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"Ev'n now the setting sun and shifting clouds,
Seen, Greenwich, from thy lovely heights, declare
How just, how beauteous the refractive law."

"To the Memory of Sir Isaac Newton"
James Thomson (1700 – 1748)
English author

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Editorial

First, Do No Harm: Why Breastfeeding Matters

Tze Tein Yong, [1]*MBBS, FRCOG, FAMS,* Liying Yang, [1]*MBBS, MRCOG, MMed (O&G)*

World Breastfeeding Week—celebrated internationally between 1st and 7th August every year—is an event supported by the United Nations Children's Fund and the World Health Organization. It aims to promote and support breastfeeding worldwide. This year's slogan is "Empower Parents, Enable Breastfeeding".

It has become necessary to advocate breastfeeding because aggressive marketing of infant formula in the 20th century has led to widespread perception by physicians and the public alike that infant formula is the preferred choice in infant feeding.[1] Free access to ready-to-feed formula and traditional hospital routines of separating mothers from their newborns have also resulted in a loss of breastfeeding skills and knowledge among women and healthcare professionals.[2] This has made it harder for women who intend to breastfeed to receive the necessary support that they need and has also led to the perception of breasts as purely sexual, rather than nutritive, organs. It is no wonder, then, that the act of breastfeeding in public often draws the ire of the uninformed.

It is not an easy task to change mindsets. Physicians are not immune to prevailing attitudes and advertising tactics, and some may still see breastfeeding as a lifestyle choice rather than an important health decision. Promises of superior intellect and academic abilities packaged in a shiny metal tin means that many parents, too, fall into the same trap. As such, it is helpful to reframe the narrative to one where breastfeeding is emphasised as the physiologic norm and breast milk is held up as the gold standard by which infant formula is compared.

Whether it is due to the disproportionately large human brain, combined with a pelvis narrowed from bipedalism—or the mother who has reached her metabolic constraints, it is a fact that human babies are born far too prematurely.[3] Unlike a calf who can walk within minutes of birthing from its mother, it will take the human baby another year or so to reach the same milestone. This state of high dependency in infancy means that much growth in humans is achieved ex utero. It is a common observation that when infants are placed on their mothers' naked chests, they will intuitively find their way to the nipple and suckle it.[4] With early skin-to-skin contact, babies are more likely to maintain their temperature and glucose levels, cry less and breastfeed for a longer duration.[5]

There are significant health risks associated with not breastfeeding. Unlike breast milk, infant formula lacks bioactive components such as lactoferrin, immunoglobulins, enzymes and growth factors that are found in the latter. It also has a much lower concentration of human milk oligosaccharides. Infants who are not breastfed are more likely to experience intestinal colonisation by pathogenic bacteria such as *Escherichia coli* rather than the beneficial microbes of the *Bifidobacteria* and *Lactobacillus* species seen in breastfed infants.[6,7] This altered gut microbiome may confer an increased susceptibility to conditions such as allergies, asthma and inflammatory bowel disease.

Infants who are not fed breast milk are at higher risk of infectious morbidity from gastroenteritis, respiratory tract illnesses and acute and recurrent otitis media. They are also at an increased risk of sudden infant death syndrome.[8,9] Preterm neonates who are not breastfed have higher intestinal permeability and are at higher risk of contracting necrotising enterocolitis.[10] Additionally, powdered formula milk is not sterile and can be contaminated by *Cronobacter sakazakii* which causes meningitis in infants.[11]

In the long term, infants who are not breastfed are at increased risk of obesity, childhood cancers, malocclusion and type 1 diabetes.[9] Their neurocognitive development may also be adversely affected due to lower concentrations and differences in composition of long-chain polyunsaturated fatty acids in infant formula compared to breast milk. The effect on neurocognitive development may persist into adulthood.[12] Mothers who do not breastfeed have a higher risk of developing postpartum depression, diabetes, hypertension, cardiovascular disease and breast and ovarian cancers.[13]

In 2011, the National Breastfeeding Survey in Singapore found that although breastfeeding initiation was high, exclusive breastfeeding rate at 6 months was only 1%.[14] Since then, laudable efforts have been made to address

[1]Department of Obstetrics and Gynaecology, Singapore General Hospital, Singapore
Address for Correspondence: A/Prof Yong Tze Tein, Department of Obstetrics & Gynaecology, Singapore General Hospital, Outram Road, Singapore 169608.
Email: yong.tze.tein@singhealth.com.sg

and improve the situation. In 2012, the first hospital in the island city-state was accredited as "Baby Friendly". Eventually, the aim of the authorities ís to get all maternity hospitals accredited as such.[15] The Sale of Infant Foods Ethics Committee of Singapore (SIFECS)—the body which regulates the appropriate promotion and distribution of breast milk substitutes—has also updated its code of ethics to align with the national agenda.[16]

Yet, on the ground, many physicians are still uncomfortable dealing with the challenges posed by breastfeeding since lactation training is sorely lacking in most medical schools and residency curricula. They may be hesitant to take a strong stand on breastfeeding because of worries about causing parental guilt. The first step that they must take to address the situation is to educate themselves in order to avoid inappropriate discouragement of breastfeeding through dispensing ill-informed advice.

Many women wean prematurely because of perceived, rather than true, low supply of their breast milk. Doctors must be aware of the physiology of breast milk production and educate women on this in order to manage their expectations. The first milk that is produced is colostrum. Though low in volume, it is dense in nutrients and is sufficient to maintain normal glucose levels in healthy-term infants without overloading their small stomachs. Babies also find it more manageable since they are still learning how to suck, swallow and breathe at the same time. It is therefore normal for women to produce a low volume of milk in the first few days after childbirth.[17]

In full-term infants, it is normal for them to experience weight loss of 5-7% during the first 3-4 days of life. This is due to physiologic diuresis and the passage of meconium, and they should regain their birth weights by 10-14 days of life.[18] Milk production slows when milk accumulates in the breast and speeds up when the breast is emptied.[19] As such, when inappropriate advice is given to supplement the perceived low supply of breast milk with infant formula, it becomes a self-fulfilling prophecy since it reduces the frequency of breast emptying and, consequently, milk production.

With the correct advice and assistance, most mother-infant dyads are successful at establishing breastfeeding. However, some will need extra attention and careful evaluation to ensure adequate infant milk intake. They include infants with hypoglycaemia, dehydration, delayed bowel movements (<4 stools at day 4 of life or meconium stools beyond day 5 of life) or hyperbilirubinaemia. Mothers with postpartum complications such as severe haemorrhage or retained placenta, breast surgery that may have affected nipple innervation (such as periareolar breast incisions) or breast hypoplasia will also require more support. Careful assessment of latch and milk transfer must be conducted by appropriately trained medical personnel. When supplementation is required, this must be done carefully with the aim of preserving breastfeeding. Cup or syringe feeding or paced bottle feeding using wide, slow-flow teats can help to prevent nipple confusion.[17]

Most medications are safe for ingestion during lactation. Iodinated and gadolinium-based contrast agents—such as those used in computerised tomography scans or magnetic resonance imaging—are not contraindicated.[20] When in doubt, physicians can consult lactation pharmacology resources such as LactMed by the United States National Library of Medicine (https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm) for accurate and evidence-based information.

Most procedures are compatible with breastfeeding. Women who were put through general anaesthesia for surgical procedures can breastfeed their healthy-term infants as soon as they are stable and alert enough to hold their babies.[21] All breast imaging studies are safe for breastfeeding women to undergo. Breastfeeding also does not need to be discontinued prior to breast biopsy since inflammation and stasis from abrupt weaning can increase the risk of fistula formation through the biopsy tract.[22] The Centers for Disease Control and Prevention (http://www.cdc.gov/breastfeeding/index.htm) and the Academy of Breastfeeding Medicine (https://www.bfmed.org/protocols) have published useful clinical information on breastfeeding issues that may be encountered in daily practice on their websites.

Based on current findings on the immunological, neurological and nutritional inferiority of breastmilk substitutes, we have an ethical obligation to equip ourselves with the knowledge and skills to help mothers make an informed choice and breastfeed successfully. For every mother who does so, her daughters and grand-daughters are likely to succeed too. As medical professionals who profess to "first, do no harm", anything less just will not do.

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Original Article

Palliative Care Awareness Among Advanced Cancer Patients and Their Family Caregivers in Singapore

Semra Ozdemir, [1,2]PhD, Chetna Malhotra, [1,2]MBBS, MD, MPH, Irene Teo, [1,2,3]PhD, Grace MJ Yang, [1,3]MBBChir, MA, MRCP, Ravindran Kanesvaran, [3,4]MD, MRCP, Alethea CP Yee, [1,3]MBBS, MRCP, Eric Andrew Finkelstein, [1,2]PhD, MHA; Cost of Medical Care of Patients with Advanced Serious Illness in Singapore (COMPASS) Study Group

Abstract

Introduction: We investigated the awareness of palliative care (PC) services in advanced cancer patients and their family caregivers and whether negative perceptions was a possible barrier to PC utilisation in Singapore. Materials and Methods: Patients with stage 4 solid cancer and their caregivers were interviewed between July 2016 and March 2018 at outpatient clinics located in the medical oncology departments of 2 major public hospitals in Singapore. Patients and caregivers were asked whether they were aware of PC services, how they first learned about them, who first recommended PC to the patient, whether the patient had received PC, and reasons for not receiving PC. Results: Awareness of PC was lower in patients compared to caregivers (43% vs 53%; *P* <0.01). The odds of being aware in patients was higher if they had higher education (odds ratio [OR] = 2.927; *P* <0.001) and higher income (OR = 1.798; *P* = 0.005). Compared to patients, more caregivers reported that a healthcare provider recommended PC to the patient (10% vs 20%; *P* <0.012). Furthermore, 7% of patients and 15% of caregivers reported that the patient received PC (*P* = 0.031). The most common reasons for not receiving PC reported by patients and caregivers (respectively) were that the patient was still receiving treatment (68% and 78%), it is not time for PC (76% and 59%) and PC would not be of help (18% and 19%). Conclusion: Less than half of patients indicated an awareness of PC. Our findings suggest that efforts should be made to increase awareness of PC and promote its acceptance in cancer patients and their family caregivers in Singapore.

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Key words: Decision-makers, End-of-life, Perceptions

Introduction

Cancer is the primary cause of death in Singapore and accounts for 30% of all deaths.[1] Patients with advanced cancer suffer from many problems including pain, side-effects from treatment and psychological distress.[2,3] To respond to the needs of these patients, international and local organisations recommend that palliative care (PC) be provided early in the course of illness and integrated with standard oncology care.[4,5] The goal of PC is to improve the quality of life of patients with any life-limiting illness and of their family caregivers by addressing physical, psychosocial and spiritual needs.[4] Several studies have shown that patients with advanced cancer who receive early integration of PC have better quality of life and less depression compared to patients who receive standard oncology care.[6-8]

Despite guidelines, the literature shows that patients lack awareness of PC and have negative perceptions about PC which, in turn, are associated with late or low utilisation of PC services.[9-11] This has been shown to be especially the case for patients with lower education or income.[12,13] Patients also perceive PC as being an alternative to life-extending treatments—that it is only for those nearing end-of-life[14] and associate it with losing hope.[9,15] Therefore, one of the goals of the National Strategy for Palliative Care (NSPC

[1]Lien Centre for Palliative Care, Duke-NUS Medical School, Singapore
[2]Programme in Health Services and Systems Research, Duke-NUS Medical School, Singapore
[3]National Cancer Centre, Singapore, Singapore
[4]Duke-NUS Medical School, Singapore
Address for Correspondence: Dr Semra Ozdemir, Lien Centre for Palliative Care, Duke-NUS Medical School, 8 College Road, Singapore 169857.
Email: semra.ozdemir@duke-nus.edu.sg

2011) in Singapore is to promote public awareness and acceptance of PC services.[16]

The NSPC also recommends promoting open communication on PC between healthcare professionals, patients and caregivers.[16] However, in Singapore, family caregivers often assume the role of being the primary decision-makers for patients and of communicating with the treating physician on the patient's behalf, especially when the patient is an elderly parent.[17-19] These caregivers—with the intention to protect the patient—may not discuss PC with their loved one and may ask physicians not to discuss it with the patient fearing that the patient may lose hope.[20,21] For the same reason, physicians may also not feel comfortable discussing PC with their patients or they may just conform to the wishes of the family.[22] The main aim of this study was to investigate the awareness of PC services in patients with advanced cancer and in their family caregivers in Singapore. We hypothesised that patients are less likely than their caregivers to be aware of PC services and that physicians are more likely to discuss PC with caregivers than patients. The secondary aim was to investigate the relationship between patient demographic characteristics and being aware of PC services. We hypothesised that patient education and income levels are significant predictors of PC awareness. Lastly, we also aimed to investigate whether negative perceptions were possible barriers to PC utilisation (and we were expecting this). The findings from this study can be used to develop strategies and interventions to increase awareness and acceptance of PC in patients with advanced cancer and in their family caregivers.

Materials and Methods

Participants and Study Setting

The data used in this study came from the baseline survey of a cohort study called Cost of Medical Care of Patients with Advanced Serious Illness in Singapore (COMPASS). The COMPASS protocol paper provides detailed information on the study design.[23] In brief, the baseline questionnaire was administered between July 2016 and March 2018 at outpatient clinics located in medical oncology departments of 2 major public hospitals in Singapore. Patients who were Singapore citizens or permanent residents, aged at least 21 years and diagnosed with stage 4 solid cancer were identified from their medical records and were approached by trained interviewers. Patients were further screened for adequate functional status for participation by: 1) having an Eastern Cooperative Oncology Group (ECOG) performance status ≤2, and 2) being cognitively intact (determined via medical record documentation or tested via the Abbreviated Mental test for those aged ≥60). The inclusion criteria for caregivers included being aged ≥21 and being one of the main persons providing care to the patient or ensuring provision of care or involved in making treatment decisions on behalf of the patient. The study was approved by the SingHealth Centralised Institutional Review Board.

Survey Development

The survey was administered in the preferred language of the participants—English, Mandarin or Malay—which covers 99.5% of language literacy in Singapore. The survey was administered via in-person interviews to the patients while caregivers could opt for completing it on their own. The patient and caregiver questionnaires were developed in consultation with oncologists—first in English and then translated into Mandarin and Malay by professional translators. The questionnaires were finalised after cognitive interviews with 10 participants for each language.

Participants were asked whether they were aware of PC services. Those who were aware about PC were further asked how they first learned about PC services, whether a physician or a healthcare provider had recommended PC to the patient and whether the patient had received PC. Reasons for not receiving PC were documented and this information provided insights on participants' perceptions about PC. The questionnaire also included questions on demographic characteristics.

Analysis

We first present the descriptive statistics on the demographic characteristics of the full sample of patients and caregivers. We then present statistics on PC awareness and if aware, how participants first learned about PC services, whether a healthcare provider recommended PC and whether the patient had received PC. Binomial logistic regression was performed to investigate the relationship between demographic characteristics and patient PC awareness (aware of PC = 1; otherwise, 0). The independent variables of interest were education level (higher than secondary education = 1; otherwise, 0) and income level (higher than median income = 1; otherwise, 0). We controlled for other demographic characteristics, such as gender, age, ethnicity and marital status.

We compared patient statistics with those of caregivers for dyads where both patients and caregivers were recruited using McNemar's test, which is the appropriate version of the chi-square test in the presence of matched pairs. Patients and caregivers who reported not receiving PC at the time of the survey were asked the main reasons for not receiving PC and were allowed to choose from multiple options. Statistical significance was measured at the 5% level. All analyses were conducted in Stata 14 (StataCorp 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Results

The survey was administered to 600 patients and 290 caregivers of these patients. The number of caregivers recruited was lower either because patients did not have a companion caregiver at the time of recruitment or caregivers did not agree to be involved in the study. Table 1 presents the demographic information of the participants.

