

Ankylosing Spondylitis in Singapore: A Study of 150 Patients and a Local Update

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Abstract

*This paper presents the results of a clinical study of 150 patients in Singapore with ankylosing spondylitis (AS) and reviews recent developments locally with regards to the disease. The patients were predominantly males (ratio 7:1) and Chinese (n = 147). The onset of disease is usually in the early twenties and there was a mean delay of 6.3 years before diagnosis was made. Peripheral joint involvement is common but apart from uveitis (17%), extra-articular manifestations are rare. AS patients have abnormal lipid profiles and lower bone mineral density compared to healthy controls. HLA*B2704 is the predominant subtype in our Chinese patients whilst HLA*B2706 was found only in healthy controls. Intensive group physiotherapy is beneficial for patients with spondyloarthropathy.*

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Key words: Bone mineral density, Dyslipidaemia, HLA B27 subtypes, Intensive physiotherapy, Peripheral joint involvement

Introduction

Back pain is a common but often self-limiting problem. However, it is important to recognise causes of chronic backache such as ankylosing spondylitis which are potentially disabling but treatable. Ankylosing spondylitis (AS) is the prototype disease in a group of disorders called seronegative spondyloarthropathy which includes psoriatic arthritis, Reiter's disease, reactive arthritis, juvenile onset spondyloarthropathy and spondylitis associated with inflammatory bowel disease. This group of inflammatory disorders share common features including a predominantly axial skeleton involvement, an association with HLA B27, familial aggregation and characteristic extra-articular manifestations e.g. uveitis.¹

In recent years, we have learned a great deal about AS in Singapore. This paper presents the clinical profile of 150 patients seen in our department and discusses the current state of knowledge about the disease and its management in Singapore.

Materials and Methods

One hundred and fifty patients with AS, who were seen in the Department of Rheumatology and Immunology, Tan Tock Seng Hospital, over a 5-year period (between April 1992 and April 1997), were included in the study. All the patients satisfied the New York criteria of definite AS.² The patients were interviewed to deter-

mine their clinical history and treatment, and a physical examination was performed. The case records and available radiographs were reviewed and all the data were entered into a standard protocol.

Results

The male to female ratio was 7:1 (131 men, 19 women). There was a predominance of Chinese patients (n = 147) with only 3 Malays. Table I shows the patients' characteristics and Table II lists the disease manifestations apart from back pain. The mean age of onset was the early twenties and the mean delay in diagnosis was 6.3 years. Peripheral joint and neck involvement were common whilst cardiac and pulmonary complications were rare. Three patients denied having any history of back symptoms. A family history of AS was present in 25 patients (17%) whilst the HLA B27 was positive in 73 of the 77 patients (95%) who had the test done. The treatment which the patients had is shown in Table III.

Discussion

Compared to our previous small cohort study of Singaporean Chinese patients with AS,³ there is a greater predominance of males in the present series. Although studies in Caucasian patients reported a male to female sex ratio closer to 3-4:1,^{4,5} racial differences may exist as the ratio was more than 11:1 in a Thai study⁶ and 16:1 in

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TABLE I: PATIENTS' CHARACTERISTICS

	Mean (years)	Range (years)
Age	33.5	15 to 75
Age of onset	23.3	8 to 52
Disease duration	10.3	1 to 45
Delay in diagnosis	6.3	0 to 36

TABLE II: DISEASE MANIFESTATIONS OF THE 150 PATIENTS EXCLUDING BACK PAIN

	Number	%
Peripheral joint involvement	100	67
Neck involvement	96	64
Anterior chest wall pain	61	41
Heel pain	36	24
Achilles tendinitis	41	27
Uveitis	26	17
Heart involvement*	1	< 0.01
Lung involvement	0	0

*Mitral valve prolapse

TABLE III: THERAPY WHICH PATIENTS HAD RECEIVED FOR THEIR DISEASE

	Number	%
NSAIDs*	134	89
Sulphasalazine	56	37
Methotrexate	2	0.01
Acupuncture	62	41
Traditional medicine	68	45

*Non-steroidal anti-inflammatory drugs .

the North Indians.⁷

The predominance of male patients in this disease may imply that sex-related factors such as hormones play a role in disease expression. Some studies have suggested an increased androgenicity to oestrogenicity in patients with AS compared to normal controls.^{8,9} In a study of our local male AS patients,¹⁰ lower levels of serum cortisol, dehydroepiandrosterone-sulphate, and prolactin but elevated levels of luteinising hormone, testosterone and follicular stimulating hormone were found in the patients compared to healthy controls. Except for serum cortisol, there was, however, no relationship between hormone levels and disease status (disease activity, functional ability and metrology).

