Pediatric Granulomatosis With Polyangiitis Mimicking IgA Vasculitis: A Case Report

Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders
Volume 13: 1–3

DOI: 10.1177/1179544120967371
SAGE

Vadood Javadi Parvaneh[1], Arezoo Shirzani[2], Khosro Rahmani[1] and Reza Shiari[1]

[1]Department of Pediatric Rheumatology, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Resident of Pediatrics, Department of Pediatrics, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

ABSTRACT

BACKGROUND: Granulomatosis with polyangiitis (GPA) is a systemic vasculitis of the upper and lower respiratory tract along with glomerulonephritis and is very rare in childhood. Its renal manifestations similarity with IgA vasculitis can be misleading.

CASE PRESENTATION: Herein, we report a 12-years-old girl with the clinical picture of IgA vasculitis and renal involvement at the time of presentation, over time, elevated cytoplasmic Anti-neutrophil Cytoplasmic Antibody (C-ANCA) and tissue biopsy confirmed GPA.

CONCLUSION: In the case of a patient with an unusual presentation of IgA vasculitis, to some degree of suspicion, the GPA should be considered. Also, in approach to non-thrombocytopenic palpable petechia and purpura a wide range of differential diagnosis such as infections, ANCA associated vasculitis, and secondary vasculitis should be considered. Therefore, 2 effective method of GPA diagnosis, the high titer of C-ANCA test and tissue biopsy, should be considered simultaneously.

KEYWORDS: Granulomatosis with polyangiitis, Wegener's Granulomatosis, IgA vasculitis, Henoch-Schonlein purpura, children/pediatrics, "case report"

RECEIVED: June 18, 2020. **ACCEPTED:** September 22, 2020.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Reza Shiari, Department of pediatric rheumatology, Shahid Beheshti University of Medical Sciences, Faculty of Medicine, Mofid Children's Hospital, Shariati Ave, Tehran, Iran. Email: shiareza@yahoo.com

Background

Overall, IgA vasculitis and GPA are not common diseases, with a worldwide annual incidence ranging from 3 to 27 and 0.1 to 1.3 cases per 100 000 individuals respectively.[1,2] IgA vasculitis (Henoch-Schonlein purpura) is one of the most common pediatric-onset vasculitides which characterized by non-thrombocytopenic palpable purpura, arthritis, bowel angina, and glomerulonephritis.[3-5] On the other hand, Granulomatosis with polyangiitis (GPA) or Wegener's Granulomatosis (WG) is a potentially life-threatening vasculitis commonly affecting upper and lower respiratory tract, kidneys, and peripheral and central nervous system.[6-8] Although it is more frequent in adult, few cases in children have been reported yet.[4,5,9] Both IgA vasculitis and GPA comprise same vasculitis syndrome in children; so, the GPA may be misdiagnosed as IgA vasculitis at the time of initial presentation. Although in a few studies, the role of Anti-neutrophil Cytoplasmic Antibody (ANCA) test and tissue biopsies to early diagnosis of GPA in children have been investigated, it is suspicious and in many medical centers can be mistaken as IgA vasculitis.[9]

Herein, we report a 12-years-old girl presented initially with the clinical picture of IgA vasculitis and only renal involvement symptoms, over time, developed the typical clinical presentation of GPA.

Case Presentation

A 12-year-old girl presented to the local general hospital with symmetric palpable purpuric lesion in lower limbs, left hip pain and also a morning stiffness for 30 minutes. She was diagnosed with IgA vasculitis and just took conservative care. She gradually improved and discharged from hospital subsequently. Nine months later, she was presented to Mofid Children's Hospital with purpuric lesion in lower limbs, significant morning stiffness (from 3 days before admission), severe parietal headache, and 3-week history of pain in the thighs, arms, and shoulders.

In physical examination there were no signs of photosensitivity, malar rash, oral ulcer, lymphadenopathy, pericarditis, and arthritis. Furthermore, there were no signs and symptoms of sinus involvement.

Due to the patient headache, brain MR imaging, and angio-MRI were done with normal results. Ophthalmology consult reported keratitis, peripheral ulcerative and episcleritis. Erythrocyte Sedimentation Rate (ESR) was 33 mm/h. Anemia, and normal leukocyte and platelets number were finding of complete blood count (CBC) test.