Table 1. Patient and Caregiver Demographic Characteristics

	Patient (n = 600)	Caregiver (n = 290)
Age, mean (SD)	61 (11)	51 (14)
Female (%)	54	65
Education (%)		
No formal	10	2
Primary and secondary	59	42
Above secondary	31	56
Ethnicity (%)		
Chinese	79	76
Malay/Indian/Others	21	24
Marital status (%)		
Married	73	78
Others	27	22
Employment (%)		
Full-time, part-time	36	60
Others (homemaker, retired, unemployed)	64	40
Median household income ($)*	3500	3500
Religion (%)		
Buddhist	35	30
Christian	22	23
Muslim	16	18
Others	12	11
No religion/free thinker	15	18
Relationship to patient (%)		
Spouse	NA	47
Child	NA	37
Others	NA	16
Primary cancer site, n (%)		
Respiratory	169 (28)	NA
Gastrointestinal	156 (26)	NA
Breast	96 (16)	NA
Genitourinary	78 (13)	NA
Gynaecological	53 (9)	NA
Others†	48 (8)	NA

NA: Not applicable; SD: Standard deviation

*n = 523 for patients; 72 patients reported not knowing their household income and 5 patients did not answer the question. n =189 for caregivers; the income question was only asked to those who worked full- or part-time (n = 195). Among these caregivers, 6 reported not knowing their household income and 2 did not answer the question.

†Including head and neck, musculoskeletal, neurological and skin.

The mean age for the patient and caregiver samples was 61 and 51 years, respectively. The majority of the patients and caregivers were female (54% and 65%), Chinese (79% and 76%) and married (73% and 78%). Most patients had only primary or secondary education (59%) and were not in the workforce (64%) while the majority of caregivers had above secondary education (56%) and were full- or part-time employed (60%). The most prevalent religion was Buddhism among patients (35%) and caregivers (30%). Almost half of the caregivers (47%) were spouses of patients. The most common site of the primary cancer was lung (28%), followed by gastrointestinal (26%) and breast (16%).

Almost half of the patients (46%) were aware of PC (Table 2). Among patients who were aware of PC (n = 274), about half (49%) had first heard about it from their family and friends; only 12% had heard from a physician or other healthcare provider. Among those who were aware of PC, only 8% reported that a physician or a healthcare provider had recommended PC and 4% reported receiving PC. As expected, having secondary education or higher (odds ratio [OR] = 2.927; P <0.001) and having higher than median income (OR = 1.798; P = 0.005) were significant predictors of PC awareness among patients (Table 3).

As hypothesised, PC awareness was lower among patients compared to caregivers (43% vs 53%; P <0.01) among patient-caregiver dyads (n = 290) (Table 2). Both groups reported family and friends to be the primary source of information on PC (51% vs 40%). Among dyads who were aware of PC (n = 81), compared to patients (10%), more caregivers (20%) reported that a physician or a healthcare provider had recommended PC to the patient (P = 0.012). This finding is consistent with our hypothesis. When asked if the patient had received PC, 15% of caregivers reported that the patient had received PC while only 7% of patients stated that they did (P = 0.031).

The reason reported for not receiving PC by 68% of patients (n = 263) and 78% of caregivers (n = 69) was that the patient was still receiving treatment (Table 4). The second most cited reason reported by 76% of patients and 59% of caregivers was not believing that it was time for PC. Participants also either reported that PC would not be of help (18% of patients and 19% of caregivers) or that patient's physicians do not think that PC would be of help (7% of patients and 16% of caregivers). A smaller percentage of patients (6%) and caregivers (10%) also reported that getting PC means giving up on life. Study participants also cited other reasons such as PC being expensive (10% for both groups) and not knowing much about PC (8% of patients and 7% of caregivers).

Table 2. Awareness of PC Services

	Full Patient Sample	Dyad		
		Patient	Caregiver	*P* Value
Aware of PC services? (%)	n = 600	n = 290		*P* <0.001
Yes	46	43	53	
No	49	52	34	
Not sure	5	5	10	
(If aware) How first learned about PC services? (%)	n = 274	n = 81		*P* = 0.090
Physician or other healthcare provider	12	19	28	
Family/friends	49	51	40	
Personal research	6	2	5	
Internet/media	29	23	20	
Others	4	5	7	
(If aware) Physician or healthcare provider recommended PC? (%)	n = 274	n = 81		*P* = 0.012
Yes	8	10	20	
No	92	90	78	
Not sure	<1	0	2	
Whether patient received PC? (%)	n = 274	n = 81		*P* = 0.031
Yes	4	7	15	
No	96	93	85	

PC: Palliative care

Table 3. Odds Ratios for Patients Being Aware of PC as a Function of Demographic Characteristics (n = 523)*

	Odds Ratio (SE)	*P* Value
Higher education (higher than secondary education)	2.927 (0.652)	0.000
Male	0.833 (0.164)	0.354
Age	1.005 (0.010)	0.585
Chinese ethnicity	0.729 (0.168)	0.172
Married	0.739 (0.161)	0.165
Higher income (higher than median income)	1.798 (0.372)	0.005
Having comorbidities (other than cancer)	1.017 (0.230)	0.942
Constant	0.656 (0.406)	0.496

PC: Palliative care; SE: Standard error

*n = 523 for patients; 72 patients reported not knowing their household income and 5 patients did not answer the question.

Table 4. Reasons for Patients Not Receiving PC at the Time of the Survey

	Patient, % (n = 263)	Caregiver, % (n = 69)
Patient is still receiving treatment for patient's disease	68	78
Do not believe it's time for hospice palliative care	76	59
Do not think that hospice palliative care would be of help to the patient	18	19
Patient's doctors do not think that hospice palliative care would be of help to the patient	7	16
Getting hospice palliative care will be like giving up on life	6	10
It is expensive	10	10
Do not know much about it	8	7

PC: Palliative care

Discussion

Less than half of patients in our sample reported being aware of PC and the odds of awareness was higher among those with higher income and education levels. Our findings also show that compared to patients, more caregivers reported that they first learned about PC from a healthcare provider. In addition, more caregivers reported that a physician or a healthcare provider recommended PC to the patient and that the patient received PC services. Our study also revealed negative perceptions of PC in cancer patients and their caregivers.

Awareness of PC services among patients in our study was 46%. This is lower than other developed countries such as the United States where PC awareness was reported to be as high as 77% in outpatient cancer patients.[10] The odds of PC awareness in patients was higher if they had higher education and income. This is consistent with findings from previous studies which showed that education and income levels are positively correlated with PC awareness.[10,12,13]

We also found that, among the patient-caregiver dyads who were aware of PC, only 10% of patients and 20% of

caregivers reported that a physician or a healthcare provider recommended PC. Considering the international guidelines on integrating PC into standard care early in the course of advanced cancer, most patients in our sample should have been recommended PC. The low rates might be due to factors related to healthcare providers and the healthcare system.[24] Referrers may be concerned about limited availability of PC specialist teams and other PC resources or they may be unsure on when it is appropriate to refer a patient to a PC specialist team. In addition, not all physicians are equipped with communication skills to discuss PC referral with patients.[25] It is also possible that primary referring oncologists may have negative perceptions about PC or on the roles of the PC team.[26,27]

Our findings also show that compared to patients, more caregivers reported that they first learned about PC from a healthcare provider, that a physician or a healthcare provider recommended PC to the patient and that the patient had received PC services. These findings suggest that healthcare providers are more likely to talk to caregivers than patients about PC. Although providers may feel more comfortable discussing this topic with caregivers than patients, patients may have different treatment preferences from their caregivers[28] and should be informed of the available care options.

Our study revealed perceptions of cancer patients and their caregivers about PC. The majority of patients and caregivers reported "patient still receiving treatment" as a reason for the patient not receiving PC. This shows that participants perceive that patients have to stop treatment to receive PC. In addition, about 20% of patients and caregivers reported that PC would not be of help. Similar findings were found in a survey of the general public by Lien Foundation. When asked why participants would not consider PC for a life-threatening illness, 26% of respondents reported that they would focus on curing the illness and 35% reported that there is no need or no use for PC.[29] The negative perception of PC in patients and the general population suggests demand-side barriers to PC utilisation in Singapore.

The cost of PC services also seems to be a concern for about 10% of patients and caregivers. Although patients and their families can use their MediSave (a Singapore national medical savings scheme that sets aside part of an individual's income to help pay for certain medical expenses) to pay for PC services (and up to 80% subsidies are provided for PC-related services), some families may not be able to afford PC services or may not be aware of the available subsidies. Consulting patients and caregivers on financial matters and increasing government subsidies for PC may help to alleviate this problem.

Our study is not free of limitations. The rates of PC recommendation and utilisation might be underreported in the survey because some patients and caregivers might not know what PC entails although the patient was referred to and/or received PC services. This might especially be the case if PC services were provided by the oncology team.

PC in Singapore started as charities initiated by volunteers which developed into professional services in less than 10 years.[30] It is now recognised as an essential part of the healthcare system and has been offered in hospitals, hospices and at home for over 30 years.[16] National guidelines recommend making PC as part of standard care for those who are likely to die within the next 12 months.[5] In order to achieve these objectives, efforts should be made to increase awareness of PC services in Singapore in order to be on par with other developed countries,[31] and to understand why patients and their caregivers think PC are not helpful. Future research should be conducted to understand the perceptions of referring physicians about PC, whether there is a need for training programmes to help healthcare providers assess when to refer patients to PC and develop skills and confidence to discuss PC-related issues more comfortably with their patients.[32] Further research can also explore other potential barriers from the healthcare system's perspective.

Conclusion

Our findings suggest that efforts should be made to increase awareness of PC and to promote its acceptance among cancer patients and their family caregivers in Singapore. Based on our findings, awareness campaigns should focus on explaining how PC services can help patients and their families throughout the course of advanced cancer—not just at end-of-life—and that PC can be received with standard care.

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Original Article

Impact of Knowledge and Attitudes on Lifestyle Practices in Preventing Type 2 Diabetes Mellitus

Benson WG Ang, [1], Mui Yee Tan, [1], Cheryl MY Goh, [1], Sylwan Rahardja, [1], Beatrice Y Lim, [1], Wenqi Chiew, [1], Thurston YJ Heng, [1], Kuang Ian Tan, [1], Jenies HX Foo, [1], Sarah ZL Tham, [1], Jason KS Chng, [1], Wei Jie Seow,[1,2] *BSc, MSc, ScD*, Nan Luo,[1,2] *BSc, MSc, PhD*

Abstract

Introduction: Diabetes mellitus is a major public health issue in Singapore. To shape healthcare policies for the primary prevention of diabetes, it is crucial to understand Singaporeans' knowledge, attitudes and practices related to diabetes and its prevention. This study aimed to assess the knowledge, attitudes and lifestyles of individuals without diabetes. Materials and Methods: A cross-sectional household survey was performed between 31 January to 3 February 2019 to examine knowledge, attitudes and practices related to diabetes. Inclusion criteria of the participants included: 1) Singaporeans/ permanent residents, 2) between 30 to 64 years old, and 3) who did not have a diagnosis of diabetes. Logistic and linear regression models were used to analyse the association of knowledge and attitudes with physical activity and diet habits, respectively. Results: Among 806 participants, 72.2% did not meet the Health Promotion Board's physical activity recommendation. Physical activity was associated with better diabetes knowledge (odds ratio [OR] 5.38, 95% confidence interval [CI] = 1.65-17.53, *P* = 0.049), stronger beliefs in diabetes prevention (OR 3.36, 95% CI = 1.02-11.12, *P* = 0.047) and lower levels of worry about diabetes (OR 0.41, 95% CI 0.17-1.00, *P* = 0.049). Neither knowledge nor beliefs or worries about diabetes was associated with diet. Conclusion: There is a need to reinforce the importance of physical activity and healthy diet in preventing diabetes. Although improving the knowledge level of diabetes may increase physical activity of the population, it is unlikely to improve dietary choices without effective behaviour change interventions.

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Key words: Healthy diet, Physical activity, Singapore, "War on Diabetes"

Introduction

Diabetes mellitus is a chronic disease that affects the body's metabolism of sugar. Type 2 diabetes involves insulin resistance and is preventable. Worldwide, type 2 diabetes accounts for the majority of diabetes cases.[1] It is a disease of multifactorial pathogenesis[2] and modifiable lifestyle factors include obesity,[3] physical inactivity,[4] diet[5] and alcohol consumption.[6] Diabetes leads to debilitating complications like chronic renal failure,[7] acute myocardial infarction and stroke.[8] It is a worldwide epidemic that affected 422 million adults (8.5% of the world's population) in 2014[9] and is listed as 1 of 4 priority non-communicable diseases by the World Health Organization (WHO).[9]

Diabetes also poses a significant burden in Singapore. It accounts for 10% of Singapore's disease burden[10] and cost Singapore over 1 billion dollars in 2010.[11] In fact, the prevalence of diabetes in Singapore is higher than that of the world's average.[10,12] The number of Singaporeans living with diabetes might surge from 440,000 in 2014 to 1 million by 2050,[12] with 1 in 3 Singaporeans having a lifetime risk of developing diabetes.[13]

In 2016, Singapore's Ministry of Health (MOH) declared a "War on Diabetes" (WoD) to address the magnitude of the problem, implementing preventive interventions targeting modifiable risk factors. These include primary preventive measures for diet control (e.g. Healthier Dining Programme,

[1]Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[2]Saw Swee Hock School of Public Health, National University of Singapore, Singapore
Address for Correspondence: A/Prof Luo Nan, Saw Swee Hock School of Public Health, National University of Singapore, #10-01, Tahir Foundation Building, 12 Science Drive 2, Singapore 117549.
Email: ephln@nus.edus.sg

Healthier Choice Symbol identifier) and exercise (e.g. National Steps Challenge), as well as secondary preventive measures to increase screening uptake and early detection (e.g. Diabetes Risk Assessment Tool, Screen for Life subsidies). Since the start of the WoD, the 2018 National Nutrition Survey showed an overall improvement in Singapore's dietary practices compared to 2010, with Singaporeans consuming food with fewer calories and carbohydrates, though there was still high sugar and salt intake.[14] With regard to exercise, more than a third (36.5%) of Singaporeans still have insufficient physical activity.[15] However, there are no formal studies conducted to assess the effects of the WoD on the knowledge and attitudes of the population.

Hence, this study aimed to assess the knowledge, attitudes and lifestyles of diabetes-free Singaporeans and permanent residents, in an attempt to evaluate the early impact of the WoD on healthy lifestyle adoption, with the hope of informing the design of future primary preventive interventions against diabetes. The study objectives were: 1) to assess the current physical activity level and dietary habits and identify suboptimal practices despite ongoing awareness campaigns, and 2) to determine the association of knowledge and attitudes of diabetes with lifestyle practices.

Materials and Methods

Study Design, Case Definition and Data Collection

This study used data collected from a cross-sectional, questionnaire-based survey administered by trained interviewers between 31 January and 3 February 2019. Inclusion criteria were Singapore citizens or permanent residents without diabetes, aged 30-64 years and who could comprehend and communicate in English or Mandarin. The age group of 30-64 years old was chosen to represent the young and middle-aged population, with the age bracket of 30-39 years representing the first big jump in prevalence.[16] Ethical approval was obtained from the National University of Singapore (NUS) Institutional Review Board. Informed consent was obtained from each individual prior to participation.

Six Housing and Development Board (HDB) estates were selected via simple random sampling out of 23 HDB towns and 3 HDB estates.[17] Thirty blocks per estate and 50 units per block were randomly selected. Selected units were approached in order until 10 responses were obtained per block.

The survey was conducted over 2 weekdays from 5 pm to 9 pm and 2 weekends from 9 am to 6 pm to avoid underrepresentation of the employed. In households with multiple eligible individuals, the most willing individual was surveyed.

Interviewers were trained to ensure uniformity in questionnaire administration. Interviewers manually entered participants' responses with smartphones into a secure NUS MySurvey portal, in compliance with the Personal Data Protection Act.

Selected questions from the Diabetes Knowledge Questionnaire (DKQ)[18] and Diabetes Knowledge Test (DKT)[19,20] were modified to suit the local population to assess general knowledge on diabetes and its management. A total score for diabetes knowledge was calculated from the questionnaire: 16 items from DKQ and 8 items from DKT. Items were scored 1 for a correct response and 0 for incorrect and "I don't know" responses. Participants' scores were represented as a percentage of the total score of 24 (i.e. if a participant answered 16 items correctly, their total score is 16/24 x 100 = 66.7%).