It is notable that the prevalence of Malays in our patients was disproportionately lower than that of the general population¹¹ and there were no Indian patients at all. Racial differences in prevalence of AS and related spondyloarthropathies have been highlighted by Nasution et al,¹² who found that HLA B27 positive Chinese Indonesians have a greater relative risk of developing the disease compared to native Indonesians,

although the prevalence of HLA B27 in the latter group is more than twice that of the Chinese Indonesian. The reason for the absence of Indian patients in our series is not clear, because AS has been reported in Indians in South Asia.⁷ Selection bias is unlikely because our department is a tertiary referral centre for rheumatic diseases for the whole of Singapore. Whether the prevalence of AS in our local Indian population is truly low needs further investigation.

The presence of family history of AS was higher than our earlier smaller study³ but the prevalence of HLA B27 in the patients is similar to previous report.¹³ Further insight into ethnic differences in AS may be provided by recent studies of HLA B27 subtypes. Presently 11 subtypes (HLA B2701 to B2711) have been identified¹⁴ and it has been suggested that certain subtypes may not be associated with the disease.^{15,16} The predominant subtypes vary with different racial population and in Singaporean patients the main subtypes are HLA B2704 and B2705 whilst HLA B2706 is only found in our healthy controls with HLA B27.¹⁶

Our patients tend to have an early age of onset usually in their twenties. Reasons for the long delay in diagnosis may include the disease manifesting initially and perhaps mildly with only peripheral joint involvement which may contribute to delay in seeking treatment. It is also noteworthy that Mau et al¹⁷ have reported a long delay in radiographic changes of the disease which may have hampered the diagnosis in some patients.

Peripheral joint involvement is present in about two-thirds of the patients and the diagnosis of spondyloarthropathy should always be considered in a young male who presents with peripheral arthritis. Back pain occurred in all but three patients. The nature of inflammatory back pain is usually characteristic. In a patient with persistent localised vertebral pain, other complications such as osteoporotic vertebral fracture^{18,19} should be excluded. Osteoporosis is not an uncommon feature of long standing AS but recently it has also been recognised in patients with early disease.²⁰ In a study of local Oriental male AS patients without radiological evidence of spinal ankylosis, bone mineral density (BMD) measurements at the lumbar spine and neck of femur were found to be significantly lower compared to controls.²¹ The factors contributing to the lower BMD are not clear but there were no relationship between BMD and sex hormone status, disease severity or IL-6 and TNF- α levels.

The prevalence of uveitis in our patients is higher than previously thought²² and is in keeping with reports in Caucasian patients.^{22,23} Other extra-articular manifestations were uncommon in our patients. Only one patient had heart involvement relevant to the disease although the prevalence has been quoted to be as high as 10%.^{24,25} Abnormal lipid concentrations have been reported in

patients with rheumatic diseases.²⁶ For example, patients with active rheumatoid arthritis have lower levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) compared to healthy controls.^{27,28} In a recent study, 70% of our local AS patients had abnormal lipid profiles and of these patients, more than half had at least one other risk factor for coronary artery disease.²⁹ Compared to controls, the patients studied had significantly lower HDL levels and higher total cholesterol/HDL ratios. It has been suggested that there is an increased mortality in AS patients relative to the general population with excess death resulting from cerebrovascular and circulatory disease.³⁰ Whether dyslipidaemia in AS patients contribute to this excess mortality deserves further evaluation.

Majority of patients were on a non-steroidal anti-inflammatory drug (NSAID) at the time of the study and more than a third required a second line agent. Many of the patients had also tried acupuncture and traditional medicine; and it is possible that this may have contributed to a delay in their diagnosis and treatment. Fatigue is recognised as a significant problem in AS.³¹ Recently, low dose amitriptyline has been reported to be useful for alleviating fatigue as well as improve pain and stiffness scores.³² In our experience with local patients, low dose amitriptyline is a useful adjuvant therapy and is well tolerated.

Apart from drug treatment, physiotherapy plays an important role in the management of patients with AS. Intensive group physiotherapy has been reported to be beneficial³³ and this was introduced in Singapore in 1995 at Tan Tock Seng Hospital. A ten-day out-patient programme consisting of daily physiotherapy, hydrotherapy and patient education has since been conducted quarterly. Patients who underwent the programme showed improvement in terms of disease activity, functional ability and metrology.³⁴

In conclusion, AS in Singapore is a disease that predominantly affects young male adults, and is associated with peripheral joint involvement in the majority of patients. The long delay in diagnosis in many of the patients calls for the need to be aware of the disease amongst doctors and patients. AS is a potentially treatable disease and with proper therapy, gross spinal deformity may be preventable.

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