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IgA Vasculitis in Adults & Outcome - A Retrospective Observational Study from a Tertiary Care Centre in South India

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Abstract: ***Adult Ig A vasculitis is rare and has a heterogeneous presentation with more severe systemic involvement than childhood onset IgA vasculitis. It is characterized by severe gastrointestinal and renal manifestations along with atypical skin lesions. Management of adult IgA vasculitis is considered difficult as there is no correlation between initial presentation and long term renal outcome. There are limited studies on adult IgA vasculitis from India. The objective of our study was to describe epidemiology, clinical profile, laboratory parameters and the outcomes in the South Indian cohort presenting with adult IgA vasculitis.***

Keywords: Adult Ig A vasculitis, systemic involvement, outcome

1. Introduction

Ig A vasculitis formerly known as Henoch - Schonlein purpura vasculitis, is the most common systemic vascultitis in childhood. It is usually seen between the age group of 4 to 7 years. The annual incidence varies from 3 to 26 per 100000 children. Ig A vasculitis is rare in adults, with an annual incidence 0.1 - 1.8 per 100000 persons[1, 2]. It is characterized by cutaneous, gastrointestinal, musculoskeletal and renal manifestations.

Previously IgA vasculitis was thought to be a childhood disease and was underdiagnosed in adults. There are characteristic differences that exist between children and adults with vasculitis. The disease is more frequent in males with male: female ratio being 1: 5[3]. Adult Ig A vasculitis presents with more severe multisystem involvement. The incidence of renal involvement is more (45 - 85%) in adult Ig A vasculitis as compared to (20 - 54%) in children [3.] Adult Ig A vasculitis with renal and cutaneous involvement is more prone for relapses[4]. It has a poor long term outcome in comparison to children. Aggressive therapy is needed for adult IgA vasculitis.[4]

Adult IgA vasculitis presents with heterogeneous features with varying severity. Since this disease can be polyphasic in adults[5], it is challenging to treat organ threatening manifestations in adults. There are limited studies on adult IgA vasculitis from India. This study is performed in Indian patients with adult IgA vasculitis to describe the epidemiology, clinical profile, laboratory parameters and outcome in a South Indian cohort.

2. Methodology

A retrospective observational study of adult IgA vasculitis patients was conducted in SRIHER Chennai in a South Indian cohort over 4 years. Patients (>18 years) who fulfilled the EULAR/PRINTO/PRES (Ankara, 2008) [6] criteria were included in the study. Patients with incomplete data, pregnancy, lost to follow up, medication non adherence were excluded. Other causes of vasculitis were also ruled out. Demographic data, various clinical presentations, comorbities, laboratory parameters, treatment and outcomes were described in this cohort.

3. Results

35 patients were included in our study and were followed up for a mean duration of 2.8 years. The mean age at presentation was 36 years. Male to female ratio was 1.3: 1. The most common clinical presentation was cutaneous followed by constitutional (fever), gastrointestinal and articular manifestations, 100%, 70%, 65%, 50% respectively. The most common comorbidities seen in our cohort were diabetes mellitus (10, 31%), hypertension (3, 10%) and hypothyroidism (4, 13%).

In our study, the most common cutaneous feature was palpable purpura (26, 74%) FIGURE 2. It was a non blanching purpura seen predominantly over both lower limbs. It was associated with pruritus and burning in nature. Other skin findings seen were in the form of maculopapular rash (2, 5%), multiple ulcers (2, 5%) FIGURE 1, blisters/ haemorrhagic bullae (2, 5%) FIGURE 4 and pustules (2, 5%). One patient had gangrene of both lower limbs (FIGURE 3). Constitutional feature in form of fever was present in 70% of patient in our study.

Gastrointestinal manifestation were seen in 68%. The most common gastrointestinal presentation was abdominal pain and melena. It was present in 20% of patients, mainly in epigastric region and was burning in nature. Diarrhoea was another manifestation seen in 17% of patients. Other findings were abdominal pain (17%) in combination with nausea/ vomiting and abdominal pain (14%). It was watery in consistency. Upper/ lower gastrointestinal endoscopy was done in 31%. The most common finding in upper gastrointestinal endoscopy was duodenitis (15%) and pan gastritis (15%). In lower gastrointestinal endoscopy, the predominant finding showed ulcers in ileal mucosa (25%). Fatty liver was the most common finding in ultrasound abdomen. Computed tomography scan abdomen was suggestive of thickening of ileum and jejunum loops which were observed in three patients. Ileal nodularity was seen in two patients on imaging. This patient was subjected to ileal biopsy which showed leucocytoclastic vasculitis.