To assess attitudes, the team generated questions about worries and beliefs regarding diabetes based on the Tripartite Model of Beliefs.[21] Questions assessing physical activity were adapted from the Health Promotion Board (HPB)'s Diabetes Risk Assessment Tool and WHO's Global Physical Activity Questionnaire.[22] Barriers to physical activity were sought using the Health, Knowledge & Practices Questionnaire 1999 by The Australian Diabetes, Obesity and Lifestyle Study.[23] To assess diets, questions were modified from the Dietary Screener Questionnaire[24] in the National Health and Nutrition Examination Survey (NHANES), and the Health at Work Questionnaire[25] by the British Heart Foundation. Sociodemographic information and past medical history were also collected.

To facilitate administration, the questionnaire was translated from English to Chinese. Both language versions of the questionnaire were tested with interviewers' families before data collection. Subsequently, questions were rephrased to reduce ambiguity and to omit medical jargon. The final questionnaire included a total of 47 questions (see Appendix: Questionnaire).

Statistical Analysis

Participants' knowledge, attitudes and diet habits were assessed using percentage scores based on their responses to relevant questions. For diet habits, its association with all sociodemographic and past medical characteristics was first examined using one-way analysis of variance (ANOVA). All statistically significant or borderline-significant variables ($0.05 < P \leq 0.10$) in the univariate analyses were included in a multivariate linear regression analysis, with knowledge and attitudes scores (including beliefs and worries about diabetes) included as covariates.

Exercise was coded as a binary categorical variable (meets or does not meet HPB's recommendations for physical activity, which is defined as at least 150 minutes of moderate intensity exercise or 60 minutes of high intensity exercise per week). Its association with sociodemographic

and medical characteristics was first examined using simple logistic regression. Subsequently, all statistically significant or borderline significant variables were included in a multiple logistic regression model, together with knowledge and attitudes scores to identify factors independently associated with meeting recommended physical activity. Statistical Package for the Social Sciences (SPSS) version 23 was used for data analysis. A value of P <0.05 was considered statistically significant for univariate and multivariate analyses.

Results

Of the 5400 household units that had been approached, 3526 were contactable, of which 1541 residents were eligible. Of those eligible, 806 agreed to participate and completed all questions without missing responses, yielding a response rate of 52.3%.

The mean age (standard deviation [SD]) of the study sample was 57.2 ± 12.5 years. The majority of participants were females (60.7%), had qualifications above primary level (87.1%), monthly household incomes of less than S$10,000 (88.0%) and lived in housing units of 4-room or smaller (78.0%); 35.1% of participants had a family history of diabetes and 19.7% had high blood pressure (Table 1).

Diabetes Knowledge and Attitudes

The mean knowledge score (SD) of the participants was 59.2 ± 15.1%, with the minimum of 0.0%, maximum of 100.0% and median of 58.3%.

Generally, participants had good knowledge about the impact of diabetes mellitus on health. For example, 90.8% of participants answered correctly that "Cuts and abrasions on patients with diabetes heal more slowly". However, only 14.4% knew that "Eating too much sugar and sweet foods is a cause of diabetes" was false.

A total of 49.8% of participants were worried about a future diagnosis of diabetes. The majority of participants possessed strong beliefs about diabetes prevention (Fig. 1). For example, 86.1% and 87.1% of the participants (strongly) agreed that their risk of diabetes can be controlled by exercising regularly and maintaining healthier diets, respectively.

Practices

A total of 27.8% of participants met the HPB's recommendations for physical activity.[26] The majority of participants exercised for more than 60 minutes per week (63.4%) and most did light to moderate exercise (85.4%).

For dietary practices, responses were varied. Most participants chose not to "eat at western fast food outlets or quick-service restaurants" (92.8%), "consume sweetened beverages" (87.0%) or "consume sweet cakes, desserts, sweets, chocolates or confectionery" (87.1%) at least half the time. Most participants also chose wholemeal bread over white bread more than half the time (68.2%). However, a majority had suboptimal dietary practices regarding carbohydrates and fats, choosing to base their main meals around starchy foods at least half the time (64.3%). The distribution of responses to all diet questions are shown in Figure 2.

Factors Associated with Practices

Simple logistic regression analyses showed that Chinese (P = 0.052), females (P <0.001) and participants with primary or secondary qualifications (P = 0.043) exercised less. Participants living in Yishun exercised more (P = 0.093, OR 1.55, 95% CI 0.93-2.58) compared to those in Ang Mo Kio. In multivariate analysis, participants who had higher knowledge scores (P = 0.005, OR 5.38, 95% CI 1.65-17.53), stronger beliefs (P = 0.047, OR 3.36, 95% CI 1.02-11.12), or less worries (P = 0.049, OR 0.41, 95% CI 0.17-1.00) exercised more (Table 2).

In the analyses of dietary practices, we found that older participants (P = 0.002) and participants in Clementi (P = 0.020) and Yishun (P = 0.002) had healthier dietary practices. There was no statistically significant association of knowledge or attitudes with dietary practices (Table 3).

Race, marital status, household income, type of housing, family history of diabetes and personal history of hypertension were not significantly associated with physical activity or dietary practices (Tables 2 and 3).

Barriers to More Physical Activity and Healthier Diets

The 3 most commonly cited barriers to increasing physical activity were "work" (25.3%), "lack of time" (24.2%) and "other priorities" (15.0%). Common barriers to a healthier diet included "lack of time" (20.7%), "other priorities" (18.5%) and "lack of access from workplace" (15.5%). Participants' responses are shown in Figure 3.

Discussion

More Singaporeans had suboptimal exercise levels compared to a recent study published in "The Lancet Global Health" (2018) describing worldwide trends in insufficient physical acitvity,[15] which found that 33.3% of populations in South Asian countries had insufficient physical activity. This could be due to differences in their study population which included participants as young as 18 years old who would be more physically active. Singaporeans in our study are mostly from the working class, where lack of time was commonly cited as a barrier to more exercise. As overseas studies and trials have shown that workplace interventions significantly increase the level of physical activity[27] and overall physiological health,[28,29,30] quick and easy activities

Table 1. Sociodemographics of Sample Population

Demographic	n	%	Singapore Population Distribution*
Age (years)			
30 – 44	299	37.1	42.7
45 – 64	507	62.9	57.3
Race			
Chinese	621	77.0	75.0
Malay	84	10.4	12.1
Indian	80	9.9	9.3
Others	21	2.6	3.6
Gender			
Male	317	39.3	48.7
Female	489	60.7	51.3
Marital status			
Single	131	16.3	15.5
Married	642	79.7	77.0
Divorced/widowed	33	4.1	4.7
Highest qualification			
Primary	104	12.9	21.1
Secondary	236	29.3	18.6
Postsecondary	199	24.7	25.7
University	267	33.1	34.6
Monthly household income			
<$2000	214	26.6	19.1
$2000 – $4999	242	30.0	15.8
$5000 – $7999	171	21.2	15.8
$8000 – $10,000	82	10.2	9.6
>$10,000	97	12.0	39.8
Type of housing			
2-room flat	61	7.6	4.7
3-room flat	200	24.8	19.1
4-room flat	368	45.7	43.0
5-room, executive, maisonette flats	177	22.0	33.1
Family history of type 2 diabetes			
Yes	283	35.1	
No	509	63.2	
I don't know	14	1.7	
Hypertension			
Yes	159	19.7	
No	638	79.2	
I don't know	9	1.1	
Area of Singapore			
Ang Mo Kio (north)	168	20.8	15.7
Bedok (east)	128	15.9	26.6
Bukit Merah (south)	130	16.1	14.3
Bukit Panjang (west)	128	15.9	13.6
Clementi (west)	126	15.6	8.8
Yishun (north)	126	15.6	21.0

*Department of Statistics, Singapore. Singapore Census Data. Available at: https://www.tablebuilder.singstat.gov.sg/publicfacing/createSpecialTable.action?refId=15454. Accessed on 22 February 2019.

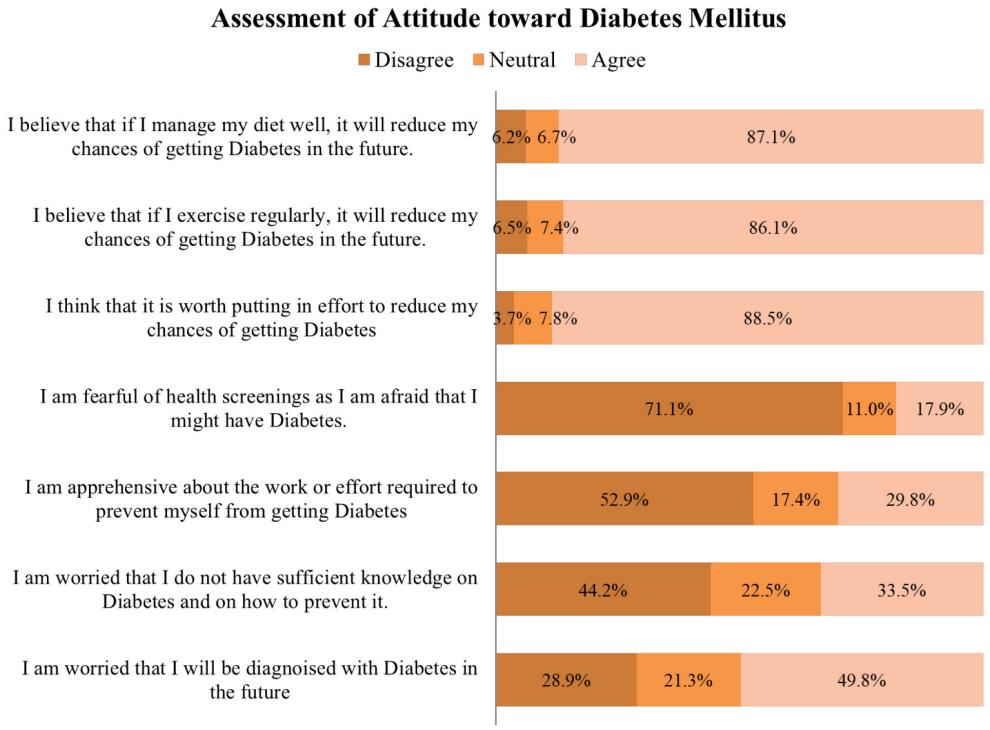

Fig. 1. Participants' attitudes towards the prevention of diabetes mellitus.

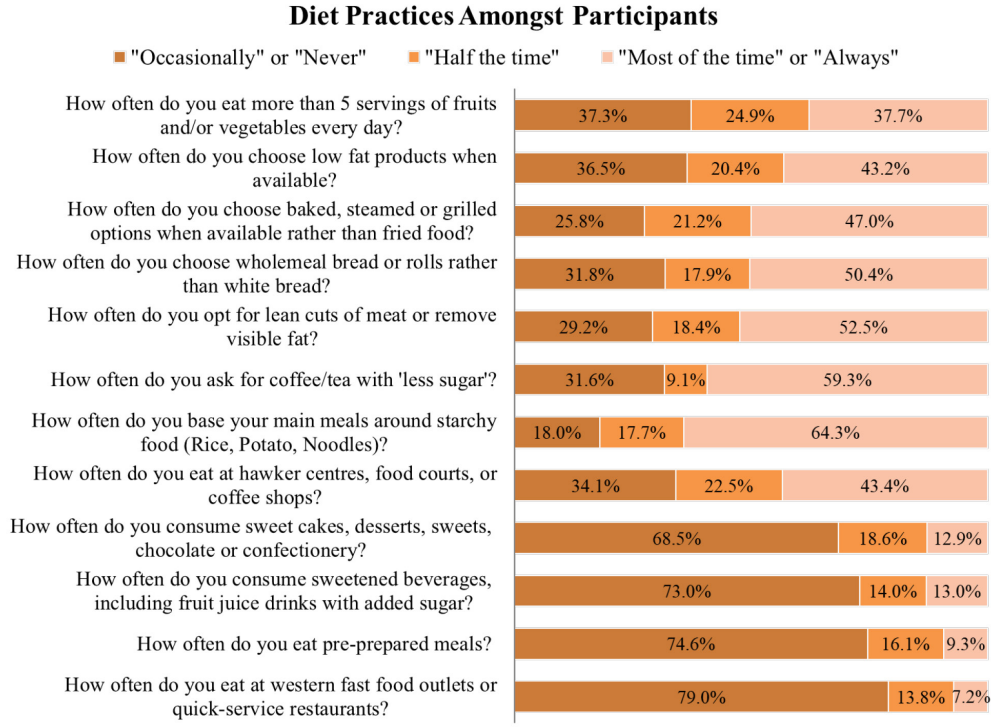

Fig. 2. Responses to questions on dietary practices of participants.

Table 2. Association of Knowledge and Attitudes with Exercise

Demographic	% Meets Recommendation (n)	Univariate *P* Value	Odds Ratio (95% CI)	Multivariate *P* Value*
Age (years)		0.148		
30 – 44	31.4 (94)			
45 – 64	25.6 (130)			
Race		0.052		0.059
Chinese	26.9 (167)			
Malay	31.0 (26)		1.25 (0.73 – 2.13)	0.423
Indian	31.3 (25)		1.26 (0.74 – 2.15)	0.404
Others	28.6 (6)		3.39 (1.35 – 8.53)	0.009
Gender		<0.001		<0.001
Male	36.3 (115)			
Female	22.3 (109)		0.48 (0.34 – 0.66)	<0.001
Marital status		0.746		
Single	33.6 (44)			
Married	26.6 (171)			
Divorced/widowed	27.3			
Highest qualification		0.043		0.477
Primary	22.1 (23)			
Secondary	26.3 (62)		1.00 (0.55 – 1.80)	0.991
Postsecondary	26.1 (52)		1.39 (0.76 – 2.55)	0.281
University	32.6 (87)		1.27 (0.68 – 2.22)	0.500
Monthly household income		0.336		
<$2000	25.7 (55)			
$2000 – $4999	28.1(68)			
$5000 – $7999	31.6 (54)			
$8000 – $10,000	25.6 (21)			
>$10,000	26.8 (26)			
Type of housing		0.803		
2-room flat	32.8 (20)			
3-room flat	26.0 (52)			
4-room flat	28.5 (105)			
5-room, executive, maisonette flats	26.6 (47)			
Area of Singapore		0.057		0.054
Ang Mo Kio (north)	24.4 (41)			
Bedok (east)	18.0 (23)		0.65 (0.36 – 1.18)	0.156
Bukit Merah (south)	31.5 (41)		1.49 (0.87 – 2.53)	0.147
Bukit Panjang (west)	30.5 (39)		1.17 (0.68 – 2.01)	0.565
Clementi (west)	30.2 (38)		1.07 (0.62 – 1.84)	0.818
Yishun (north)	33.3 (42)		1.62 (0.94 – 2.79)	0.084
Family history of type 2 diabetes		0.853		
Yes	27.6 (78)			
No	27.3 (139)			
I don't know	50.0 (7)			

CI: Confidence interval

*Only variables that were statistically significant or borderline-significant in univariate analysis were included in the multivariate analysis.

Table 2. Association of Knowledge and Attitudes with Exercise (Cont'd)

Demographic	% Meets Recommendation (n)	Univariate *P* Value	Odds Ratio (95% CI)	Multivariate *P* Value*
Hypertension		0.190		
Yes	22.6 (36)			
No	29.2 (186)			
I don't know	22.2 (2)			
Knowledge			5.38 (1.65 – 17.53)	0.005
Worries			0.41 (0.17 – 1.00)	0.049
Beliefs			3.36 (1.02 – 11.12)	0.047

CI: Confidence interval
*Only variables that were statistically significant or borderline-significant in univariate analysis were included in the multivariate analysis.

