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Case Report

Co-occurrence of Immunoglobin A Vaculitis and Immunoglobulin A Nephropathy Suggesting Common Pathogenesis: A Case Report

Sweta Mishra[1*], **Lipsa Priyadarshini**[1], **Subal Kumar Pradhan**[1]

1. Division of Paediatric Nephrology, Department of Paediatrics, SVP Post Graduate Institute of Paediatrics & SCB Medical College, Cuttack, India.

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Corresponding Author:
Sweta Mishra
Address: Division of Paediatric Nephrology, Department of Paediatrics, SVP Post Graduate Institute of Paediatrics & SCB Medical College, Cuttack, India.
E-mail: mswetamishra112@gmailcom

ABSTRACT

Immunoglobulin A (IgA) vasculitis, also known as Henoch-Schönlein purpura, and IgA nephropathy are two different diseases of the same clinical spectrum. They may occur sequentially in the same patient and exhibit overlapping clinical presentations, immunological characteristics, and pathological features. The clinical presentation and the degree of severity are different for individual cases. In this study, we report a girl who initially presented with Henoch-Schönlein purpura, and on follow-up, renal biopsy was suggestive of IgA nephropathy. Accordingly, this presentation suggests the common pathogenesis of both diseases and the need for long-term follow-up of patients with Henoch-Schönlein purpura.

Keywords: Henoch–Schönlein purpura (HSP), HSP nephritis, Immunoglobulin A nephropathy (IgAN), IgA vasculitis

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Introduction

Immunoglobulin A (IgA) vasculitis is a small vessel vasculitis mediated by galactose-deficient IgA with a predilection for skin, joints, gastrointestinal tract, and kidney. To the best of our knowledge, there are currently no diagnostic criteria for IgA vasculitis. We follow the classification criteria defined by the European League Against Rheumatism (EULAR), Paediatric Rheumatology International Trial Organisation (PRINTO), and Paediatric Rheumatology European Society (PRES) [1]. This disorder includes the presence of palpable purpura and one of the following criteria: diffuse abdominal pain, arthritis or arthralgia, renal involvement (haematuria/proteinuria) and a renal biopsy showing predominant IgA deposition in immunofluorescence microscopy [2]. On the other end of the spectrum, IgA nephropathy is the most common chronic glomerular disease in childhood. Usually, there is an absence of any systemic disease with predominant IgA deposition in renal histopathology. There are unusual cases of IgA nephropathy in literature, which subsequently develop a purpuric rash and systemic features. In this study, we report a girl who presented with recurrent episodes of purpuric rash and subsequently developed hypertension, sub-nephrotic range proteinuria, gross haematuria, and renal biopsy suggestive of IgA nephropathy.

Case Presentation

A 12-year-old girl presented with erythematous pruritic rashes over the extensor surface of both lower limbs (Figure 1) with gross haematuria and haematochezia. She had a similar history of recurrent episodes of rash involving both lower limbs for the last two years. The rash was not associated with fever, joint pain, or abdominal pain. On examination, the patient had stage 1 hypertension with some pallor but no organomegaly or lymphadenopathy. Urine analysis revealed haematuria and significant proteinuria. Serum creatinine was 4.9 mg/dL (reference: 0.3-0.7 mg/dL) along with blood urea of 127 mg/dL (reference: 5-18 mg/dL). Serum albumin was 3.9 g/dL (reference: 3.6-5.2 g/dL). Meanwhile, serum cholesterol was 252 mg/dL (Reference: <170 mg/dL). Anti-streptolysin O titer was negative. Meanwhile, antinuclear antibodies were negative and serum complements (C3 and C4) levels were normal. Persistent proteinuria with gross haematuria with normal complements and negative anti-streptolysin O prompted do renal biopsy. Renal biopsy showed global tuft sclerosis in 4/8 (50%) glomeruli, secondary segmental sclerosis in 4/8 (50%) capillary tuft and a mild increase in mesangial matrix/cellularity in viable glomerular areas along with patchy acute tubular injury was noted and a moderate increase in tubulointerstitial chronicity was observed suggestive of IgA nephropathy (Figure 2). Immunostaining pattern indicated IgA deposits (3+ staining) in mesangium and granular C3 (1+) deposits and the mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S) and tubular atrophy/interstitial fibrosis (T) and (fibro)cellular crescents (C) scores (Oxford classification of IgA nephropathy)=M0, E0, S1, T1, C0. Immunostaining patterns were observed: Ig A=3+ mesangial (granular/confluent); IgG=negative; IgM=Negative; C3=1+ mesangial; C1q=negative; kappa light chain= 1+ mesangial; lambda light chains=3+ mesangial. Given proteinuria and hypertension, she was