Urinalysis revealed proteinuria (1+) and hematuria (Blood 3+ and red blood cell (RBC) 70-80/hpf). Proteinuria was calculated quantitatively (300 mg per 24 hours). Blood Urea Nitrogen (BUN) and Creatinine (Cr) were in normal range. Lupus profile autoantibodies, Perinuclear Anti-neutrophil

Table 1. Reported cases about pediatric GPA mimicking IgA vasculitis.

NUMBERS	FIRST AUTHOR	TITLE	JOURNAL	YEAR OF PUBLICATION	REFERENCE NUMBER
1	May	Henoch-Schonlein Purpura Followed by Wegener's Granulomatosis	Clin Pediatr (Phila)	1993	4
2	Miyata	A patient with Wegener's granulomatosis with initial clinical presentations of Henoch-Schönlein purpura	Intern Med	2001	5
3	Bui	Granulomatosis with polyangiitis presenting as Henoch-Schönlein purpura in children	J Clin Rheumatol	2013	9
4	Zhang	Significance of antineutrophil cytoplasmic antibody in adult patients with Henoch-Schönlein purpura presenting mainly with gastrointestinal symptoms	World J Gastroenterol	2008	14

Cytoplasmic Antibody (P-ANCA), immunologloblins (Igs) level, wright, 2-mercaptoethanol (2ME), and anti-streptolysin O antibody (ASO) titer level were normal. C-ANCA was highly positive (C-ANCA > 300 U/ml, cut-off >18 positive). Considering hematuria, proteinuria, and high level C-ANCA renal biopsy was considered. Its result revealed focal crescentic and sclerosing glomerulonephritis ANCA associated with pauci-immune vasculitis.

Regarding the C-ANCA assay which was significantly positive and the histopathologic findings in the renal biopsy, the GPA was diagnosed. Subsequently, the patient treated with azathioprine (100 mg/day), prednisolone (27.5 mg/day), and captopril (12.5 mg/day). After 6 months follow-up, the symptoms resolved, inflammatory marker dropped, and the disease was in remission. After 2 years, the patient is in the complete remission with azathioprine (50 mg/day) and prednisolone (5 mg/day).

Discussion and Conclusion

IgA vasculitis is a systemic vasculitis with unknown etiology, with immune complex damage to the post capillary venules. Renal involvement, usually with the proteinuria or hematuria, is seen in up to 40% of patients.[10] The disease is usually self-limited, with resolution in 3 to 6 weeks. Fortunately, progression to end-stage renal damage is rare in children. Biopsy reveals deposit of Ig_s principally granular IgA in the vessel.[11]

GPA is an ANCA-associated primary small vessels vasculitis. It has the diagnostic triad of upper and lower respiratory tract inflammation and renal disease.[12] Clinical feature of renal involvement include abnormal urinalysis, biopsy proven glomerulonephritis, and elevated serum creatinine. According to Vasculitis Clinical Research Consortium (VCRC) Scheme for staging GPA, there are limited and severe GPA. The patient had limited GPA with hematuria, proteinuria, glomerulonephritis, with normal serum creatinine without rising from baseline.

Searching the key words related to the WG, GPA, IgA vasculitis, and Henoch-Schonlein purpura in pediatric at the English literatures and scientific web sites like PubMed, Scopus, Science Direct, Wiley, Ovid, Springer, Web of Science, Clinical Key, Google scholar, and also the Google research engine revealed that just a few cases have been reported until September 2018. These cases have been shown in Table 1. Table 1 shows the data extracted from each article by authors, title, journal, year of publication, and place of study.

In a recent report, Bui and colleagues emphasized the role of ANCA test and tissue biopsy in establishing the diagnosis of GPA at the time of initial presentation in patients that GPA masqueraded as IgA vasculitis. They concluded that ANCA test is useful in GPA diagnosis but for confirming needs tissue biopsy.[9] Because some conflicting data, some authors suggest that the presence of IgA-ANCA might be useful for diagnosis of Henoch Shonlein purpura (HSP).[3,13] Miata and colleagues reported a GPA young case (19-years-old) who initially diagnosed as HSP.[5] Four years later, the appearance of polyarthralgia which followed by skin purpura and melena suggested recurrence of IgA vasculitis; however, with time, massive lesion in the sinuses and cavities in the lung which appeared in the age of 28 her sinus biopsy revealed that she suffered from GPA. In other case report, a case of IgA vasculitis followed by WG was described.[4] The authors reported a case of a 13-years-old girl who presented with arthritis, abdomen pain, palpable purpura, and hematuria with proteinuria. Her skin biopsy revealed leukocytoclastic vasculitis and the C-ANCA test was negative. She was diagnosed with IgA vasculitis. With time, she presented with pan sinusitis. Her sinus biopsy and high titer of C-ANCA test revealed the GPA.