Table 3. Association of Knowledge and Attitudes with Diet

Demographic	Mean Score (%)	Univariate *P* Value	Regression Coefficient	Multivariate *P* Value*
Age (years)		0.002	0.024 (0.009 – 0.040)	0.002
30 – 44	45.4			
45 – 64	47.9		0.024 (0.009 – 0.040)	0.002
Race		0.912		
Chinese	46.9			
Malay	47.7			
Indian	46.6			
Others	47.1			
Gender		0.503		
Male	47.3			
Female	46.7			
Marital status		0.509		
Single	46.0			
Married	47.1			
Divorced/widowed	48.0			
Highest qualification		0.481		
Primary	47.2			
Secondary	46.9			
Postsecondary	47.8			
University	46.2			
Monthly household income		0.335		
<$2000	47.5			
$2000 – $4999	46.5			
$5000 – $7999	45.8			
$8000 – $10,000	47.9			
>$10,000	48.1			
Type of housing		0.136		
2-room flat	44.1			
3-room flat	47.5			
4-room flat	46.8			
5-room, executive, maisonette flats	47.6			

*Only variables that were statistically significant or borderline-significant in univariate analysis were included in the multivariate analysis.

Table 3. Association of Knowledge and Attitudes with Diet (Cont'd)

Demographic	Mean Score (%)	Univariate *P* Value	Regression Coefficient	Multivariate *P* Value*
Area of Singapore		0.016	0.008 (0.003 – 0.012)	0.001
Ang Mo Kio (north)	45.4			
Bedok (east)	46.3		0.007 (-0.017 – 0.032)	0.562
Bukit Merah (south)	46.0		0.007 (-0.018 – 0.031)	0.580
Bukit Panjang (west)	46.8		0.015 (-0.010 – 0.039)	0.241
Clementi (west)	48.5		0.030 (0.005 – 0.055)	0.020
Yishun (north)	49.3		0.038 (0.014 – 0.063)	0.002
Family history of type 2 diabetes		0.591		
Yes	46.5			
No	47.1			
I don't know	48.8			
Hypertension		0.240		
Yes	46.9			
No	46.9			
I don't know	53.0			
Knowledge			0.021 (-0.030 – 0.072)	0.421
Worries			0.010 (-0.029 – 0.049)	0.610
Beliefs			<0.001 (-0.051 – 0.050)	0.997

*Only variables that were statistically significant or borderline-significant in univariate analysis were included in the multivariate analysis.

could be introduced to encourage more exercise among busy working adults. Workplace-focused exercise and fitness programmes with easy accessibility to exercise avenues such as gyms could be viable options to overcome this barrier and positively impact their practices. Additionally, a potential reason for females in our study to engage in less physical activity (compared to their male counterparts) could be due to the difference in societal gender roles where women are expected to bear greater responsibilities at home and with childcare,[31] and hence less time is dedicated to exercise. With regard to older participants making healthier choices, possible reasons for it include: 1) being more health conscious as they age, 2) having more family members/ friends diagnosed with diabetes, and 3) having more leisure time than younger people.

Our study showed that the majority of Singaporeans are making healthier diet choices regarding food high in sugar,[14] suggesting that HPB's "Life's Sweeter with Less Sugar" campaign launched in 2014[32] has been effective. Despite better choices, total sugar intake of Singaporeans increased to 60 g[14] which suggests that Singaporeans are consuming more sugars per serving from their food. There is thus a need to improve Singaporeans' food choices as they could have a misperception of the amount of sugar that they are consuming. Most Singaporeans still have suboptimal diet practices, choosing to base their main meals around carbohydrates most of the time. Lack of time, lack of access from home and workplace, cost and other priorities are possible reasons for unhealthy diet choices.[33] Furthermore, rice and noodles are staples in Asian cuisine, making it harder to find alternatives. As such, cheaper and more convenient access to main meals without starchy food items could be introduced to overcome these barriers.

Singaporeans with better knowledge or stronger beliefs about diabetes prevention tend to exercise more as they could be more health conscious and motivated.[34] An Australian study reported that one of the main motivators for people to engage in physical activity is to improve overall health.[35] Therefore, efforts should be aimed at improving knowledge, which can potentially result in an increase in exercise at the population level.

This is further reinforced by HPB's campaigns promoting physical activity such as the "National Steps Challenge".[36] Additionally, due to the beliefs that they are taking active steps in preventing diabetes, these individuals also tended to worry less about developing diabetes as opposed to those who exercised less.

The lack of significant association between knowledge or attitudes towards diabetes and diet could be due to ingrained cultural food habits. HPB has implemented initiatives such as "Healthier Hawker Centre" and "Finest Food" programmes to increase provision of healthy food[37] and "My Healthier Plate", "Healthier Choice Symbol" and "Healthy 365" diet journal to promote healthy eating.

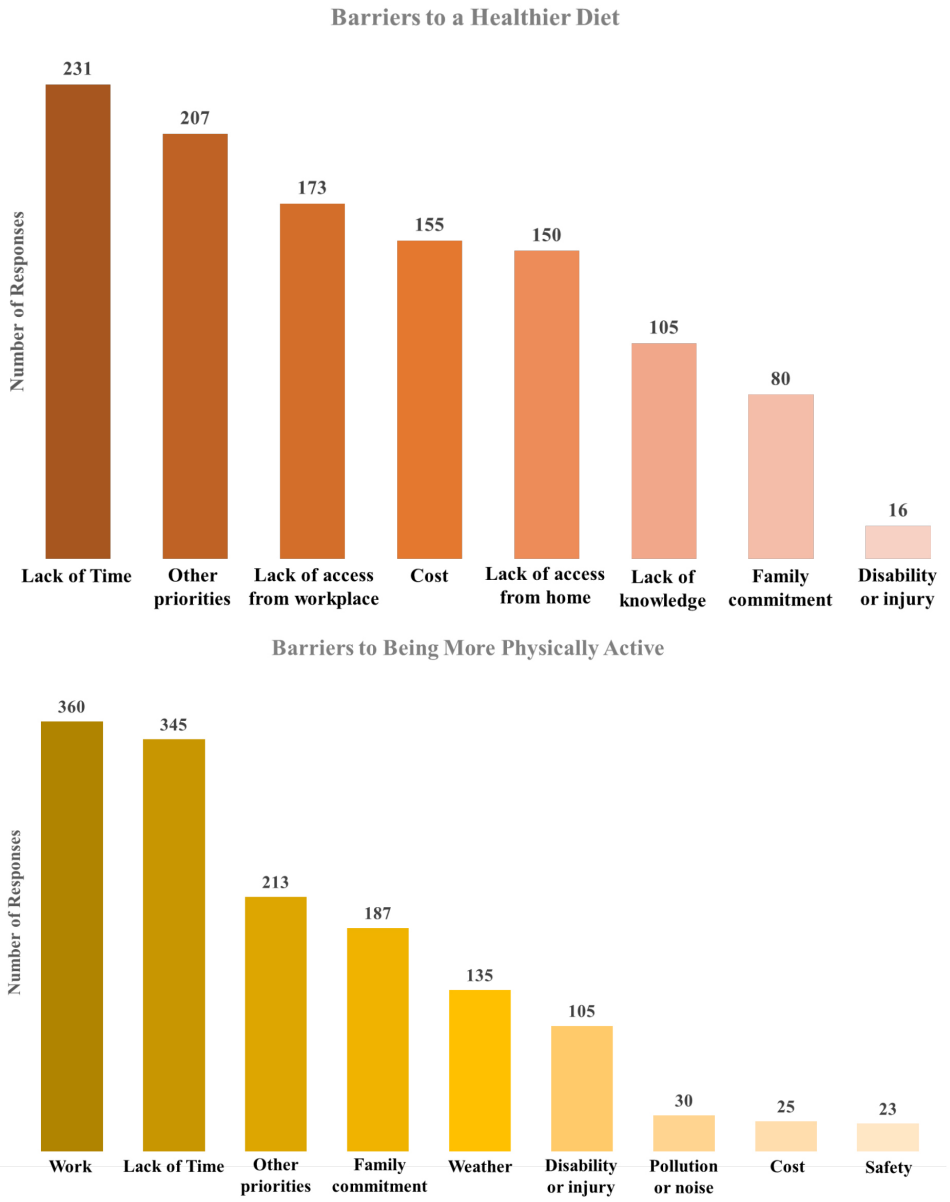

Fig. 3. Barriers to healthy practices.

However, more could be done to improve the accessibility and convenience of healthy eating options and to promote healthier eating habits. For the latter, some suggestions would be to host reality cooking television programmes or to create interactive videos on HPB's websites to reach out to a wider audience. Building on the success of switching to wholegrain food, more specific suggestions on food replacement options such as having fruits for dessert (instead of sweet soup) can be recommended through the abovementioned platforms.

Being a cross-sectional study, causalities between knowledge, attitudes and practices cannot be determined. Residents living in private properties, institutions and the homeless were not sampled due to limited time and resources. Data collection was carried out only in English or Chinese due to the lack of Malay- and Tamil-speaking interviewers, excluding residents who could not converse in either language.

Residents living within the same unit were not randomly selected for participation. We had disproportionately more females as women were more likely to answer the door and agree to participate. Our survey questions were adapted from various validated sources and several new questions were crafted to assess the attitudes of Singaporeans.

Conclusion

This cross-sectional study assessed the association between diabetes knowledge and attitudes, and the preventive practices among middle-aged people without diabetes in Singapore. Our findings suggest that Singapore is headed in the right direction following the declaration of the WoD in 2016. However, individual commitment to healthier lifestyle for diabetes prevention needs to be further strengthened. It is pertinent to encourage both policymakers and researchers to design and implement more effective interventions that are directed towards healthier dietary practices and higher physical activity levels among Singaporeans.

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Appendix: Questionnaire

A. Inclusion Criteria

Are you a Singapore Citizen or a Permanent Resident?	Yes / No
Have you been diagnosed with Diabetes Mellitus by a Healthcare Professional?	Yes / No
Are you between 30 years old and 64 years old?	Yes / No

B. Demographics

Area:		**Date:**	
Gender	Male / Female	**Race**	Chinese / Malay / Indian / Others
Age:		**Marital Status**	Single / Married / Divorced / Widowed
Education Level	Primary / Secondary / Tertiary / University / Others		
Monthly Household Income	Below 2k / 2k to 5k / 5k to 8k / 8k to 10k / Above 10k		
Type of Housing	2-Room Flat / 3-Room Flat / 4-Room Flat / 5-Room Flat / Mansionette / Executive Flat		

C. Past Medical History

1. **Do you have a parent, sibling and/or child diagnosed with Type 2 Diabetes?**
   您是否有父母，兄弟姐妹和/或孩子被诊断患有 2 型糖尿病？
   a. Yes 是
   b. No 否
   c. I do not know. 我不知道

2. **Have you been told by your doctor that you have high blood pressure?**
   您是否被医生诊断过有高血压吗？
   a. Yes 是
   b. No 否
   c. I do not know. 我不知道

D. Diabetes Knowledge

Part 1

Note to Interviewer:

The following section is for the purpose of evaluating the participant's knowledge regarding diabetes. Go through the following questions with the participants and record down their response.

Instructions to Participant:

We would like to know how much you know about diabetes. I will be asking you a series of questions regarding Diabetes. Please answer "Yes" if you agree with the statement, "No" if you do not agree with the statement. If you are unsure of the answer, answer "I Don't Know".

	Question	Options		
1	**Eating too much sugar and other sweet foods is a cause of diabetes.** 过量的甜食会造成糖尿病。	Yes 是	No 否	I Don't Know 不知道
2	**In untreated diabetes, the amount of sugar in the blood usually increases.** 如果糖尿病患没治疗，血液中的糖含量通常会增加。	Yes 是	No 否	I Don't Know 不知道
3	**If I am diabetic, my children have a higher chance of being diabetic.** 父母如有糖尿病，孩子患糖尿病的风险通常会增加。	Yes 是	No 否	I Don't Know 不知道
4	**Diabetes can be cured.** 糖尿病是可以治好的。	Yes 是	No 否	I Don't Know 不知道
5	**A fasting blood sugar level of 11.6 mmol/L is too high.** 如果某人的空腹血糖是 11.6 mmol/L，可算是过高的血糖水平。	Yes 是	No 否	I Don't Know 不知道
6	**The best way to check my diabetes is by testing my urine.** 检查糖尿病的最好方式是检测尿液。	Yes 是	No 否	I Don't Know 不知道
7	**There are two main types of diabetes: Type 1 (insulin dependent) and Type 2 (noninsulin dependent).** 有两种主要类型的糖尿病：1 型（胰岛素依赖型糖尿病）和 2 型（非胰岛依赖型糖尿病）。	Yes 是	No 否	I Don't Know 不知道
8	**Medication is more important than diet and exercise to control my diabetes.** 如要控制糖尿病， 药物治疗比饮食治疗和运动治疗重要。	Yes 是	No 否	I Don't Know 不知道
9	**Diabetes often causes poor circulation.** 糖尿病往往导致血液循环不良。	Yes 是	No 否	I Don't Know 不知道
10	**Cuts and abrasions on diabetics heal more slowly.** 糖尿病患者的伤口往往需要更多时间愈合。	Yes 是	No 否	I Don't Know 不知道
11	**The way I prepare my food is as important as the foods I eat.** 食物煮的方法（列如：蒸，油炸，烤） 与吃的食物种类一样重要。	Yes 是	No 否	I Don't Know 不知道
12	**Diabetes can damage my kidneys.** 糖尿病若控制不好，可能会损伤肾脏。	Yes 是	No 否	I Don't Know 不知道
13	**Diabetes can cause loss of feeling in my hands, fingers and feet.** 糖尿病若控制不好，可能导致手，手指和脚失去感觉。	Yes 是	No 否	I Don't Know 不知道
14	**Shaking and sweating are signs of high blood sugar.** 发抖和出冷汗是高血糖的症兆。	Yes 是	No 否	I Don't Know 不知道
15	**Frequent urination and thirst are signs of low blood sugar.** 尿频和口渴是低血糖的症兆。	Yes 是	No 否	I Don't Know 不知道
16	**A diabetic diet consists mostly of special foods.** 为糖尿病患者准备的饮食主要是特别的食物。	Yes 是	No 否	I Don't Know 不知道

Part 2

Note to Interviewer:

The following section consists of multiple choice questions evaluating the participant's knowledge of diabetes. Go through the following questions with their corresponding options with the participants and record their response.

Instructions to Participant:

I will now ask you a few multiple-choice questions. Please choose the most suitable answer for each question.

	Question
17	**The diabetes diet is:** **为糖尿病患者准备的饮食：** a. a healthy diet for most people 对大多数人来说，是健康的饮食。 b. too high in carbohydrate for most people 对大多数人来说，碳水化合物过高。 c. too high in protein for most people 对大多数人来说，蛋白质过高。 d. I do not know 我不知道。
18	**What does 'sugar-free' on a food label indicate?** **食物标签上的‘无糖’ 表示什么？** a. No added sugar or unsweetened food 产品无加糖份。 b. Contains 0g of sugar 产品无含糖。（0 克） c. Contains equal or less than 0.5g of sugar per 100g or 100mL 每 100g/100mL 产品里含有 0.5 克 一下的糖份。 d. Low calorie food 产品是低卡路里。 e. I do not know 我不知道。
19	**Which is the best method for home glucose testing?** **一下哪个选择是在家测试血糖最佳方法？** a. Urine testing 尿液检测 b. Blood testing 血液检测 c. Both are equally good 尿液检测或血液检测都一样好 d. I do not know 我不知道
20	**What effect does unsweetened fruit juice have on blood glucose?** **不加糖的果汁对血糖有什么影响？** a. Lowers it 降低血糖 b. Raises it 升高血糖 c. Has no effect 没有影响 d. I do not know 我不知道
21	**What effect does exercise have on a person's blood glucose?** **运动对与某人的血糖有什么影响？** a. Lowers it 降低血糖 b. Raises it 升高血糖 c. Has no effect 没有影响 d. I do not know 我不知道
22	**Eating foods lower in fat decreases your risk for:** **食用低脂肪食物可降低患下以下风险：** a. Nerve disease 神经系统疾病 b. Kidney disease 肾脏疾病 c. Heart disease 心脏病 d. Eye disease 眼病 e. I do not know 我不知道
23	**Numbness and tingling may be symptoms of:** **麻木和刺痛可能是什么的症状？** a. Kidney disease 肾脏疾病 b. Nerve disease 神经系统疾病 c. Eye disease 眼病 d. Liver disease 肝病 e. I do not know 我不知道

24	**Which of the following is usually not associated with Diabetes:** **哪一种问题通常跟糖尿病无关？** a. Vision problems 眼视影响 b. Kidney problems 肾脏影响 c. Nerve problems 神经系统影响 d. Lung problems 肺影响 e. I do not know 我不知道

E. Attitude & Practices

Part 1: Diabetes Perspective & Attitude
Note to Interviewer:
The following section consists of questions evaluating the participant's perspective and attitude on Diabetes. Go through the following questions with the participants and record their response on a scale of 1 to 5.
Instructions to Participant:
I would like to know more about your views and feelings towards Diabetes. Please let me know how much you disagree or agree with the following statements.