Renal involvement was present in 50 % of patients in our study. The most common renal involvement was in the form of nephrotic range proteinuria (26 %) followed by nephritic syndrome (11%). Haematuria was present in 8% of patients. Deranged renal function test was seen in 5% of patients and one patient needed maintenance haemodialysis. One patient underwent renal biopsy which was suggestive of IgA nephropathy (M1E1T1S0).

In our cohort, polyarthalgia in 8 patients (22%) was the characteristic feature seen. The second common articular feature was oligoarthritis which was observed in 17 % of patients. It mainly consisted of large joint (knee joint) involvement which was symmetrical in nature. Polyarthritis was present in 8% involving knees, elbows and ankle joints.

Anaemia and thrombocytosis were seen in 54% and 20% patients respectively. White cell count was elevated in 46% of patients. Acute phase reactants (ESR, CRP) were raised in all patients (100%). Nine patients were subjected to skin biopsy. Leucocytoclastic vasculitis was present in six patients (out of nine) FIGURE 5. Serum Ig A was elevated in 7 out of 10 patients (70%).

All patients were followed up for a total of 4 years. All patients received oral steroids (0.5 - 1 mg/kg). Three patients were given pulse steroids of 1gm methyl prednisolone for 3 days in view of nephrotic and nephritic range proteinuria and resistant haemorrhagic bullous lesion. After pulse steroid therapy, patients were switched to oral steroid 1 mg/kg /day. MMF was given in 20 % of the patients. One patient was given colchicine in view of cutaneous involvement. Another patient was given azathioprine in view of severe cutaneous involvement (bullae, ulcers).

