

Clinical features and outcomes of the adult Singapore IgA vasculitis cohort

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Dear Editor,

Immunoglobulin A (IgA) vasculitis (IgAV), formerly known as Henoch-Schönlein purpura, is an immune-mediated small vessel vasculitis that has a predilection to affect the joints, kidneys, gastrointestinal tract and skin.^{1,2} It is the most frequent systemic vasculitis in children, and while less common in adults, it is often associated with more severe disease. Geographical differences have been reported in the prevalence of adult IgAV including male predominance, gastrointestinal involvement and musculoskeletal complications among Europeans, and lower propensity for genitourinary involvement among Americans.³ The frequency of glomerulonephritis (referred to as IgAV nephritis) in adults is higher than in children and tends to present more severely, with approximately 10–30% of those affected eventually progressing to end-stage renal disease.⁴ There have been several published case series and cohort studies of adult IgAV from the Asia-Pacific region, predominantly from East and Central Asia, but with a paucity of reports from Southeast Asia.^{5,6}

We hereby report our findings from the Singapore IgA Vasculitis Cohort (SIgAVasC), which is a retrospective case records review of consecutive adult patients tagged ≥ 21 years hospitalised in Tan Tock Seng Hospital, a tertiary adult hospital, with the main diagnosis of IgAV during the study period between 2007 and 2020. Included patients fulfilled the 2010 European Alliance of Associations for Rheumatology/Paediatric Rheumatology International Trials Organisation/Paediatric Rheumatology European Society classification criteria for IgAV.⁷ Demographic characteristics, clinical features, therapies and outcomes of all patients were analysed. Ethics approval was granted by National Healthcare Group Domain Specific Review Board (2018/00721).

The SIgAVasC comprised 136 IgAV patients: median (interquartile range) age 43 (29–57) years, with 23 (16.9%) aged ≥ 65 years at the time of incident admission. Majority were female (74, 54.4%), 91 were Chinese (66.9%), 18 (13.2%) of other ethnicities, 14

(10.3%) Malays and 13 (9.6%) Indians. The median (IQR) time from initial symptom onset to presentation was 14 (7–31) days. Disease manifestations comprised cutaneous (136, 100.0%), renal (57, 41.9%), gastrointestinal (50, 36.8%) and articular (19, 14.0%). Preceding fever (5, 3.7%) and sore throat (13, 9.6%) were uncommon. Microscopic haematuria (41, 30.1%) and proteinuria (14, 10.9%) were the most common renal manifestations. Renal function during the incident admission was as follows: 8 (5.9%) patients had estimated glomerular filtration rate (eGFR) of < 30 mL/min/1.73m²; 5 (3.7%) had an eGFR 30–59; and 106 (77.9%) had an eGFR ≥ 60 . There were 25 (18.4%) with underlying hypertension, and 18 (13.2%) with diabetes mellitus. Among 9 (6.7%) patients who underwent renal biopsy, 7 (77.8%) had histological features of crescentic glomerulonephritis and 5 (55.6%) had segmental sclerosis. There were 2 (1.5%) deaths during the incident admission. Among 117 patients with at least 1 year of follow-up data, 5 (4.3%) had an eGFR < 30 , 8 (6.8%) had an eGFR in the range 30–59, and 76 (65.0%) had an eGFR of ≥ 60 mL/min/1.73m². One patient developed kidney failure requiring dialysis within a year from incident hospitalisation.

Immunosuppressive therapy comprised prednisolone/methylprednisolone (61, 44.9%), intravenous hydrocortisone (31, 22.9%), oral cyclophosphamide (5, 3.7%) and azathioprine (4, 2.9%). One year after inpatient discharge, 15/117 (12.8%) patients required non-corticosteroid immunosuppressive therapies to maintain disease remission (azathioprine [14, 12.6%], mycophenolate mofetil [2, 1.7%], cyclophosphamide [2, 1.7%] and ciclosporin [1, 0.9%]). The remaining patients achieved drug-free remission. Table 1 summarises the characteristics of the SIgAVasC at incident admission.

Systemic or organ-specific autoimmune disease was diagnosed prior to incident admission in 2 (1.5%) patients who had rheumatoid arthritis and systemic lupus erythematosus with antiphospholipid syndrome. Malignancy was diagnosed in 4/136 (2.9%) prior to or during incident admission, comprising malignant

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Table 1. Characteristics of SIgAVasC cohort at time of incident admission.