Part A: Feelings or Emotions linked to Diabetes Mellitus						
	Questions 1) Strongly Disagree 强烈反对 2) Somewhat Disagree 不太同意 3) Neutral 中性 4) Somewhat Agree 有点同意 5) Strongly Agree 非常同意	**Options**				
25	**I am worried that I will be diagnosed with Diabetes in the future.** 我担心将来会被诊断出患有糖尿病。	1	2	3	4	5
26	**I am fearful of health screenings as I am afraid that I might have Diabetes.** 我害怕健康检查，因为我担心我可能患有糖尿病。	1	2	3	4	5
27	**I am apprehensive about the work or effort required to prevent myself from getting Diabetes.** 我对防止自己患糖尿病所需的工作或努力感到担忧。	1	2	3	4	5
28	**I am worried that I do not have sufficient knowledge on Diabetes and on how to prevent it.** 我担心我对糖尿病以及如何预防糖尿病的知识不足。	1	2	3	4	5
Part B: Beliefs or thoughts associated with Diabetes Mellitus						
	Questions 1) Strongly Disagree 强烈反对 2) Somewhat Disagree 不太同意 3) Neutral 中性 4) Somewhat Agree 有点同意 5) Strongly Agree 非常同意	**Options**				
29	**I believe that if I manage my diet well, it will reduce my chances of getting Diabetes in the future.** 我相信如果我能很好地管理我的饮食，它将减少我将来患糖尿病的机会。	1	2	3	4	5
30	**I believe that if I exercise regularly, it will reduce my chances of getting Diabetes in the future.** 我相信，如果我经常运动，它将减少我将来患糖尿病的机会。	1	2	3	4	5

31	**I think that it is worth putting in effort to reduce my chances of getting Diabetes.** 我认为值得投入努力减少患糖尿病的机会。	1	2	3	4	5

Part 2: Physical Activity

Note to Interviewer:

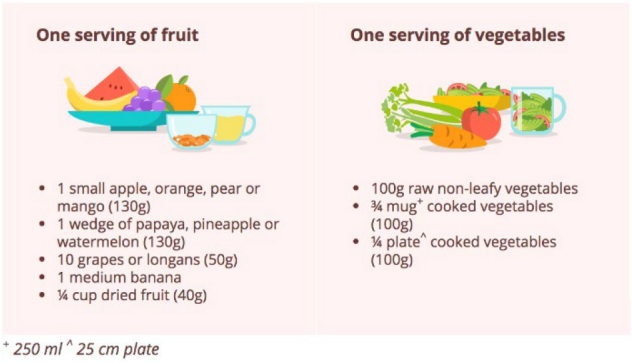
The following section consists of multiple-choice questions evaluating the participant's level of physical activity. Go through the following questions with the participants and record their responses.

Instructions to Participant:

I would like to know more about how much physical activity you do every week. Please answer the following questions and choose the option that best represents your current level of physical activity.

	Questions
32	**On average, how much time do you spend on physical activity in a week?** 您平均每个星期花在运动上的时间有多少？ **1.** Less than 30 minutes 少过 30 分钟 **2.** Between 30 minutes to 60 minutes 30 到 60 分钟 **3.** Between 60 minutes to 100 minutes 60 到 100 分钟 **4.** Between 100 minutes to 150 minutes 100 到 150 分钟 **5.** More than 150 minutes. 150 分钟以上
33	**On average, how strenuous are your physical activities in a week?** 您每个星期所做的运动有多剧烈？ 1. Light Intensity 轻度 Example: Cooking, Mopping/Sweeping, Leisure Stroll 例如：烹饪，拖地/清扫，休闲漫步 2. Moderate Intensity 中等强度 Example: Brisk walking (6km/h or 400m in 4 minutes), Light effort cycling, Recreational Badminton 例如：轻快步行（6 公里/小时或 4 分钟走 400 米），轻松骑行，休闲羽毛球 3. High Intensity 高强度 Example: Jogging/Running (9km/h or 400 m in 3 minutes), Heavy effort cycling, Football, Basketball, Tennis 例如：慢跑/跑步（9 公里/小时或 3 分钟跑 400 米），重体力骑车，足球，篮球，网球

Part 3: Diet
Note to Interviewer:
The following section consists of questions evaluating the dietary habits of the participants. Go through the following questions and record their response on a scale of 1 to 5.
Instructions to Participant:
I would like to know more about your diet. Please answer the following questions and choose the option that best represents your current diet.

	Questions 1) Never 从来没有 2) Occasionally 偶尔 3) Half the time 一半时间 4) Most of the time 大多数时候 5) Always 每次都有	**Options**				
34	**How often do you eat more than 5 serving of fruits and/or vegetables every day?** 您多经常每天吃 5 份以上的水果和/或蔬菜？ Example of 1 Serving: 一份量的例子：  	1	2	3	4	5
35	**How often do you ask for coffee/tea with 'less sugar'?** 您会不会时常要求“少糖”的咖啡/茶？	1	2	3	4	5
36	**How often do you base your main meals around starchy food (Rice, Potato, Noodles)?** 您会不会经常以淀粉类食物（米饭，马铃薯，面条）作为主要食物？	1	2	3	4	5
37	**How often do you choose low fat products when available?** 您是否经常选择低脂肪产品？	1	2	3	4	5
38	**How often do you choose baked, steamed or grilled options when available rather than fried food (such as crisps and snacks, or fish and chips)?** 您是否经常选择烤制，蒸制或烤制选择而不是油炸食品（如薯片和零食，或鱼柳薯条）？	1	2	3	4	5
39	**How often do you consume sweet cakes, desserts, sweets, chocolate or confectionery? For example, Kueh, Chendol, Cheng Teng?** 你多常吃甜食，例如蛋糕，甜点，糖果，巧克力？（如 粿，珍多，清汤）	1	2	3	4	5
40	**How often do you eat pre-prepared meals? For example, pre-prepared sandwiches, ready meals or canned soups.** 你多经常吃加工食物？例如：三明治，即食食品或罐头汤。	1	2	3	4	5

41	**How often do you opt for lean cuts of meat or remove visible fat?For example, removing the skin on chicken or the fats on bacon?** 您多久选择一次瘦肉或去除可见脂肪？ 例如：去除鸡肉上的皮肤或培根上的脂肪？	1	2	3	4	5
42	**How often do you choose wholemeal bread or rolls rather than white bread?** 你是否经常选择全麦面包或面包卷而不是白面包？	1	2	3	4	5
43	**How often do you consume sweetened beverages, including fruit juice drinks with added sugar？ For example, cola, bubble tea, ribena, water chestnut drinks, sweetened ice tea.** 您多常饮用糖分过高的饮料，包括添加糖份的果汁饮料？例如：可乐，泡泡茶，马蹄水等.	1	2	3	4	5
44	**How often do you eat at hawker centres, foods courts or coffee shops?** 你是否经常在小贩中心，美食广场或咖啡馆用餐吗？	1	2	3	4	5
45	**How often do you eat at western fast food outlets or quick-service restaurants?** 您是否经常在西式快餐连锁店或其他快餐店用餐吗？	1	2	3	4	5

F. Exploring Reasons

Note to Interviewer:
The following section consists of questions exploring the possible reasons behind the participant's lifestyle and their outlook on Diabetes.
Instructions to Participant:
I would like to know about what is preventing from being more physically active or eating healthier food. Please select the options that best represents the current challenges you are facing.

46. Please indicate which of the following are the barriers you face in trying to be more physically active. (can circle none or >1)
请说明您在尝试更积极运动时所遇到的障碍。（可以圈无或〉1）

a. Other Priorities 其他更重要的事情
b. Disability or Injury 残疾或伤势
c. Young children or family needs 小孩或家庭需要
d. Work 工作
e. Weather 天气
f. Pollution or noise 污染或噪声
g. Lack of time 缺乏时间
h. Cost 花费
i. Safety 安全

47. Please indicate which of the following are the barriers you face in incorporating a healthy diet into your lifestyle. (can circle none or >1)
请说明您在把健康饮食习惯融入生活当中所遇到的挑战。（可以圈无或〉1）

a. Cost 花费
b. Lack of time 缺乏时间
c. Lack of access from home 住家周围缺乏资源
d. Lack of access from work place 工作地点周围缺乏资源
e. Lack of knowledge 缺乏学问
f. Other priorities 其他优先事项
g. Young children or family needs 儿童或家庭需要
h. Disability or injury 残疾或伤势

Occam's Razor or Hickam's Dictum: A Case of Myopathy Double Trouble

Dear Editor,

In clinical practice, Occam's Razor is a principle that can usually be applied to diagnose patients with rare neuromuscular conditions. However, a second aetiology needs to be considered if a single cause cannot account for all the symptoms seen in patients. We report the rare case of a patient who developed acute progressive generalised myopathy associated with fever and eosinophilia shortly after returning from a tropical island endemic for muscular sarcocystosis. Subsequently, she was diagnosed with possible coexistent renal cell carcinoma (RCC)-associated antinuclear matrix protein 2 (antiNXP2) myositis with muscular sarcocystosis. She was successfully treated with immunomodulatory treatment, tumour resection and antiparasitic treatment. She made a full and complete clinical recovery.

Case Presentation

A 35-year-old teacher with no past medical history presented with acute progressive generalised myopathy. She was well before symptom onset. Prior to admission, she had visited Tioman Island in West Malaysia for 3 days. A week after her return, she noted episodic fever on alternate days associated with relapsing-remitting cough, rhinorrhoea and migratory myalgia. Each episode lasted a few hours. Before presenting to our institution 10 days later, she developed severe, generalised myalgia and arthralgia with progressive bulbar, limb and truncal weakness.

On clinical examination, her temperature was 38.1°C and her vital signs were stable. Neurological examination showed mild bifacial weakness with normal tongue and palatal movement. Swallow assessment revealed delayed swallows, reduced laryngeal excursions and mild nasal regurgitation. Neck flexion and extension measured 4/5 on the Medical Research Council Scale for Muscle Strength. Tone and deep tendon reflexes were normal. Proximal muscle power was 3/5 and distal power was 4/5. Cerebellar and sensory examinations were normal. Systemic examination was also normal with no evidence of skin rash, joint tenderness or swelling, muscle tenderness or lymphadenopathy. Abdominal and chest examinations were normal. Serum creatine kinase (CK) was 3264 IU/L but it increased to 10,216 IU/L on day 8 of admission. Needle electromyography of the right deltoid, biceps, quadriceps and tibialis anterior muscles indicated generalised, irritable myopathy. The laboratory investigations are summarised in Table 1.

In view of her eosinophilia, recent travel history and relapsing-remitting symptoms, an infective aetiology was considered. While on Tioman Island, she engaged in hiking, snorkelling and had contact with domesticated cats. There was no history of animal bites, sick contact or consumption of uncooked meat or seafood. She was in a monogamous relationship and did not have a history of sexually transmitted diseases. No traditional medication, illicit drug or supplement use was reported.

Serum myositis panel returned strongly positive for anti-NXP2 antibody (EUROLINE Autoimmune Inflammatory Myopathies, EUROIMMUN, Lübeck, Germany). Muscle biopsy showed scattered necrotic and regenerating fibres with no endomysial or perimyseal inflammation. Major histocompatibility complex class 1 expression was upregulated diffusely in the sarcolemma and in some areas of sarcoplasm. Paraffin section showed 2 intrasarcoplasmic, cyst-like structures that contained numerous merozoites (Fig. 1). Subsequent serum specimen showed immunoglobulin G but no immunoglobulin M (IgM) antibody to *Sarcocystis nesbitti* (in-house assay, Department of Medical Microbiology, University of Malaya, Kuala Lumpur, Malaysia). Other systemic blood infective and autoimmune markers tested negative.

Computed tomography (CT) scan of the abdomen, pelvis and thorax showed a left renal lower pole lesion measuring 1.9 × 1.7 × 1.9 cm which showed heterogeneous enhancement, suggesting a hypovascular RCC. There was no radiological evidence of interstitial lung disease.

On day 8 of admission, she was started on parenteral methylprednisolone (1 g/day for 5 days), intravenous immunoglobulin (2 g/kg weight) and oral albendazole (400 mg twice a day for 14 days). A partial nephrectomy and resection of the renal lesion was performed 7 weeks after admission. Histology revealed a localised, chromophobic RCC. Treatment led to rapid resolution of fever and improvement of weakness which were accompanied by normalisation of CK and serum eosinophilia (Table 1). She was treated with a tailing dose of oral prednisolone and was completely weaned off immunosuppressants 9 months

Table 1. Serial Laboratory Investigations

Variable (Unit)	Range	On Admission	Day 8	Day 42	Month 9
WBC count (× 10^3/μL)	4.0 – 10.0	5.2	3.3	10.6	
Haemoglobin (g/dL)	11.5 – 15.0	13.4	12.2	10.4	
Platelet (× 10^3/μL)	150 – 450	267	120	264	
Absolute eosinophil (× 10^3/μL)	0.0 – 0.4	0.6	0.5	0.0	
Absolute neutrophil (× 10^3/μL)	2.0 – 7.5	2.5	7.4	14.7	
C-reactive protein (mg/L)	<10.0	0.6			
ESR (s)	3 – 15	62		39	
Creatinine (μmol/L)	50 – 90	58			
Total bilirubin (μmol/L)	5.0 – 30.0	3.7	2.5	4.7	
ALT (U/L)	10 – 55	117	358	31	
AST (U/L)	10 – 45	151	560	16	
TSH (mIU/L)	0.40 – 4.0	1.0			
FT4 (pmol/L)	10.0 – 20.0	12.6			
CK (U/L)	38 – 164	3264	10,216	62	
ANA, Anti-dsDNA, anti-HMGCR antibody, ENA, RF		Negative			
Extended myositis panel*		Strong positive for NXP2			Negative for NXP2
Dengue IgG/IgM antibody/NS1 antigen, hepatitis A IgG antibody, hepatitis B surface antigen, hepatitis C EIA, hepatitis E IgG/IgM antibody, HIV serology, rubella IgG/IgM serology		Negative			
CMV PCR, parvovirus B19 PCR, serum EBV PCR, tuberculosis T-spot		Negative			

ALT: Alanine transaminase; ANA: Antinuclear antibody; Anti-dsDNA: Antidouble stranded deoxyribonucleic acid; AST: Aspartate transaminase; CK: Creatine kinase; CMV: Cytomegalovirus; DNA: Deoxyribonucleic acid; EBV: *Epstein-Barr* virus; EIA: Enzyme immunoassays; ENA: Extractable nuclear antigen; ESR: Erythrocyte sedimentation rate; FT4: Free thyroxine; HIV: Human immunodeficiency virus; HMGCR: 3-Hydroxy-3-methylglutaryl-*CoA reductase;* IgG: Immunoglobulin G; IgM: Immunoglobulin M; NSI: Non-structural protein 1; NXP2: Nuclear matrix protein 2; PCR: Polymerase chain reaction; RF: Rheumatoid factor; TSH: Thyroid stimulating hormone; WBC: White blood cell

*Qualitative immunoblot assay was performed on EUROLINE kit (EUROIMMUN, Lübeck, Germany) for myositis-associated antigens (IgG) with a titre limit of 1:101 for the following antibodies: EJ, Jo-1, Ku, MDA5, Mi-2a, Mi-2b, NXP2, OJ, PL-7, PL-12, PM-Scl70, PM-Scl100, Ro52, SAE1, SRP and TIF1g.

