Case Series
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Atypical Characteristics of Skin Eruption in Adult Iga Vasculitis should not Deter from Diagnosis: Observations from a Retrospective Case Series

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Abstract

IgA vasculitis is poorly understood in adults and there is a greater need for randomized control trials to identify the clinical course and proper management of the disease. This is especially critical for adults with IgA vasculitis, given the association with worse outcomes and greater morbidity and mortality related to the diseaseâ€™s comorbidities. For this reason, prompt identification and diagnosis of the vasculitis is critical. Importantly, cutaneous eruption is the most common presenting sign of IgA vasculitis, and it may be the only feature available to determine initial suspicion for IgA vasculitis. Atypical cutaneous features, such as necrotic or hemorrhagic purpura, bullae, or pustules, are more common in the cutaneous eruption of adult IgA vasculitis. This complicates identifying an already rare vasculitis in adults and could lead to delays in identification and management of the associated comorbidities. In this retrospective case series, we studied 34 adult patients with biopsy proven IgA vasculitis and divided each case into one of three different groups based on the dermatology providersâ€™ differential diagnosis and initial clinical suspicion for IgA vasculitis at the time of biopsy. We then evaluated whether the proportion of patients with atypical cutaneous features differed across the groups. Atypical cutaneous features were significantly more common in cases where IgA vasculitis was not included in the differential compared to cases where IgA vasculitis was included. This suggests that atypical cutaneous features could be deterring clinicians from considering and identifying the vasculitis. This has implications for patient care related to the diseaseâ€™s comorbidities and steps should be taken to emphasize that atypical cutaneous features are a common occurrence in adult IgA vasculitis.

Keywords: Adult • IgA vasculitis • Rheumatology • Prevalence • Patient care

Introduction

Palpable purpura or petechiae with lower limb predominance are the classic skin eruptions associated with IgA vasculitis (IgAV); however, skin eruption in adult onset IgAV is more likely to present with atypical features that deviate from this presentation. For example, roughly one-third of adults present with necrotic or hemorrhagic purpura [1,2]. Adults are also more likely to have bullae, pustules and urticarial wheels [3,4]. In contrast, a recent study found that only two out of 113 children with IgAV presented with atypical skin eruptions such as hemorrhagic bullae, and skin necrosis is reported to occur in less than 5% of childhood cases [2,5-7]. Currently, there is no specific criterion for diagnosing IgAV in adults and clinicians often rely on the childhood diagnostic criteria to identify the disease in adults. This has implications since the most updated childhood IgAV diagnostic criterion, created by the European League against Rheumatism/Pediatric Rheumatology International Trials Organization/Pediatric Rheumatology European Society (EULAR/PRINTO/PRES), does not account for differences between children and adults, such as the higher prevalence of atypical cutaneous features. Additionally, the accuracy of diagnosing IgAV in adults with the childhood criterion has been divergent [8,9] and several have called for a specific adult criterion [10]. Recognizing the differences in clinical spectrum between adults and children with IgAV is essential for diagnostic accuracy and patient care, especially since IgAV is diagnosed largely by clinical criteria [11]. Importantly, IgAV is affiliated with renal, articular, gastrointestinal (GI) and other comorbidities, which frequently manifest after the initial skin lesions. Adults are more likely to have severe and relapsing disease related to these comorbidities [10]. This underscores the importance of identifying the disease early, as this alerts clinicians to look for systemic involvement and initiate appropriate management as needed. Since skin eruption is the presenting sign of IgAV in around 75% of cases, it may be the only feature available to determine initial suspicion for IgAV. Clinicians are taught to recognize adult IgAV based on childhood criteria; however, they might be missing cases if they do not affiliate atypical cutaneous features as a common part of the clinical spectrum in adults. Additionally, although providers may recognize that atypical cutaneous features can occur in adult IgA vasculitis, prior studies have not examined whether this recognition actually is applied in clinical practice.