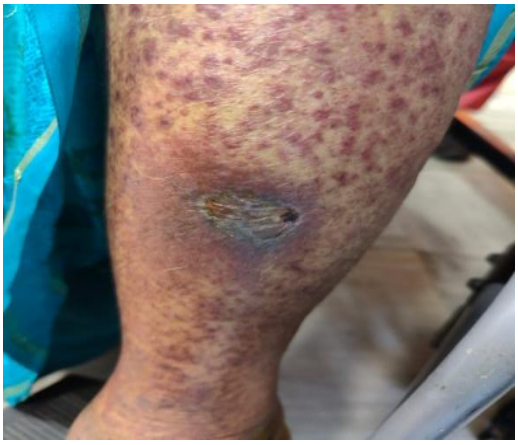

Figure 1: Palpable purpura with ulcer

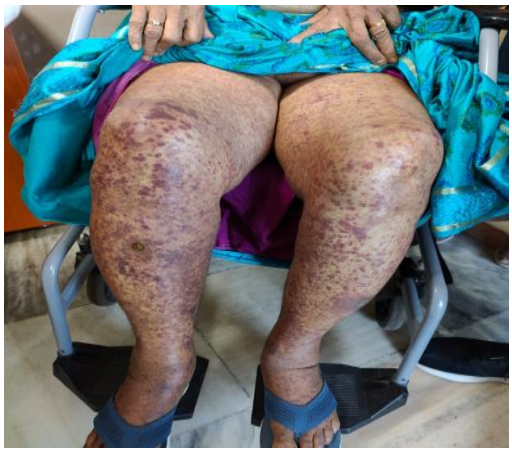

Figure 2: palpable purpura

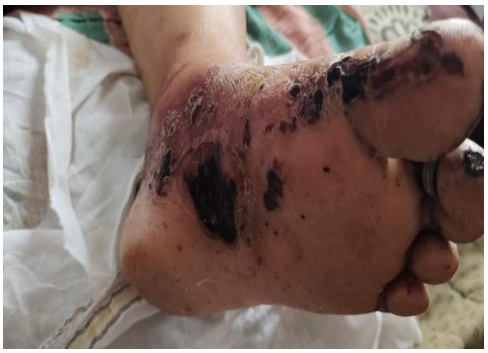

Figure 3: Gangrene lesion

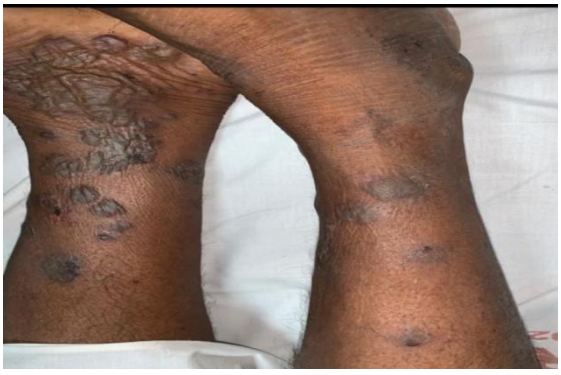

Figure 4: Haemorrhagic bullae

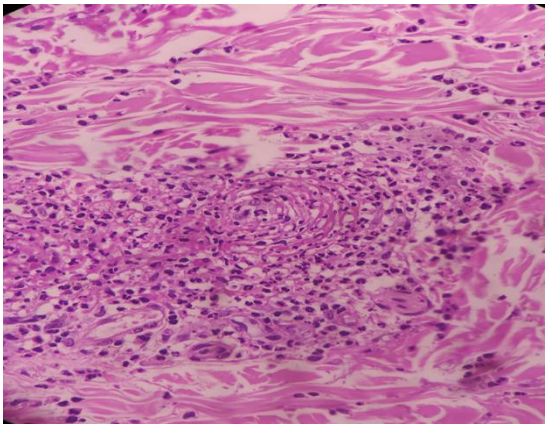

Figure 5: Skin histopathology - leucocytoclastic vasculitis

Table 1

Characteristics	N (35)	Percentage (%)
DEMOGRAPHIC DATA		
Mean age	36.96 yrs	-
Male: Female	1.3: 1	-
CLINICAL FEATURES		
Constitutional (Fever)	24	68%
Cutaneous	35	100%
Maculopapular	2	5%
Palpable purpura	26	74%
Multiple ulcers	2	5%
Blisters & Haemorrhagic bullae	2	5%
Pustules	2	5%
Gangrene	1	2%
Musculoskeletal	17	48%
• Polyarthralgia	8	22%
• Oligoarthitis	6	17%
• Polyarthritis	3	8%
Gastrointestinal	24	68%
Abdominal pain	6	17%
Abdominal pain + Nausea /vomiting	5	14%
Abdominal pain + Melena	7	20%
Diarrhoea	6	17%
Renal	18	50%
Nephrotic range proteinuria	4	11%
Sub Nephrotic range proteinuria	9	26%
Nephritic	3	8%
RPGN	2	5%
Comorbidities		
Diabetes mellitus	12	34%
Hypertension	4	11%
Hypothyroidism	4	11%
Secondary infection	9	26%
Sepsis	4	11%
Urinary tract infection	4	11%
Upper respiratory tract infection	1	2%

Table 2

Laboratory Parameters	N (35)	Percentage (%)
Anaemia	19	54%
Leucocytosis	16	46%
Thrombocytosis	7	20%
Elevated inflammatory markers		
ESR	35	100%
CRP	35	100%
Elevated renal parameters	2	5%
Elevated SIgA levels	7/10 (70%)	-
Abdominal Imaging (bowel wall thickening)	4/4	23%
Upper GI endoscopy (Erosive gastritis) erosive duodenitis	5/5	-

Treatment	N (35) %	Indication
STEROIDS	35 (100%)	GI/ MSK
Oral steroid	32 (75%)	Extensive Skin rashes
Pulse steroid followed by oral steroids	3 (10%)	Nephrotic range proteinuria
		Resistant haemorrhagic bullous lesion
		RPGN
Mycophenolate mofetil (MMF) (+ steroids)	7 (20%)	Severe GI involvement
		Persistent proteinuria and hematuria
		Refractory skin lesions
Azathioprine	1 (2%)	Refractory skin lesions
Colchicine	1 (2%)	Refractory Skin lesions

4. Discussion

There are only few studies on adult IgA vasculitis from India. Our study comprised of 35 patients with a mean age of 36.96 years and female: male 1: 1.3. This ratio is similar to the studies mentioned in the table 4 [7, 8].