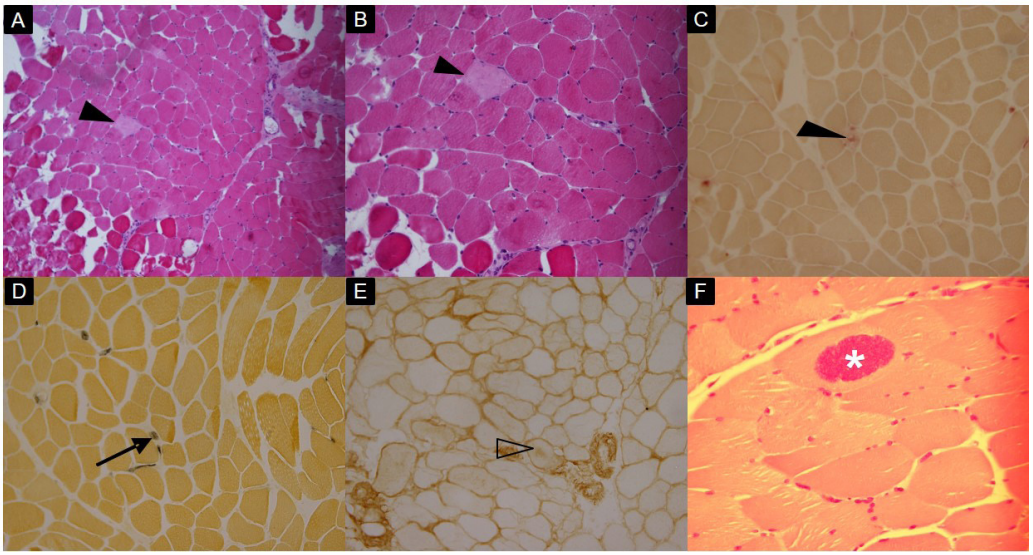


Fig. 1. Left bicep muscle biopsy. A-D: Scanty necrotic fibres (arrowheads) with scattered regenerating fibres (long arrow). Note the absence of a primary inflammatory infiltrate. E: Diffused increased MHC-1 expression of sarcolemma and some areas of sarcoplasm (hollow arrowhead). F: Cyst-like structure (∗) contains numerous merozoites. (A: HE stain, original magnification × 10; B: HE stain, original magnification × 20; C: Acid phosphatase stain, original magnification × 20; D: Alkaline phosphatase stain, original magnification × 20; E: MHC-1 stain, original magnification × 20; F: Paraffin stain, original magnification × 40). HE: Haematoxylin and eosin; MHC-1: Major histocompatibility complex class 1

after presentation. She remained in biochemical and clinical remission 12 months after presentation. Repeat antiNXP2 antibody test at 9 months postsymptom onset was negative.

Discussion

AntiNXP2 antibodies are associated with dermatomyositis and, less commonly, with polymyositis.[1,2] Symptom duration ranges from 2-23 months and fever, myalgia and bulbar, proximal and distal limb weakness are presenting features.[1,3] Serum CK levels range from 1500-26,000 IU/L.[1] Pathological findings include perifascicular atrophy and perivascular inflammation, but these findings are found only in 32% and 53% of 1 patient cohort, respectively.[3]

Although an association with various types of primary malignancies was reported in adult patients,[4] only 1 case of antiNXP2 myositis associated with RCC had been reported.[5] The disappearance of antiNXP2 antibodies following resection of RCC, in tandem with clinical remission, suggests an association between antiNXP2 antibody and RCC in our patient.[6] Although myositis antibodies can be positive in other systemic autoimmune conditions and in infective myopathies, strongly positive myositis antibody levels such as those seen in our patient were shown to be specific in the diagnosis of inflammatory myopathies.[7]

Muscular sarcocystosis secondary to *Sarcocystis nesbitti* has been reported in Tioman Island and Pangkor Island in West Malaysia.[8,9] Snakes are definitive hosts for *Sarcocystis nesbitti* and humans are intermediate hosts.[9] Infection follows consumption of food or water contaminated with faeces of the definitive host. Ingested sporocysts develop in circulating monocytes and blood vessel endothelium before sarcocysts form in the skeletal muscle of the intermediate host.[10] The incubation period ranges from 9-13 days. Early manifestations include fever, headache, joint pain and myalgia while dysphagia and weakness are not prominent features. A relapsing-remitting course is ob-served in more than half of patients. Serum CK is usually elevated to between 200-900 IU/L but it was markedly raised in our patient. Eosinophilia is seen in two-thirds of patients during the course of illness.[9]

A definitive diagnosis is made through histological identification of intrasarcoplasmic sarcocysts. Merozoites are found in a cyst and are encapsulated within a thin membrane. Usually, there is minimal inflammatory change around a cyst.[9,11] In our patient, her serum was non-reactive to IgM antibody to *Sarcocystis nesbitti*, but it must be stressed that current *Sarcocystis* serology is still at an experimental phase. Evidence-based treatment for both muscular sarcocystosis and antiNXP2 myositis is not established. Treatment of muscular sarcocystosis with antiparasitic agents such as albendazole has been attempted with varying results. The mainstay of treatment for inflammatory myopathies involves immunosuppression and, in the case of paraneoplastic inflammatory myopathies, treatment of the associated malignancy. Corticosteroids and steroid sparing agents, including intravenous immunoglobulin, have been used for immunosuppression.

This case highlights several important clinical points. In patients with inflammatory myositis who are seropositive for antibodies associated with cancer, a thorough search for malignancy is mandatory. When a malignancy is found, effective treatment of the underlying malignancy may lead to clinical and serological remission. Additionally, it is important to consider a parasitic aetiology in patients with inflammatory myositis, especially when there is a history of residence in or travel to an endemic region and there is a relapsing-remitting course with associated eosinophilia. Lastly, a second aetiology should be excluded if a single cause cannot account for all the symptoms in patients.

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Zhiyong Chen, [1]*MBBS, MRCP*, Monica Saini, [2]*MD*, Kalimullah Jan, [2]*MBBS, MD, MRCP*, Josiah YH Chai, [1]*MBBS, FRCP*

[1]Department of Neurology, National Neuroscience Institute, Singapore
[2]Department of General Medicine, Changi General Hospital, Singapore

Address for Correspondence: Dr Chen Zhiyong, Department of Neurology, National Neuroscience Institute, 11 Jalan Tan Tock Seng, Singapore 308433. Email: chen.zhiyong@singhealth.com.sg

Partial Patella Tendon Tear in a Middle-Aged Man with No Previous Knee Injuries: A Non-Surgical Approach

Dear Editor,

Patella tendon (PT) rupture is an uncommon cause of anterior knee pain[1] and is reportedly 6 times less frequent than patellar fracture, making it a rare injury.[2] Although most PT ruptures are unilateral, case studies that described simultaneous bilateral tendon ruptures have been reported.[3-5] PT tears can be classified as partial or complete and typically occur in active individuals <40 years old. We describe an unusual case of unilateral PT injury in a 39-year-old Chinese man.

Case Presentation

The patient presented to the specialist outpatient clinic after he sustained a fall when he was commuting on public transport. He reported that he was standing in a bus when it braked suddenly, causing him to lose his balance and fall. Due to the sudden impact, his lateral right knee struck the edge of a step. Although he could ambulate initially, he developed considerable swelling and bruising around the joint which worsened progressively. Prior to this incident, he had no history of trauma or symptoms and had no pre-existing medical conditions. He was not on any long-term medications such as steroids that would compromise his tendon.

On clinical examination, there was limitation to right hip flexion and knee extension. Pain was localised to the anterior-lateral border of the right PT. Ultrasound examination revealed near full thickness tear to the lateral half of the right PT that began one-third from the distal insertion. There were hypoechogenic changes that were suggestive of fluid within the substance of the tendon and areas of neovascularity (Fig. 1).

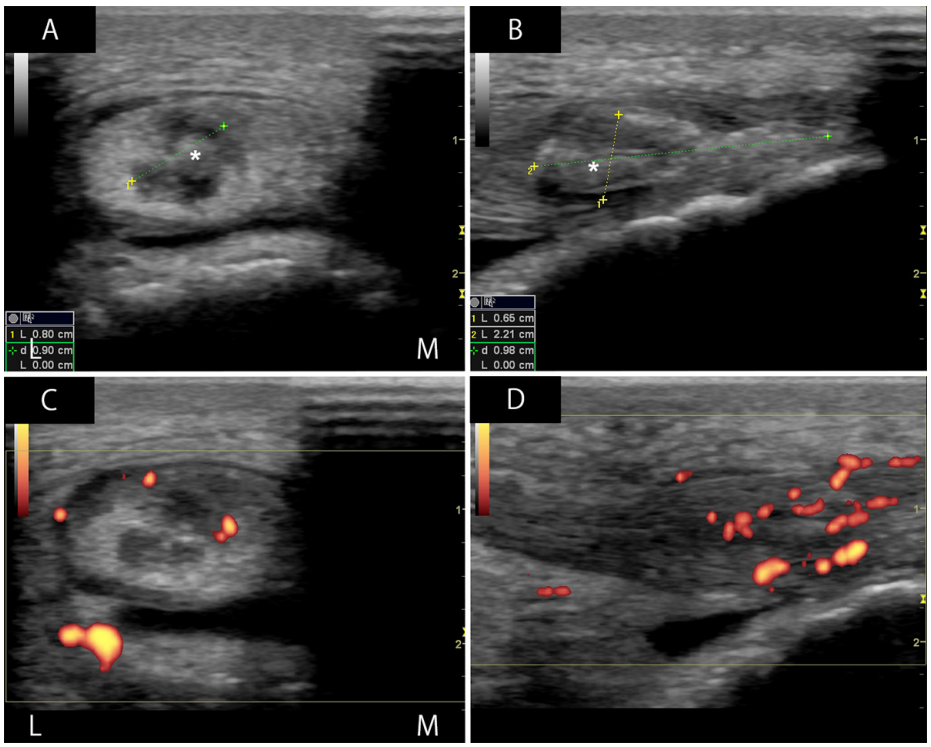

Fig. 1. Lateral and short axis ultrasonography of the right patella tendon. A and B: An 8 × 6.5 × 22 mm tear (∗) is seen in the lateral segment with a thickened but still intact tendon medially. C: Hypoechogenic areas indicate fluid within the substance of the tendon that represent a near full thickness tear. D: Considerable neovascularity seen in the region of interest does not tract proximally and is suggestive of acute injury as opposed to underlying tendinopathy.

Operative repair was discussed with the patient but he opted for conservative management. The right knee was immobilised in full extension for 2 weeks with a cast and he was allowed to weight bear. Upon removal of the cast after the acute phase of injury, he used a hinge brace as it was more comfortable and it was easier to monitor his recovery. The same position was maintained after the hinge brace was locked into full extension. Repeat ultrasound examinations at 2 (Fig. 2), 4 (Fig. 3) and 12 (Fig. 4) weeks demonstrated good healing within the substance of the tendon.

At the second consultation, platelet-rich plasma (PRP) therapy was discussed and offered as part of conservative management but in view of the healing, it was not adopted. Knee movement increased to 45 and 90 degrees flexion at 4 and 12 weeks, respectively. Upon complete healing, physiotherapy was commenced to restore full range of movement and quadriceps and hamstring strength. Over the next 3 months, he gradually returned to normal activities and eventually resumed his chosen sport of distance running.

Discussion

PT rupture is usually caused by direct or indirect trauma to the knee. The latter is more common[4] and involves a sudden contraction of the quadriceps with the knee in slight flexion caused by, for example, sudden movement, sprint and avoidance of a fall.[2] Biomechanical analysis has shown that a force equivalent to 17.5 times that of normal body weight can easily rupture the PT in healthy young individuals.[6] Traumatic ruptures are usually preceded by structural abnormalities in the tendon and 3 primary causes were identified:[7-9] 1) systemic disorders such as chronic renal insufficiency, diabetes mellitus, hyperparathyroidism, lupus erythematosus and rheumatological diseases; 2) chronic local stress to both knees leading to repeated microtraumas and inflammatory and degenerative changes; and 3) local or systemic administration of steroids.

Our patient did not have a history of systemic disorders, steroid use or symptoms in the tendon that would suggest microtrauma prior to his injury. Nevertheless, this case was still unusual after a partial width and near full thickness tear—normally caused by longstanding tendinopathy and subsequent intra-substance tearing—that was sustained upon direct impact to the tendon.

Complete PT ruptures typically present with patella alta and inability to initiate active knee extension due to disruption of the knee extensor mechanism. On the other

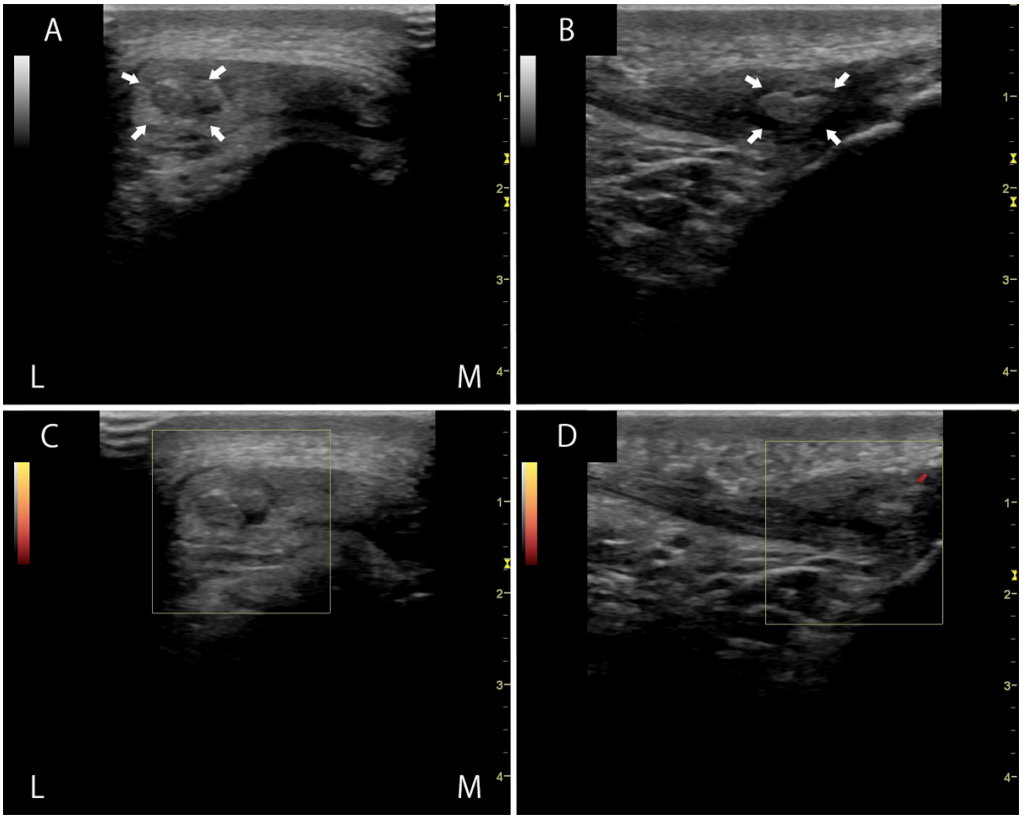

Fig. 2. Lateral and short axis ultrasonography of the right patella tendon at 2 weeks. A and B: Hypoechogenic areas seen in the initial images have lessened in both short and long axes. The hyperechogenic areas (white arrows) represent organisation of a haematoma. C and D: Initial hypervascularity has also settled following a period of mobilisation.