Demographics (N=136)	
Female, no. (%)	74 (54.4%)
Age at incident admission, years	
Mean (SD)	44.4 (17.4)
Median (IQR)	43 (29–57)
Age group, no. (%)	
21–44 years	72 (52.9%)
45–54 years	23 (16.9%)
55–64 years	18 (13.2%)
65–74 years	17 (12.5%)
≥75 years	6 (4.4%)
Ethnicity, no. (%)	
Chinese	91 (66.9%)
Malay	14 (10.3%)
Indian	13 (9.6%)
Others	18 (13.2%)
Median no. of days from symptoms onset to admission, no. (IQR)	14 (7–31)
Manifestations	
Cutaneous, no. (%)	136 (100%)
Constitutional, no. (%)	58 (42.6%)
Musculoskeletal, no. (%)	75 (55.1%)
Renal, no. (%)	57 (41.9%)
Respiratory, no. (%)	38 (27.9%)

neoplasm of the stomach, lung, nasopharynx and thyroid. One additional patient developed prostate cancer from the time of incident admission.

The demographic profile of our adult patients with IgAV was similar to that reported in other Asian series, differing in that our series had marginally more females.^{5,6} Extracutaneous involvement occurred in less than 50% of the SIgAVasC, with only 47% requiring systemic corticosteroids (CS) and 5% requiring non-CS induction immunosuppressive therapy (cyclophosphamide or azathioprine) at the incident admission. This observation reflects the presence of both severe (major organ involvement) and non-severe phenotypes (skin-limited with/without joint involvement) in our cohort, which differs from

Table 1. Characteristics of SIgAVasC cohort at time of incident admission. (Cont'd)

Manifestations	
Gastrointestinal, no. (%)	50 (36.8%)
Neurological, no. (%)	12 (8.8%)
Mucous membranes/eye, no. (%)	18 (13.2%)
Cardiovascular, no. (%)	6 (4.4%)
Ear, nose and throat, no. (%)	6 (4.4%)
Others, no. (%)	4 (2.9%)
Treatment	
Any glucocorticoid, no. (%)	
Prednisolone (including methylprednisolone), no. (%)	64 (47.1%)
Dexamethasone, no. (%)	61 (44.9%)
Hydrocortisone, no. (%)	1 (0.7%)
Azathioprine, no. (%)	31 (22.8%)
Cyclophosphamide, no. (%)	4 (2.9%)
Methotrexate, no. (%)	5 (3.7%)
Colchicine, no. (%)	1 (0.7%)
NSAIDs, no. (%)	14 (10.3%)
Haemodialysis, no. (%)	49 (36.0%)
Plasmapheresis, no. (%)	2 (1.5%)
Mortality	
Deaths during incident hospitalisation, no. (%)	2 (1.5%)

IQR: interquartile range; NSAIDs: non-steroidal anti-inflammatory drugs; SD: standard deviation; SIgAVasC: Singapore IgA Vasculitis Cohort

the majority of published adult series, where most patients were described as having a severe phenotype, predominantly attributed to renal involvement. The use of non-CS immunosuppressive therapies 1 year after the incident admission, predominantly azathioprine, reflects the mild-to-moderate severity of patients with extracutaneous involvement in a sub-population of the SIgAVasC.

Renal involvement was the most common extracutaneous involvement, similar to most Asian and non-Asian cohorts.^{5,6} However, the majority in our cohort had mild renal involvement in the form of asymptomatic haematuria and proteinuria, with none requiring long-term renal replacement therapy for up to 5 years following incident admission. Only 6.7% required renal

biopsy, of which the most common histological finding was crescentic glomerulonephritis. The presence of segmental sclerosis reflected underlying chronic kidney disease (9.7%) in the Singapore cohort—contributed by underlying age, hyper-tension and diabetes mellitus. Adult IgAV-related nephritis patients with more crescents have more severe renal manifestations and worse treatment responses, whereas the proportions of crescents were not associated with higher risks for end-stage renal disease (ESRD) or 50% decline in renal function. A more suitable pathological classification standard is needed to predict renal prognosis.⁸ The modest severity of renal involvement in our cohort contrasts with the higher prevalence of 63% in another report.⁸ IgAV associated with malignancy was uncommon in our cohort, similar to the case reports published in the literature on solid organ and haematological cancers.⁹

The treatment of adult IgAV ranges from supportive therapy in mild disease to definitive therapies including CS and non-CS immunosuppressive therapies, biologics (e.g. rituximab), intravenous immunoglobulins and plasma exchange depending on disease severity.^{10,11} In contrast to paediatric IgAV where there has been an attempt at creating consensus guidelines on treatment, there have not been any similar consensus guidelines for adults.

The majority of our adult IgAV cohort did not require long-term immunosuppressive therapy; had generally good renal outcomes at 1 year with only 1 patient requiring renal replacement therapy; and had a low incidence of progressive chronic kidney disease and mortality. The incidence of a concurrent neoplastic trigger was low. The SIgAVasC comprised a heterogeneous cohort of adults with IgAV, with a range of non-severe to severe phenotypes and as reflected by the varying types of immunosuppressive therapies used. End-organ damage, in particular chronic kidney disease was overall uncommon.

Ethics statement

Ethics approval was granted by NHG DSRB (2018/00721).

Declaration

The authors declare there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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