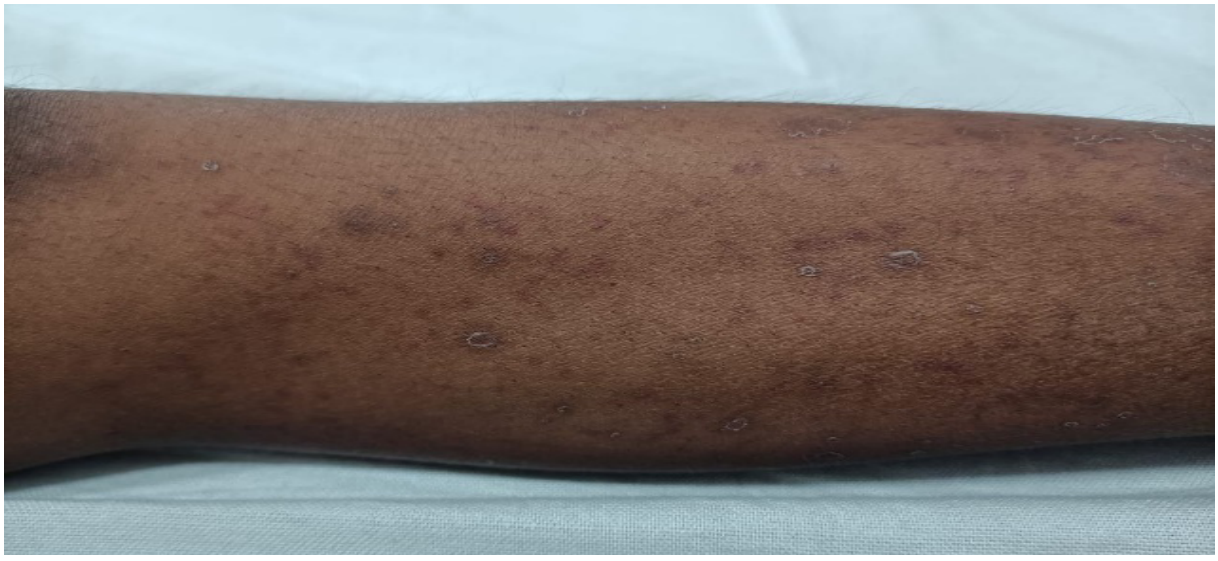

Figure 1. Erythematous rash over the extensor surface of left lower limb

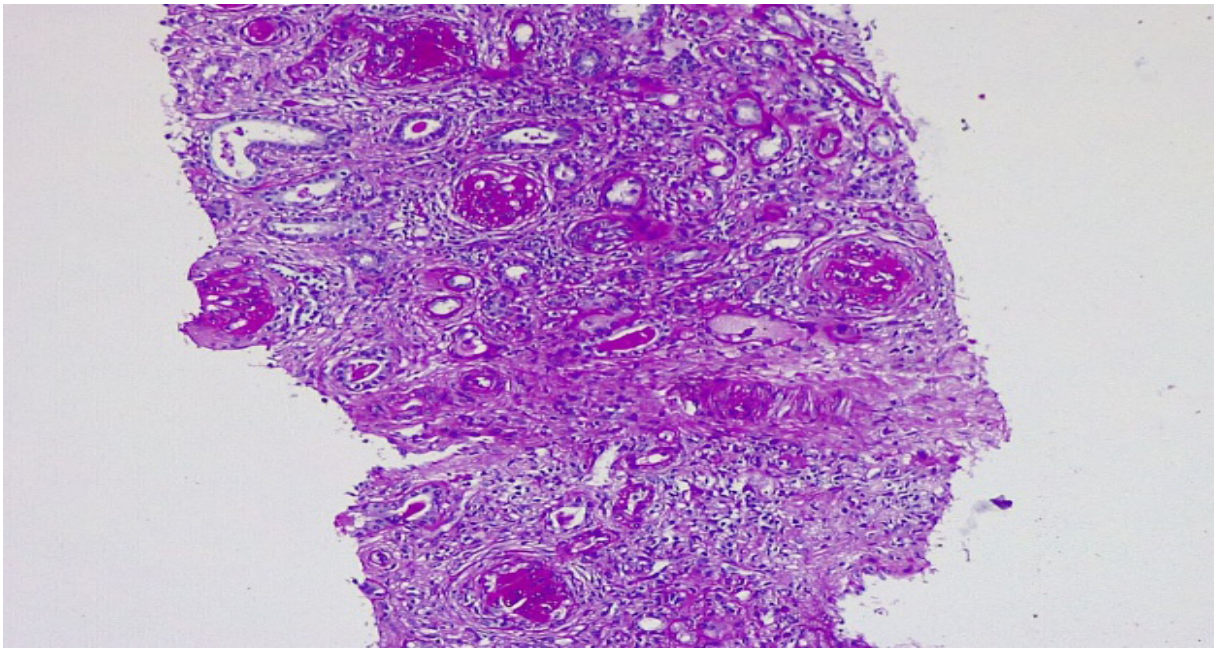

Figure 2. LM showing global tuft sclerosis in glomeruli, mild increase in mesangial matrix/cellularity

treated with angiotensin-converting enzyme inhibitors. However, subsequently, the patient progressed to chronic kidney disease and is on regular follow-ups.

Discussion

The global incidence of Henoch–Schönlein purpura (HSP) is 10 to 20 cases per 100000 children annually. Almost 20%-55% of patients presenting with HSP have renal involvement [10]. Various clinical presentations of HSP nephritis can range from haematuria (88.6%), haematuria with sub nephrotic proteinuria (66.7%), nephrotic syndrome (13.3%), and acute nephritic syndrome (8.9%) [11, 12]. Both diseases have a predilection for the male sex, are usually preceded by an upper respiratory tract infection, and are also associated with increased serum Ig A levels (Table 1).

Table 1. Characteristics of IgA nephropathy and of Henoch–Schönlein purpura vasculitis

Similarities Between IgAN and Henoch–Schönlein Purpura Vasculitis		
Clinical features	More common in males Haematuria after an upper respiratory tract infection (synpharyngitic) Can progress to End-stage kidney disease	
Histology	Mesangial IgA_1 deposits	
IgA	Abnormal glycosylation pattern of IgA_1 Raised levels of plasma IgA	
Differences Between IgAN and Henoch–Schönlein Purpura Vasculitis		
Clinical features	IgAN	Henoch–Schönlein purpura nephritis
Extrarenal symptoms	Rare	Usually, present
Age of onset	More common in adolescents or adults	3-15 years
Histology	Mesangial proliferation, sclerosis and renal tubular atrophy	Neutrophil infiltration, endocapillary proliferation and crescent formation
Treatment modalities	Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers; Corticosteroids and cyclophosphamide in severe cases	
Outcome	Can progress to ESKD	