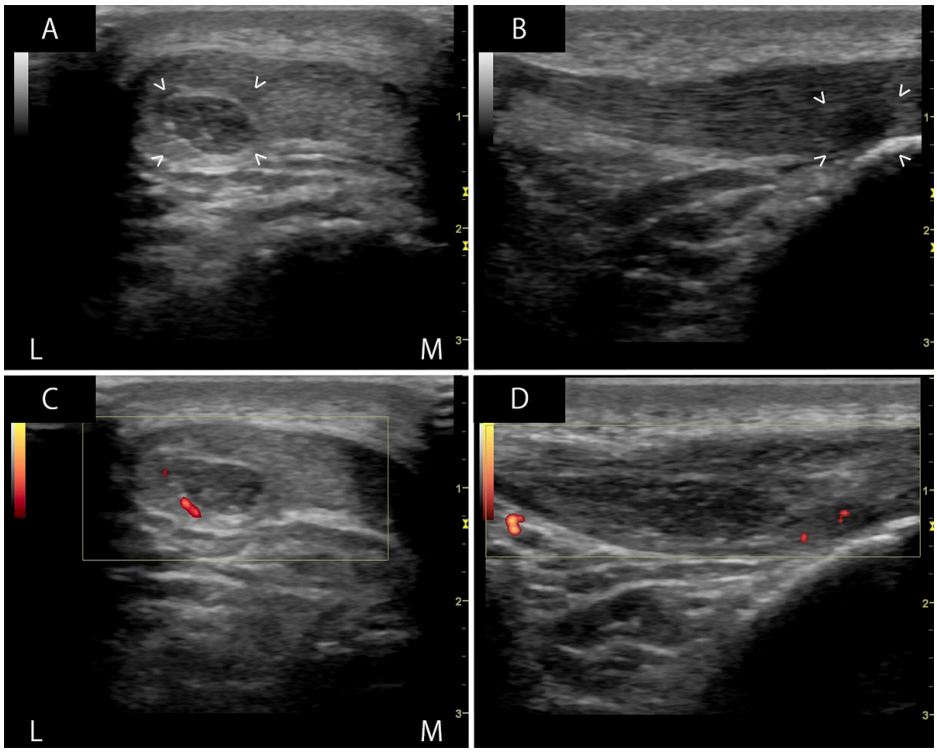

Fig. 3. Lateral and short axis ultrasonography of the right patella tendon at 4 weeks. A and B: The area of injury is almost fully filled and is well defined (^) compared to the normal tendon architecture. This is most evident on the short axis. C and D: Compared to the ultrasound images taken at 2 weeks, there is a slight increase in vascularity and it was attributed to the commencement of physiotherapy.

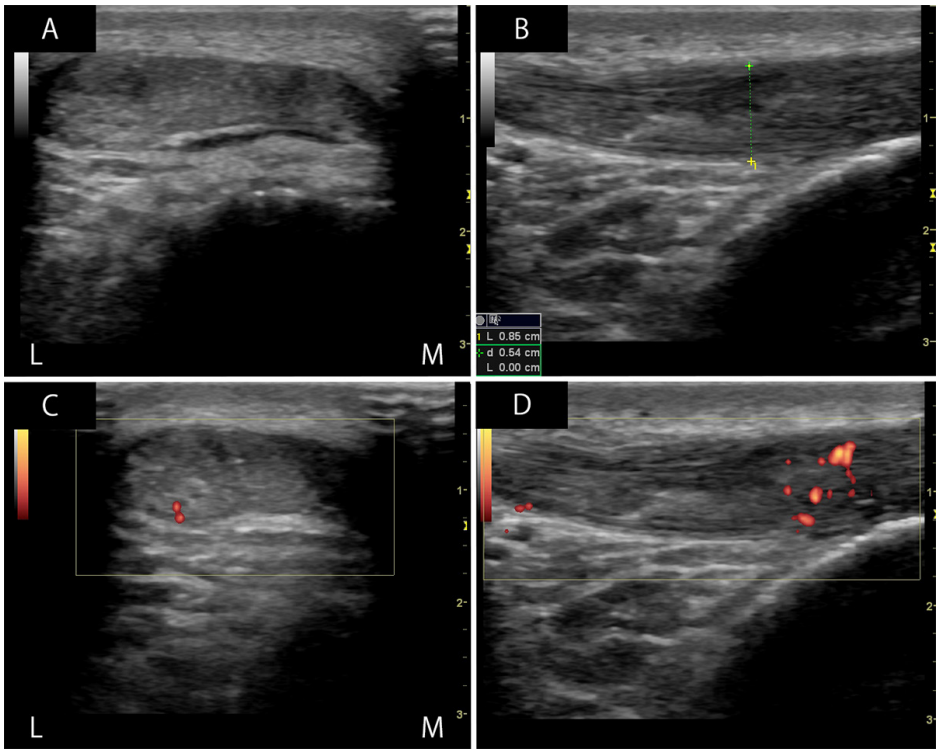

Fig. 4. Lateral and short axis ultrasonography of the right patella tendon at 12 weeks. A and B: The injury has healed well and shows similar echotexture as the uninjured portion of the tendon. This is evident on the short and long axes. The distal region remains thickened at 8.4 mm. C and D: Residual vascularity was attributed to ongoing physiotherapy and was not associated with pain symptoms.

hand, a partial tear has clinical features that resemble patellar tendinosis: preservation of active initiation of knee extension and aggravation of symptoms by movements such as jumping or navigating stairs.[10] Despite these features, the likelihood of a wrong diagnosis being made based only on clinical signs can be high.[11] This is because the presence of intact retinacular fibres in haemarthrosis or preserved active knee extension can limit the findings of a physical examination.

Imaging Patella Tendon Injuries

A plain radiograph is an appropriate first-line imaging modality for PT injuries since it can identify tibial tuberosity fractures, patellar avulsions or patella alta. These bony injuries are suggestive of a rupture.[12] Other findings that can be identified include joint effusion, poorly defined suprapatellar masses and calcific densities but they are frequently missed.[11] A diagnosis can be confirmed with either an ultrasound or magnetic resonance image (MRI) for cases that present with equivocal clinical and radiograph findings. Both are non-invasive and do not utilise ionising radiation. Over the past 2 decades, improvements in MRI have greatly reduced the need for invasive arthroscopies to examine the ligaments and menisci of the knee.[13-5] It is considered the gold standard in imaging PT injuries and reconstructing 3-dimensional images to facilitate preoperative planning.

Significant improvements in ultrasound technology and training have led to its widespread use in musculoskeletal medicine. Although it is difficult to visualise articular or particularly deep structures, ultrasound is still an excellent modality to diagnose superficial pathologies such as tendinopathies, ligament tears, joint degeneration and impingement. It is used to visualise any disruption in the tendon's fascicular pattern, which is indicative of a tear, and other pathological changes such as increased space between echogenic fibres and decreased echogenicity. In particular, power Doppler sonography is used to image neovascularisation. Given its low cost, healing can be monitored with regular imaging at follow-up examinations and changes such as the organisation of anechoic fluid following an acute injury can be observed.

Ultrasound imaging can also identify changes that are indicative of pre-existing pathologies such as thickening and calcification in tendinopathy, fusiform thickening and loss of normal fibrillar echotexture in inflammatory enthesitis.[16] Another unique feature of ultrasound is the ability to perform dynamic assessments and to guide interventions. According to Girish et al,[17] it is the investigation of choice in the examination of the extensor mechanism of the knee.

The literature on the accuracy of ultrasound imaging in diagnosing PT tears is mixed. In their retrospective review of clinical, MRI and ultrasound findings in patients who had undergone surgical repair of quadriceps and PT ruptures, Swamy et al[11] concluded that ultrasound was unreliable in the identification of acute injuries to the extensor mechanism of the knee in obese and muscular patients. They suggested that an MRI could be done when there is clinical ambiguity and before any surgical treatment is undertaken. Conversely, Warden et al[18] reported greater accuracy in the use of ultrasound than MRI to diagnose PT pathologies. Other studies have also advocated the use of ultrasound in early assessment and management of PT injuries.[19-21]

In their report on the intraoperative findings in 7 patients, La et al[20] concluded that ultrasound, including the use of dynamic evaluation, was helpful in the diagnosis of partial thickness tears of the quadriceps tendon and may aid in the differentiation of such cases from complete quadriceps tendon tears, particularly in acute cases. However, scar tissue in chronic injury may represent a potential pitfall in the assessment of partial versus full quadriceps tears. Lee et al[21] have suggested high-frequency ultrasound as an effective method to detect and localise disruption of the quadriceps and PT. However, its efficacy is dependent on the skill of the user.

Due to its high cost and long wait time, many patients are reluctant to undergo MRI. As such, the use of ultrasound imaging in outpatient clinics can assist clinicians to reach an earlier diagnosis and expedite treatment. When there is clinical suspicion of a significant rupture based on ultrasound findings and surgical intervention is deemed necessary, the findings can be discussed with the radiologist or surgeon and further imaging studies can be requested.

Clinical Management and Platelet-Rich Plasma

Our case highlights the propensity of PT to heal through immobilisation without any need for further intervention. Treatment for a partial PT tear overlaps with that for tendinopathy, which is conservative management that comprises rest, stretching and eccentric quadriceps strengthening exercises. However, this treatment is prescribed according to the experience of physicians and is not based on clinical data and findings. As such, its efficacy remains undetermined.[22] Traditionally, surgical intervention is considered for partial tears that do not respond to conservative treatment.[23,24] However, the emergence of PRP therapy has been hailed as an alternative, but less invasive, treatment option.

The increasing popularity of PRP therapy is attributed to the fact that it is a simple procedure and is one of the few established treatments that can hasten healing in musculoskeletal injuries. It involves the administration of concentrated PRP—which contain growth factors that are derived from the patient's own blood—into the injury site to promote healing. It is manufactured from the centrifugation

of blood. There are a myriad of PRP samples that contain varying amounts of platelets and leukocytes, and the platelet levels can be as high as 9 times that of whole blood.[25] Due to its autologous nature, PRP therapy has minimal side effects and can be classified into 4 groups: acute ligament injury, chronic tendinosis, intraoperative tissue repair augmentation and muscle injury.[26]

Contraindications to PRP therapy include allergies to any manufacturing components (such as dimethyl sulfoxide), concurrent illnesses, local infection around the site of injection and recent malignancy due to the hypothetical risk of injecting malignant cells back into the body. It is not recommended in patients with thrombocytopaenia or in those who are on regular nonsteroidal anti-inflammatory drugs due to altered platelet numbers and function.[27]

Although the results from in vitro and in vivo studies are promising and there are anecdotal cases of tendon recovery following PRP therapy,[10,28-31] multiple systemic reviews of the use of PRP therapy paint a controversial picture. Collectively, PRP therapy is beneficial in the treatment of patellar tendinosis and lateral epicondylitis but not for Achilles tendinosis.[29,32,33] There is also a lack of consensus on the use of PRP therapy in the treatment of muscle injuries. Reurink et al[34] did not find a significant difference in healing between patients with acute hamstring injuries on PRP therapy and those who were on placebo. Although some researchers have reported on the risk of fibrosis and scar tissue development,[32] others reported faster recovery and a return to normal sporting activities in patients who were treated with PRP therapy,[35] especially after it was combined with rehabilitative therapy.[36]

In surgical augmentation such as anterior cruciate ligament reconstructions and rotator cuff repairs, PRP therapy has shown mixed results and is therefore not recommended in routine clinical practice.[29,32] This could be due to 2 factors. First, there is a lack of a standard protocol on how PRP is obtained and used. As such, there are variations in platelet-to-leukocyte ratios, PRP volumes and usage techniques.[29,30,33] Second, patient factors such as age and activity levels can influence potential healing. The disease stage can also impact treatment timing.[29]

PRP therapy was discussed with our patient as a potential treatment modality but due to improvement in the tendon architecture seen on serial ultrasound findings, it was abandoned. It could be considered if the findings had demonstrated poor recovery.

Surgical repair of an acute, partially torn PT is rarely indicated, especially when active knee extension is still intact. When direct repair cannot be achieved, it may be augmented with tendon grafts but the method and procedure can vary depending on factors such as the location of the injury and chronicity of the lesion.[2,12,37-40] Early surgery is indicated after a complete rupture is identified and the outcome is generally positive.[40]

Conclusion

Our case demonstrates an unusual injury to the PT following direct trauma and the propensity for partial tendon injuries to heal without any clinical intervention. Although our patient did not require further intervention beyond immobilisation and rehabilitative therapy, PRP therapy or surgical intervention must be discussed early with patients on a case-by-case basis using tissue healing and functional recovery as a treatment guide. Additionally, it is important to conduct dynamic musculoskeletal ultrasound imaging studies in a high-volume orthopaedic or sports clinic in order to expedite treatment. They are preferred to MRI which is more costly and requires a longer wait time.

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Nicole YY Choi, [1]*Diploma (BMS)*, Shauna HS Sim, [2]*MBBS*,
Alvin CK Tan, [3]*MRCS, MMed, FRCS*,
Dinesh Sirisena, [2]*MSc (SEM), FFSEM (Ire), FFSEM (UK & Ire)*

[1]Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[2]Sports Medicine Centre, Khoo Teck Puat Hospital, Singapore
[3]Department of Orthopaedic Surgery, Khoo Teck Puat Hospital, Singapore

Address for Correspondence: Dr Dinesh Sirisena, Sports Medicine Centre, Khoo Teck Puat Hospital, 90 Yishun Central, Singapore 768828.
Email: dinesh.sirisena@ktph.com.sg

White Matter Disease in a Young Adult Presenting as Rapidly Progressive Parkinsonism

A 36-year-old Chinese lady presented with bilateral hand tremors and difficulty in performing simple tasks such as typing and handling of utensils. She also reported short-term memory loss over the last 3 months. On initial examination, bradykinesia was observed in her upper limbs which was slightly more pronounced on the left. This was associated with postural and intention tremors as well as left upper limb dystonia, posturing and apraxia. Brisk tendon reflexes were also elicited. Her sensory and motor power and coordination examinations were unremarkable. Her gait and speech were normal.

Within 1 year of her initial presentation, her symptoms progressed rapidly. Her speech became impaired with hypokinetic dysarthria. She had difficulty initiating speech and features such as festination and reduced volume were observed. Emotional lability was also noted. Additionally, she developed postural instability and was unable to stand independently. There was progression of bilateral upper limb dystonia with increased rigidity and spasticity. Two years after symptom onset, she required assistance in most of her activities of daily living.

Notably, her mother passed away at the age of 55 in another country and was suspected to be suffering from an undetermined neurodegenerative disease. No definite family history of Parkinsonism was otherwise present. There was no history of consanguinity. Her father and 3 siblings were healthy.

What do her serial magnetic resonance imaging (MRI) show?

A. Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP)
B. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
C. Multiple sclerosis (MS)
D. Central nervous system (CNS) vasculitis
E. Adult-onset Krabbe disease

Workup and Findings

The initial clinical diagnosis was asymmetrical Parkinsonism syndrome. Cerebrospinal fluid (CSF) and serum workups for MS, vasculitis, infective and other immune-mediated causes (both paraneoplastic and non-paraneoplastic) were negative. Initial MRI done in a private hospital showed bilateral white matter hyperintensities on T2-weighted axial images and fluid-attenuated inversion recovery (FLAIR) coronal images, predominantly in the frontoparietal lobes, and included the corticospinal tracts at the posterior limbs of the internal capsules (Fig. 1). Additionally, multiple foci of restricted diffusion were present in the bilateral centrum semiovale (Fig. 1), corona radiata and splenium of the corpus callosum. There was also frontal atrophy which is rare in someone of her age (Fig. 1). No abnormal parenchymal or leptomeningeal enhancement was identified. The basal ganglia, brainstem and cerebellum were not involved. Computed tomography (CT) of the brain and angiogram study showed confluent white matter changes that were similar in appearance and distribution to that seen on MRI. A calcific focus was seen in the right frontal lobe periventricular white matter. There was normal contrast opacification and calibre of the anterior and posterior circulations. No stenosis or beading was seen that would otherwise suggest vasculitis.