Case Series

In this retrospective case series we aimed to evaluate whether atypical cutaneous characteristics, such as necrotic or hemorrhagic purpura, bullae, or pustules, influenced clinical suspicion for IgAV. Our study included 34 patients ≥18 with biopsy-proven IgAV (defined as skin biopsy showing leukocytoclastic vasculitis with predominant IgA deposits OR kidney biopsy with proliferative glomerulonephritis with predominant IgA deposits) seen at our institution between 2016 and 2021. We then classified each case into one of three different groups based on the providers' differential diagnosis (DDX) and suspicion for IgAV at time of biopsy (Table 1). The DDX and clinical suspicions were those determined by University of Arizona dermatology residents in conjunction with their attendings at time of consultation. We then evaluated whether the proportions of patients with atypical skin eruption features differed across the groups by the likelihood-ratio-based exact G-test

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Table 1. Biopsy proven adult IgA vasculitis cases divided into groups based on clinician inclusion of IgA vasculitis in differential diagnosis at time of initial biopsy.

Group	Description	Example	n
Group 1	IgAV [†] not included in DDX[‡] and no mention of any clinical suspicion for IgAV.	"septic vasculopathic phenomenon *vs.* vasculitis *vs.* adult onset stills."	11
Group 2	IgAV included in the DDX, along with other diagnoses.	"IgAV vs. pigmented purpura dermatitis."	15
Group 3	Only IgAV included in DDX.	"Rule out IgAV."	8

[†]IgAV: IgA vasculitis; [‡]DDX: differential diagnosis

Table 2. Partitioned analysis comparing proportions across groups based on initial IgA vasculitis inclusion in DDX[†] at time of initial biopsy.

Tests		Total Cases (n)	Cases with Atypical Rash (n)	%
Omnibus test	IgAV[b] not in DDX	11	6	0.54545
	IgAV in DDX	15	4	0.26667
	IgAV only DDX	8	1	0.12500
g[§]=2.81968, df[¶]=2, p=0.244				
Poolability test	IgAV in DDX	15	4	0.26667
	IgAV only DDX	8	1	0.12500
g=0.52763, df=1, p=0.46761				
Comparison test	IgAV not in DDX	11	6	0.54545
	IgAV in/only DDX	23	5	0.21739
g=75.15424, df=1, p<0.00001				

(G=2*Sum[Observed*ln[Observed/Expected]]), in a Bonferroni-corrected (α <0.01667) partitioned analysis with an omnibus test of proportions, a subsequent poolability analysis of the closest proportions (IgAV in DDX and IgAV only DDX), and a final analysis comparing the pooled ("in/only") to the (IgAV not in DDX) case (Table 2).

The omnibus and poolability tests were not significant, yet the comparison of Group 1 (IgAV not in DDX) to the pooled data (Groups 2 and 3) was statistically significant (p<0.00001). The results suggest that atypical cutaneous features were significantly more common in cases where IgAV was not considered in the DDX, compared to cases where IgAV was included in the DDX. These findings suggest that atypical characteristics may deter clinicians from considering the diagnosis of IgAV upon initial assessment. For example, in one case where IgAV was not included in the DDX, the clinician remarked that their "concern for medium vessel vasculitis came from the presence of hemorrhagic bullae and ulceration." This statement emphasizes that providers may not associate atypical features, such as hemorrhagic bullae or ulceration, with small vessel vasculitides such as IgAV.

Results and Discussion

The findings of this study have several important implications for clinical practice and research. Importantly, Adult IgAV is considered a rare disease, although it may be more common than initially thought [12]. Because of its perceived rarity, clinicians may be more likely to consider other vasculitides than IgAV when first evaluating a patient with palpable purpura. This becomes even more of a possibility if a patient presents with atypical cutaneous features that are more reflective of another vasculitis than IgAV. The results of our study indicate that this is plausible since providers were more likely to consider a different diagnosis in the presence of atypical cutaneous features. Prior studies have also shown discrepancies in the clinical and histopathologic diagnosis of adult IgAV. For example, a 2018 study by Lath, et al. suspected IgAV clinically in 65 patients of which only 40 (61.5%) were confirmed on DIF. Furthermore, 20 cases that were not originally suspected of HSP/IgAV were later found to be DIF proven IgAV. This study did not examine potential reasons for the missed clinical diagnosis of IgAV in these 20 cases; however, this may reflect difficulties in identifying the disease that could be reflective of atypical cutaneous eruptions.