Table 4

Study data	Our study (2024)	Ramnath et al (2017)	Garcia et al (2002)	Uppal et al (2006)
N	**35**	**30**	**31**	**20**
Mean age	**36**	**33 ± 12.1 years**	44 ± 17 years	**32.1 +/ - 11.7**
Male: Female	**1.3: 1**	**1.5: 1**	2.4: 1	0.5: 1
Cutaneous	**33 (100%)**	**30 (100%)**	**31 (100%)**	20 (100%)
Musculoskeletal	15 (75%)	27 (90%)	20 (65%)	11 (55%)
Gastrointestinal	**22 (66 %)**	**20 (66%)**	26 (84%)	11 (55%)
Abdominal pain	**18 (54%)**	**19 (63%)**	26 (84%)	8 (40%)
Melena	**07 (21%)**	**8 (26%)**	13 (42%)	3 (15%)
Diarrhoea	06 (18%)	-	-	5 (25%)
Renal	**16 (48%)**	18 (60%)	18 (54%)	18 (90%)
Nephrotic range proteinuria	4 (12%)	6 (20%)	6 (26%)	6 (30%)
Sub Nephrotic range proteinuria	**8 (24%)**	16 (53%)	**8 (26%)**	23 (75%)
Nephritic	3 (9%)	10 (33%)	-	17 (85%)
RPGN	**2 (5%)**	**1 (3%)**	4 (12%)	2 (10%)
Elevated Serum IgA	10 (30%)	20 (66%)	5/11 (46%)	-
Abdominal Imaging (bowel wall thickening)	4/4 (23%)	10 (34%)	-	-
Skin biopsy Leucocytoclastic vasculitis (LCV)	6/9 (66%)	20 (66%)	-	-

The most common clinical feature was palpable purpura (100%) predominantly over the lower part of both legs which was consistent in all studies[7, 8]. It was the first presenting clinical feature in adult IgA vasculitis. In our study multiple ulcers, blisters/ haemorrhagic bullae and pustules were seen in 5% each respectively. We observed gangrene of lower limbs in one patient, a very rare finding in IgA vasculitis. Atypical skin lesions reflect a more severe course of disease[11]. One patient with pustules also had renal involvement (sub nephrotic proteinuria). Atypical lesions like blisters, haemorrhagic bullae and pustules were seen in 35% [9, 10]. Some bullous lesions lead to necrosis resulting in scarring and/or hyperpigmentation but they commonly resolved within a few weeks[11].

In our study, we noticed atypical skin lesions in association with severe extra cutaneous features (renal, gastrointestinal) comparable to the study by Tatiana Koleva et al[11]. All patients underwent skin biopsy with the consistent finding of IgA vasculitis. Serum IgA was elevated in two patients with atypical lesions.

The second most common clinical feature was gastrointestinal which predominantly consisted of nausea/ vomiting and melena in 17 % and 20% respectively, as opposed to the study by Ramnath et al[6, 12]. Other gastrointestinal features were abdominal pain with melena (20%) and diarrhoea (17%) [12].

In our study the most finding in upper gastrointestinal endoscopy was duodenitis and gastritis[12]. We observed ileal nodularity in two cases and ulcers in small intestines predominantly ileum and jejunum (25%). The small bowel and especially the duodenum were most often affected in multiple case series. The spectrum of endoscopic findings was usually, irregular, ulcerating, nodular lesions or hematoma - like protrusions in the duodenum in the study done by Dharmesh Kaswala et al [12].

25 % of our patients with gastrointestinal features had renal involvement. It consisted of proteinuria – nephrotic, sub nephrotic and haematuria in 8% each respectively. Dharmesh Kaswala et al concluded that adults igA vasculitis was associated with more frequent gastrointestinal involvement and severe kidney disease[12].

The other most common manifestation observed was constitutional features which mainly presented as low grade fever (68%) lasting for less than one week as opposed to the study by Castaneda S [13] where only 20 % patients presented with fever.