Like reported cases, our patient initially presented clinical features of IgA vasculitis and finally, those of GPA. Although, in contrast to reported cases, there were no symptoms of sinuses and pulmonary involvement, but her tissue biopsy and high titer of C-ANCA confirmed the WG disease.

We concluded that the wide range of organ involvement in IgA vasculitis and its symptoms overlap with the skin vasculitis of GPA can be misleading at the time of initial presentation. The

different nature of IgA vasculitis and GPA and, also their distinct ways of treatment, suggest that in the case of a patient with an unusual presentation of IgA vasculitis, to some degree of suspicion, the GPA should be considered. Also, in approach to non-thrombocytopenic palpable petechia and purpura a wide range of differential diagnosis such as infections, ANCA associated vasculitis, and secondary vasculitis should be considered. Therefore, 2 effective method of GPA diagnosis, the high titer of C-ANCA test and tissue biopsy, should be considered simultaneously.

Author's Contribution

AS and KR drafted the manuscript. VJP and RS edited and supervised manuscript. All authors read and approved the final manuscript.

Consent for Publish

We confirm that the written informed consent form has been provided by the parents to have the case details published. Also, we restate that institutional approval is not required to publish the case details.

ORCID iDs

Vadood Javadi Parvaneh https://orcid.org/0000-0002-4159-2052
Reza Shiari https://orcid.org/0000-0002-7712-279X

REFERENCES

1. Piram M, Maldini C, Biscardi S, et al. Incidence of IgA vasculitis in children estimated by four-source capture–recapture analysis: a population-based study. *Rheumatology*. 2017;56:1358-1366.
2. Berti A, Dejaco C. Update on the epidemiology, risk factors, and outcomes of systemic vasculitides. *Best Pract Res Clin Rheumatol*. 2018;32:271-294.
3. Saulsbury FT. Henoch-Schönlein purpura in children. Report of 100 patients and review of the literature. *Medicine*. 1999;78:395-409.
4. May KP, West SG. Henoch-Schonlein Purpura Followed by Wegener's Granulomatosis. *Clin Pediatr (Phila)*. 1993;32:555-557.
5. Miyata M, Kanno K, Nishimaki T, Sakuma F, Iwatsuki K, Kasukawa R. A patient with Wegener's granulomatosis with initial clinical presentations of Henoch-Schönlein purpura. *Intern Med*. 2001;40:1050-1054.
6. Belostotsky VM, Shah V, Dillon MJ. Clinical features in 17 pediatric patients with Wegener granulomatosis. *Pediatr Nephrol*. 2002;17:754-761.
7. Cabral DA, Uribe AG, Benseler S, et al. Classification, presentation, and initial treatment of Wegener's granulomatosis in childhood. *Arthritis Rheum*. 2009;60:3413-3424.
8. Hall SL, Miller LC, Duggan E, Mauer SM, Beatty EC, Hellerstein S. Wegener granulomatosis in pediatric patients. *J Pediatr*. 1985;106:739-744.
9. Bui T, Chandrakasan S, Poulik J, Fathalla BM. Granulomatosis with polyangiitis presenting as Henoch-Schönlein purpura in children. *J Clin Rheumatol*. 2013;19:199-202.
10. Mills JA, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Henoch-Schönlein purpura. *Arthritis Rheum*. 1990; 33:1114-1121.
11. Nakamoto Y, Asano Y, Dohi K, et al. Primary IgA glomerulonephritis and Schönlein-Henoch purpura nephritis: clinicopathological and immunohistological characteristics. *Q J Med*. 1978;47:495-516.
12. Ting TV, Hashkes PJ. Update on childhood vasculitides. *Curr Opin Rheumatol*. 2004;16:560-565.
13. Zhang Y, Wu Y-K, Ciorba MA, Ouyang Q. Significance of antineutrophil cytoplasmic antibody in adult patients with Henoch-Schönlein purpura presenting mainly with gastrointestinal symptoms. *World J Gastroenterol*. 2008;14:622-626.