At follow-up 1.5 years later, MRI showed increased confluent white matter FLAIR signal abnormalities that still predominantly involved the frontoparietal lobes (Fig. 2). There was increased prominence and new foci of raised diffusion-weighted image (DWI) signal in the bilateral centrum semiovale, corona radiata and splenium of the corpus callosum. Some of these showed apparent diffusion coefficient (ADC) signal dropout that was consistent with new and persistent foci of restricted diffusion (Fig. 2). New foci of restricted diffusion were also seen in the left genu of the corpus callosum. There was generalised cerebral atrophy with frontal predominance that had progressed since the previous examination (Fig. 2).

Answer: A

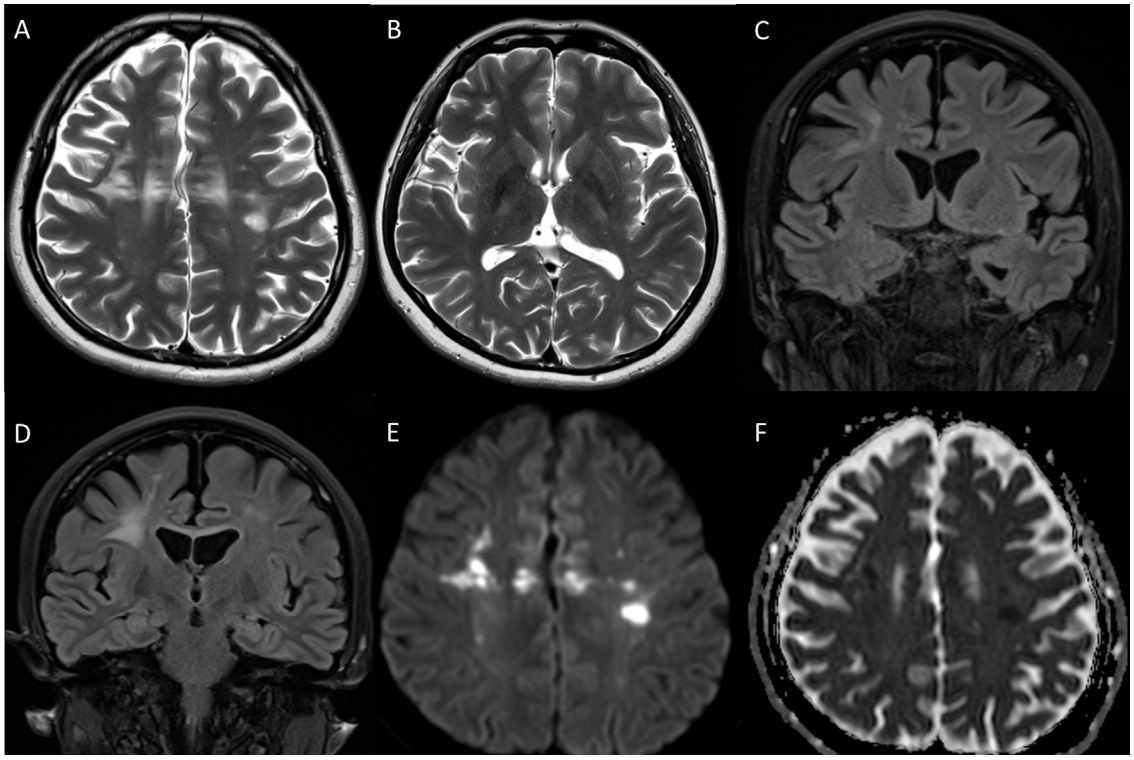

Fig. 1. Initial brain MRI. A and B: T2-weighted axial images showed signal changes in bilateral frontoparietal deep and subcortical white matter and corticospinal tracts in the posterior limb of internal capsules associated with generalised cerebral volume loss that exhibited frontal lobe predominance. C and D: Fluid-attenuated inversion recovery coronal images corroborated findings of T2-weighted images but also showed involvement of body of the corpus callosum. E and F: Diffusion-weighted and apparent diffusion coefficient axial images showed multiple areas of restricted diffusion in bilateral centrum semiovale. MRI: Magnetic resonance imaging

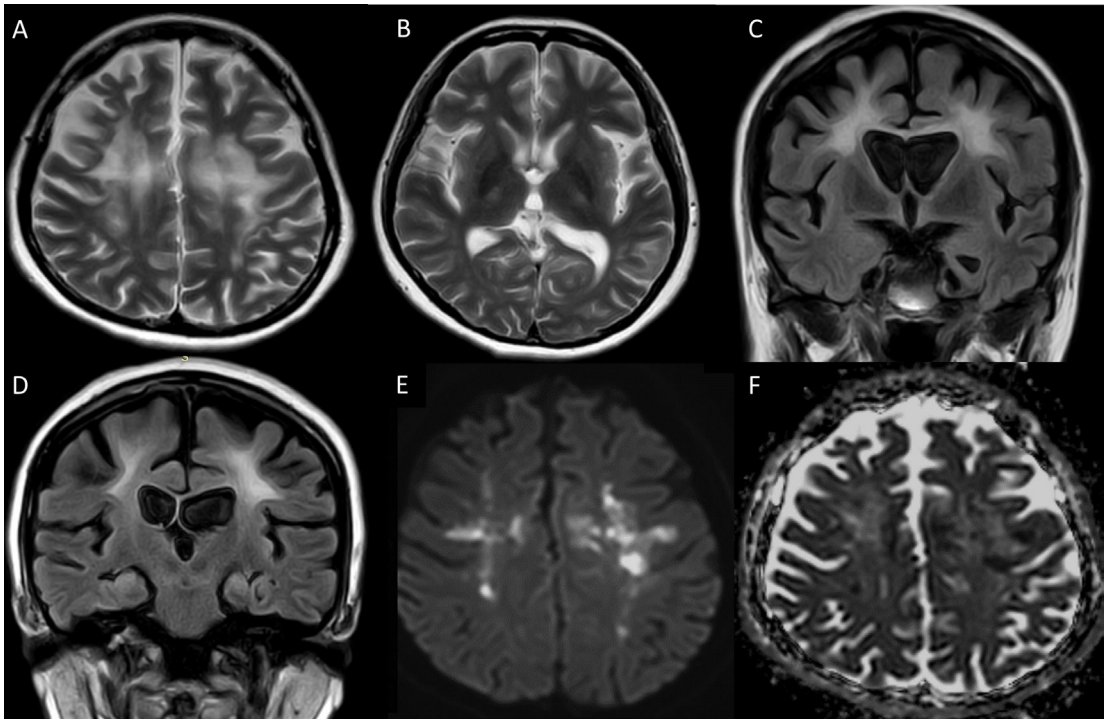

Fig. 2. Follow-up brain MRI. A and B: T2-weighted axial images showed interval progression of confluent white matter signal changes and generalised cerebral volume loss with frontal lobe predominance. C and D: Fluid-attenuated inversion recovery coronal images corroborated findings of T2-weighted images but also showed prominence of lateral ventricles from volume loss. E and F: DWI and ADC axial images showed new and increased prominence of DWI signal abnormalities, some of which showed corresponding ADC signal change that was consistent with new and persistent foci of restricted diffusion. ADC: Apparent diffusion coefficient; DWI: Diffusion-weighted image; MRI: Magnetic resonance imaging

In view of her suspected family history of neurodegenerative disease and unexplained white matter changes seen on her imaging studies, a few differential diagnoses were considered and she underwent a genetic test. Whole-genome sequencing (WGS) revealed a variant of the colony-stimulating factor-1 receptor (*CSF1R*) gene, *T567M*, that was predicted in silico to be pathogenic with a rare exome variant ensemble learner score of >0.5.[1] No other pathogenic variants or mutations were found on WGS, including in the alanyl-tRNA synthetase 2 (*AARS2*) gene that could suggest another cause of adult-onset leukoencephalopathy such as *AARS2*-related leukoencephalopathy. Her clinical syndrome and characteristic findings on imaging studies, such as bilateral frontoparietal involvement and persistent restricted diffusion, as well as the finding of the *CSF1R* gene variant on WGS and absence of other potential pathogenic variants made ALSP the likeliest diagnosis.[1]

Discussion

The term "leukoencephalopathy" encompasses an extensive group of white matter diseases that may be acquired or are congenital in origin. They may be broadly divided into demyelinating conditions that involve secondary destruction of normal myelin or dysmyelinating conditions which occur as a result of disordered myelin production.[2] The onset of presentation may range from as early as the neonatal period to adulthood. The primary focus of our discussion will be on adult-onset leukoencephalopathies. The increased use of MRI has greatly helped clinicians and radiologists to gain a better understanding of this rare subgroup of conditions.

ALSP is a rare, autosomal dominant, adult-onset leukodystrophy with a mean age of onset at 43 years old. Although it is an autosomal dominant trait, sporadic cases are common due to incomplete penetrance, genetic mosaicism and de novo mutations.[3-6] The typical imaging features include frontoparietal predominant white matter signal abnormalities that are bilateral but are not always symmetrical, corpus callosum involvement, multifocal persistent restricted diffusion on DWI, progressive volume loss and presence of calcifications that have been described in periventricular frontal and parietal subcortical white matter.[3-6] Patients usually present with early-onset cognitive dysfunction, personality changes and movement disorders including tremours, bradykinesia and rigidity that mirror features of Parkinsonism.[3-6] The neuropathological hallmark involves destruction and volume loss of cerebral white matter with a marked loss in myelin, large numbers of axonal spheroids and pigmented glia. Mutations in the *CSF1R* gene have been implicated in ALSP; most mutations were found on the tyrosine kinase domain of the protein.[3-6] Taking into account our patient's demographics, clinical presentation, preliminary genetic findings and characteristic imaging results, ALSP was suspected.

Another adult-onset inherited white matter disease is CADASIL. It may also present with confluent white matter signal abnormality, positive lesions on DWI and progressive volume loss. Although the characteristic involvement of the anterior temporal lobes and external capsules were absent in our patient, studies have shown that these manifestations may not be seen in the Asian population, particularly those with *R544C* mutations.[2,7,8] Nonetheless, CADASIL was considered as less likely given the persistent foci of restricted diffusion (atypical for infarcts) and absence of cerebral microbleeds, intracranial haemorrhage and involvement of the brainstem, which are reportedly more common in the Asian variant.[7,8]

An imaging differential of primary progressive MS was briefly considered. Demyelinating plaques are typically T1-weighted hypointense and T2-weighted hyperintense, and may show contrast enhancement in the active phase. Both high and low ADC values have been described in the active phase and are typically found in the periventricular, juxtacortical, infratentorial and spinal cord.[9,10] Additionally, compared to the Western population, Asian patients with MS tend to have optic-spinal involvement.[11] Although our patient had progressive disability and periventricular lesions on MRI, she did not respond to a trial of corticosteroids therapy. The absence of optic-spinal involvement and oligoclonal bands in CSF also rendered the diagnosis of MS as less likely.[9,11]

CNS vasculitis comprises a wide spectrum of diseases that include systemic vasculitides, connective tissue diseases, malignancies, drug- and radiation-induced infections.[12] Primary CNS vasculitis or primary angiitis of the CNS is a rare idiopathic entity that is confined to the CNS and typically presents as encephalopathy and headache in the 5th and 6th decades of life.[2,12] Imaging findings of CNS vasculitis may show microvascular ischaemic changes, infarcts, haemorrhages, white matter oedema and contrast enhancement. The cerebral arteries may have a beaded appearance that show varying degrees of stenosis, occlusion and vessel wall contrast enhancement.[12] In our patient, the clinical presentation was limited to neurological symptoms and there were no evidence of other organ involvement. Additionally, she was not on any long-term medications or radiation treatment. Serum and CSF workups did not reveal any findings that would suggest autoimmune, infective, inflammatory or malignant processes. The imaging results revealed multiple foci of restricted diffusion which could also be seen in infarcts. However, many of the foci of restricted diffusion persist over time and these are atypical

for infarcts. Other findings such as haemorrhages, contrast enhancement and vascular stenosis were also absent in our patient.

Inborn errors of metabolism (IEM) remain an important differential diagnosis in patients who present with leukoencephalopathy. IEM is a diverse group of genetic defects that result in enzyme deficiency in the metabolic pathway and in the case of leukodystrophies, it can lead to myelin disorders. These tend to produce symmetrical white matter changes in the brain.[5,6] Specifically, the more common disorders such as Krabbe disease, X-linked adrenoleukodystrophy (X-ALD) and metachromatic leukodystrophy may be considered.

Krabbe disease is an autosomal recessive lysosomal storage disease caused by beta-galactocerebrosidase enzyme deficiency. Adults with this condition present with pyramidal tract signs accompanied by spastic paraparesis or tetraparesis. Peripheral demyelinating polyneuropathy may also occur in up to 60% of patients. The clinical course is slowly progressive. MRI features include bilateral parieto-occipital white matter changes and involvement of the splenium of the corpus callosum, corticospinal tracts and optic radiation. Periventricular white matter involvement is less commonly seen. Intracranial calcifications may be seen on CT.[5,6]

X-ALD is one of the most common adult leukodystrophies that is due to mutations in the adenosine triphosphate-binding cassette subfamily D member 1 gene. On MRI, there are typically abnormalities in the parieto-occipital white matter, splenium of the corpus callosum, audio-visual pathways and occasionally the frontal lobes and corticospinal tracts. Enhancement of the lesions may be seen. Thoracic cord involvement is often seen in the adrenomyeloneuropathy form, which is the most common type of X-ALD.[5,6]

Metachromatic leukodystrophy is an autosomal recessive lysosomal disease related to arylsulfatase A gene mutations. Patients with this condition present with central and peripheral demyelination. MRI shows symmetrical and confluent frontal or periventricular white matter signal changes with sparing of subcortical U-fibres. A tigroid pattern caused by sparing of perivascular white matter may be seen.[5,6]

Our patient presented with rapidly progressive cognitive and Parkinsonian symptoms. No distal axonopathy was present. MRI showed non-enhancing frontoparietal deep and subcortical white matter signal changes, involvement of corticospinal tracts and frontal predominance cerebral volume loss. Her gender, clinical presentation, rapid clinical course and pattern of white matter involvement rendered IEM disorders such as adult-onset Krabbe disease, X-ALD and metachromatic leukodystrophy unlikely.

Currently, there is no cure for ALSP and the prognosis remains dismal. The mean disease duration is 6.8 years. Management is primarily targeted at controlling symptoms that include depression, seizures and spasticity. Additionally, conventional therapies such as levodopa and cholinesterase inhibitors have not proven beneficial for manifestations of Parkinsonism and cognitive impairment, respectively. Limited research has hinted at the potential of haematopoietic stem cell transplantation to halt disease progression in 1 patient for at least 15 years.[4] However, studies that involve large populations are required to evaluate its efficacy. Some authors have advocated early screening of *CSF1R* mutations in patients with possible CNS vasculitis or adult-onset leukodystrophy to circumvent the need for a brain biopsy with its associated risks.[3]

Conclusion

Though rare, awareness of ALSP is important as it can mimic other conditions and has a poor prognosis. In adults presenting with progressive leukoencephalopathy, more common conditions such as MS, CADASIL and CNS vasculitis should first be considered. The possibility of other adult-onset hereditary leukodystrophy, such as Krabbe disease, should also be explored. However, when characteristic imaging features such as typical frontoparietal distribution, presence of white matter calcification, temporal progression of white matter changes and cerebral atrophy are present, ALSP should be entertained. The presence of persistent foci of restricted diffusion and absence of other findings, such as contrast enhancement and vasculopathy, are important to differentiate ALSP from other disease entities. Together with biochemical, clinical and genetic findings, these characteristic imaging features can prevent a delay in diagnosis.

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Wei Ming Chua, [1]*MBBS, FRCR*, Shawn SX Kok, [1]*MBBS, FRCR*, Adeline SL Ng, [2]*MBChB (Edin), MRCP*, Wai Yung Yu, [1]*MBBS, MRCP, FRCR*

[1]Department of Neuroradiology, National Neuroscience Institute, Singapore
[2]Department of Neurology, National Neuroscience Institute, Singapore

Address for Correspondence: Dr Chua Wei Ming, Department of Neuroradiology, National Neuroscience Institute, 11 Jalan Tan Tock Seng, Singapore 308433.
Email: weiming.chua@mohh.com.sg

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