Musculoskeletal features were seen 48% in our study. It was not comparable to the below mentioned studies (table 4). The most common manifestations were polyarthralgia (22%) followed by oligoarthritis (17%) and polyarthritis (8%) respectively. It mainly comprised of large joints, predominantly lower limbs (knees, ankles) as compared to upper limbs. Porsha Roache et al's concluded that arthralgia or arthritis occurred in 75% of their patients.

Renal manifestations were present in 18 patients (50%). It was comparable to the study done by Ramnath et al[6].45% of patients had renal involvement at diagnosis in a Spanish population[15]. The most common renal feature in our study was sub nephrotic proteinuria which was seen in 9 patients (26%), as was observed by Garcia et al.7 Similarly nephrotic and nephritic syndrome was present in a quarter of patients in the Spanish cohort[14].

Rapidly progressive glomerulonephritis was seen in two patients (5%) which was similar to the study by Ramnath et al [6]. One patient underwent renal biopsy which suggested IgA nephropathy (M1E1T1S0). Severe renal involvement was seen in 5% of patients at baseline in our study, similar to the study by Hocevar A[15].

Renal function was deranged in two patients for which they underwent haemodialysis as opposed to the study by Calvo - Río V where renal insufficiency was observed in 31% [16]. We observed severe renal impairment in elderly population with nephrotic range proteinuria[17]. Giario concluded that age over 65 years, nephrotic proteinuria, acute kidney injury, and hematuria were usually associated with the worst prognosis. Serum IgA level was elevated only in only 16 % of our patients with renal involvement. Similarly Calvo - Río V et al. reported that increase in serum IgA level did not correlate with renal involvement[16].

Skin biopsy was done in 10 patients out of which 7 (70%) showing leucocytoclastic vasculitis with IgA deposits in vessel walls was comparable to the study by Ramnath et al[6]. However most cases of IgA vascultitis in adults are positive for IgA deposition. Though, few cases yield a negative DIF due to delay in skin biopsy[18].

Elevated serum IgA levels were found in 70% of adult patients with IgA vasculitis in our study. It was comparable to the study by Ramnath et al[6]. Serum IgA levels were elevated in severe cutaneous lesions and extra cutaneous features in the form of renal and gastrointestinal involvement, but do not always correlate with disease activity or severity [6].

All patients received steroids (1 mg/kg of body weight) followed by gradual tapering over 3 months. Three patients got intravenous pulse steroids followed by oral steroids for refractory skin lesions and severe renal involvement[20]. Mycophenolate mofetil was received by 18 % of patients in view of refractory skin lesions, persistent proteinuria and gastrointestinal involvement. One patient treated with azathioprine and another patient treated with colchicine for refractory skin lesions[20]. There are only few studies which have discussed treatment and outcome of IgA vasculitis[20].

Our 35 patients were followed up for a mean duration of 2.8 years. Follow up was scheduled every 2 week, 3 months, 6 months and there after annually. Relapses were found 20 % of patients.2 elderly patients had persistent renal dysfunction for which they underwent haemodialysis. The remaining five patients were having persistent and refractory skin lesions. Alojzija Hocevar et al reported 15 % relapses in igA vascultitis[15]. Advanced age (≥65 years) and proteinuria are independent prognostic factors for a decline in renal function[19].

IgA vasculitis is typically a self - limited illness that demonstrates an excellent prognosis in patients without renal involvement. Poor prognosis was found in elderly patient, nephrotic range proteinuria, haematuria and acute renal injury in our study which was similarly concluded by Garia et al. Treatment of severe organ involvement is complex and difficult and remains controversial. No evidence exists for improved long term outcome with steroids and immunosuppresants[20].

5. Conclusion

1) Cutaneous features were universal followed by constitutional and gastrointestinal features.
2) Atypical severe cutaneous lesions were seen with severe renal involvement
3) IgA vasculitis was associated with severe gastrointestinal and renal manifestations.
4) Elderly patients had severe renal involvement and were on renal replacement therapy.
5) S IgA when elevated, correlated with severe cutaneous, gastrointestinal and renal involvement.
6) Steroids and immunosuppressants were required for severe organ involvement.

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