Conclusion

One might argue that identifying IgAV based on clinical picture is not critical since DIF, which is often ordered in vasculitis and immunobullous workups, can act as a "safety net" to identify predominant IgA deposits in cases where initial clinical suspicion might be low. Although DIF is frequently contributory in cases of IgAV, this thinking is idealistic. Studies have found that there are frequently subsets of true IgAV cases in which vascular cutaneous IgA deposition is negative [13,14]. Reasons for this are not entirely clear, although timing, sampling technique and certain drugs have been implicated in affecting these results [13,14]. Therefore, providers should avoid overreliance on DIF to cement the diagnosis, especially since there other vasculitides, such as cryoglobulinemia, hypocomplementemic vasculitis and collagen vascular disease that can exhibit predominant IgA deposits as well [13] Additionally, DIF results frequently take several days to weeks to result. This can have important implications in adult IgAV given the associated comorbidities that require prompt recognition and management. For example, GI symptoms usually develop within a week of the appearance of the rash [15] and can be severe, with GI perforation representing the main life threatening complication [16]. Adults also have significantly higher rates of severe and non-severe GI bleeding [17]. Missed diagnoses of IgAV can lead to delays in screening for GI involvement and other comorbidities. In some cases, symptoms reflective of GI involvement have even been masked due to steroids [18]. Similarly, pulmonary hemorrhage which is a rare but potential complication can be seen in the early phase of IgAV and is associated with high morbidity and mortality [19]. Certain interventions have been associated with better outcomes for patients with pulmonary hemorrhage [19,20]. This further emphasizes the importance of cementing the diagnosis of IgAV as early as possible as this allows for prompt screening and identification of the comorbidities associated with IgAV. This leads to efficient treatment and management which can prevent further complications.

Limitations

Limitations of the study include the relatively small sample size and retrospective nature that may not be fully reflective of the clinicians' thought processes. Despite the small sample size, our findings suggest that IgAV may be more frequent than clinicians anticipate. Our study's strength is that we were able to observe clinicians' initial diagnostic considerations when evaluating cases of adult IgAV. This established a proportion of cases that could have been misdiagnosed if the DIF hadn't been performed to assess

for immunoglobulin deposition related to other immune-mediated diagnoses that were being considered at the time of initial evaluation. This highlights the possibility that other IgAV cases are being missed, especially if atypical features deter clinicians from considering IgAV. This clinical scenario can lead to delays in diagnoses and prompt management of associated co-morbidities.

Conflicts of Interest

Ivo Abraham reports a relationship with Matrix45 that includes: equity or stocks. Matrix45 has not provided any services to this study. Otherwise, the authors have no other conflicts of interest.