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Literature Review				
Authors	**Year and Place of Publication**	**Type of Study**	**Clinical Manifestation**	**No. of Cases**
Thorner et al. [4]	(1986) International journal of pediatric nephrology	Case report	A female child had an attack of HSP with no renal dysfunction at 4 years of age from which she recovered with conservative management. At the age of 15 years, she developed repeated bouts of gross haematuria and proteinuria, and a renal biopsy done 3 years later showed MPGN with mesangial deposits of IgA.	1
Hughes et al. [5]	(1988) Pediatric nephrology	Case report	An 8-year-old Caucasian male child presented with gross haematuria and raised serum IgA and renal biopsy consistent with IgAN. Then, 2 years later he developed pain abdomen, rectal bleeding, gross haematuria, and classic purpuric rash of HSP.	1
Ravelli et al. [6]	(1996) Nephron	Case report	A 10-year-old male child presented initially with biopsy-proven IgAN and 11 years later developed HSP.	1
Chishiki et al. [7]	(2010) Fukushima journal of medical science	Case report	A 10-year-old Japanese female child was identified with proteinuria and haematuria by school urinary screening. The 1st renal biopsy showed MPGN with immunofluorescent findings consistent with IgAN. Meanwhile, 5 years later she developed abdominal pain with a classic purpuric rash of HSP. The 2nd renal biopsy showed diffuse mesangial proliferation with crescent formation.	1
Yamabe et al. [8]	(2019) Case report in nephrology (periodical)	Case report	A 20-year-old male presented with proteinuria and haematuria and was diagnosed with IgAN. At 35 years of age, he noticed purpura in his lower extremities.	1
Weerasooriya et al. [9]	(2020) Asian journal of pediatric nephrology	Case report	A 5-year-old female child presented with acute glomerulonephritis and the biopsy showed acute diffuse proliferative IgA nephritis with crescents then 5 years later she developed HSP and proteinuria.	1

Abbreviations: IgAN: Immunoglobulin A nephropathy; MPGN: Membranoproliferative glomerulonephritis; HSP: Henoch-Schönlein purpura.

Pathogenesis of HSP is related to an increased production of abnormally glycosylated IgA_1 which is not sufficiently cleared by the liver and leads to the formation of IgA macromolecules accumulating in the circulation. These macromolecules get deposited in the vessel wall and glomerular mesangium. The renal biopsy suggests electron-dense deposits of IgA in the mesangium [13]. IgA nephropathy is also associated with excessive production of poorly glycosylated IgA_1 in the serum causing the production of IgG and IgA autoantibodies. Thus, IgA_1 is the predominant immunoglobulin deposited in the glomeruli in both conditions. Up to 30% of patients with IgA nephropathy subsequently have systemic symptoms. Dermal blood vessels of many patients with IgA nephropathy have IgA immunofluorescence like that in HSP [14].

On renal biopsy, glomerular lesions in IgA nephropathy are primarily classified based on mesangial proliferation, sclerosis, and renal tubular atrophy. In contrast, the biopsy findings of HSP usually show the presence of endocapillary and extra-capillary inflammation. Neutrophil infiltration, endocapillary proliferation, and crescent formation are more frequently observed in HSP vasculitis [10, 13]. On immunofluorescence, IgA deposits are detected in the mesangium in both IgA nephropathy and HSP vasculitis. However, in HSP nephritis, capillary wall staining for IgA is more prevalent and may even surpass mesangial IgA deposition [14]. Capillary IgA deposition in IgA Nephropathy is rare and if at all present, is associated with significantly worse outcomes [13]. Based on the pathophysiological and histopathological commonalities, HSP and IgA Nephropathy are viewed as a spectrum of IgA-mediated inflammatory syndrome [10].

Treatment protocols, as per the KDIGO recommendations, all children with IgA nephropathy and proteinuria should receive angiotensin-converting enzyme inhibitors or angiotensin receptor blockers with advice for a low sodium diet and optimal lifestyle and blood pressure control. Children with rapidly progressive IgA nephropathy should be offered treatment with glucocorticoids (methylprednisolone pulse therapy) and cyclophosphamide. HSP nephritis with persistent proteinuria should be treated with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. Children with HSP nephritis with nephrotic range proteinuria and/or rapidly deteriorating kidney function should be treated similarly to those with rapidly progressive IgA nephropathy.

Conclusion

This case report emphasizes the co-occurrence of both HSP-like cutaneous rash and renal manifestations of Ig A nephropathy in the same patient. Hence, patients diagnosed with HSP need long-term follow-up, with continuous renal parameters and blood pressure monitoring. Similarly, features of IgA vasculitis can also be seen in patients diagnosed with primary IgA nephropathy pointing toward a common pathogenesis.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research. The consent was obtained.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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