References

1. Audemard Verger, Alexandra, Evangeline Pillebout, Loïc Guillevin and Eric Thervet. "IgA vasculitis (Henoch–Shönlein Purpura) in adults: Diagnostic and therapeutic aspects." *Autoimmu Revi* 14 (2015): 579-585.
2. Pillebout, Evangéline, Eric Thervet, Gary Hill and Corinne Alberti, et al. "Henoch-Schönlein purpura in adults: Outcome and prognostic factors." *J Ame Soci Nephrol* 13 (2002): 1271-1278.
3. Nevrekar, Ramnath P., Prachi Bhandare and Anar Khandeparkar. "Clinical spectrum of Henoch Schonlein Purpura in adults: A Hospital based study." *J Assoc Phys Ind* 70 (2022): 11-12.
4. Yaseen, Kinanah, Leal C. Herlitz, and Alexandra Villa-Forte. "IgA vasculitis in adults: A rare yet challenging disease." *Curr Rheumatol Rep* 23 (2021): 1-11.
5. AlKhater, Suzan A., and Hala M. Al Moaigel. "Clinical spectrum and outcome of immunoglobulin-A vasculitis in children: A 10-year clinical study." *Intern J Clin Pract* 75 (2021): e13930.
6. Wananukul, Siriwan, Prapai Pongprasit and Wiwat Korkij. "Henoch-Schonlein Purpura presenting as hemorrhagic vesicles and bullae: Case report and literature review." *Pediatr Dermatol* 12 (1995): 314-317.
7. Saulsbury, Frank T. "Hemorrhagic bullous lesions in Henoch-Schönlein Purpura." *Pediatr Dermatol* 15 (1998): 357-359.
8. Ortiz Sanjuan, F., R. Blanco, J.L. Hernandez and M.A. González López, et al. "Applicability of the 2006 European League against Rheumatism (EULAR) criteria for the classification of Henoch-Schönlein purpura. An analysis based on 766 patients with cutaneous vasculitis." *Clin Exp Rheumatol* 33 Suppl 89 (2015): S44-7.
9. Hočevar, Alojzija, Ziga Rotar, Vesna Jurčić and Jože Pižem, et al. "IgA vasculitis in adults: The performance of the EULAR/PRINTO/PRES classification criteria in adults." *Arthr Res Ther* 18 (2016): 1-5.
10. González Gay, Miguel A., Ricardo Blanco and Santos Castaneda. "Henoch-Schönlein purpura (IgA vasculitis): The paradox of the different incidence and clinical spectrum in children and adults." *Clin Exp Rheumatol* 35 (2017): 3-4.
11. Poudel, Pooja, Steven H. Adams, Kanish Mirchia and Hanish Jain. "IgA negative immunofluorescence in diagnoses of adult-onset Henoch-Schönlein purpura." In *Bay Uni Medi Cen Proce* Taylor & Francis, (2020): pp. 436-437.
12. Hočevar, A., Z. Rotar, J. Ostrovršnik and V. Jurčić, et al. "Incidence of IgA vasculitis in the adult Slovenian population." *Brit J Dermatol* 171 (2014): 524-527.
13. Linskey, Katy R., Daniela Kroshinsky, Martin C. Mihm Jr and Mai P. Hoang. "Immunoglobulin-A–associated small-vessel vasculitis: A 10-year experience at the Massachusetts General Hospital." *J Ame Acad Dermatol* 66 (2012): 813-822.
14. Nandeesh, B. N., and Rajalakshmi Tirumalae. "Direct immunofluorescence in cutaneous vasculitis: Experience from a referral hospital in India." *Indi J Dermatol* 58 (2013): 22.
15. Esaki, Motohiro, Takayuki Matsumoto, Shotaro Nakamura and Masumi Kawasaki, et al. "GI involvement in Henoch-Schönlein purpura." *Gastroin Endosc* 56 (2002): 920-923.
16. Audemard Verger, Alexandra, Evangéline Pillebout and Zahir Amoura. "Gastrointestinal involvement in adult IgA vasculitis (Henoch-Schönlein Purpura): updated picture from a French multicentre and retrospective series of 260 cases." *Rheumatol* 59 (2020): 3050-3057.
17. Blanco, Ricardo, Víctor M. Martínez Taboada, Vicente Rodríguez Valverde and Miguel García Fuentes. "Henoch-Schönlein purpura in adulthood and childhood. Two different expressions of the same syndrome." *Arthr Rheumat Offi J Ame Coll Rheumatol* 40 (1997): 859-864.
18. Weissman, Amanda S., Viral Sanjay Patel and Omar Mushfiq. "Case of Gut Necrosis in Adult-Onset Immunoglobulin A Vasculitis (Henoch-Schönlein Purpura)." *J Investig Med Hig Imp Cas Rep* 8 (2020): 2324709620925565.
19. Rajagopala, Srinivas, Vineeta Shobha, Uma Devaraj and George D'Souza. "Pulmonary hemorrhage in Henoch-Schönlein purpura: Case report and systematic review of the English literature." In *Semi Arthri Rheumat* WB Saunders, 42 (2013): pp. 391-400.
20. Miyoshi, Seigo, Tomoaki Nagao, Masayoshi Kukida and Ken-ichi Miyoshi, et al. "A case of pulmonary hemorrhaging as a fatal complication of IgA vasculitis." *Inter Med* (2018): 0817-18.

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