Reply to Comment on "An Unusual Case of Acquired Angioedema and Monoclonal Gammopathy of Renal Significance in a Middle-Aged Caucasian Female"

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Abstract

We sincerely thank Dr Andrew Whyte, who keenly reviewed our case report and came up with critical reasoning to justify his thoughts and critique with regard to our published article, "An Unusual Case of Acquired Angioedema and Monoclonal Gammopathy of Renal Significance in a Middle-Aged Caucasian Female." We agree with the author that hypocomplementemic urticarial vasculitis can be a reasonable contender as a diagnosis in this case. There are indeed some features in this case that do not entirely fit either classic presentation of acquired angioedema or hypocomplementemic urticarial vasculitis. Both diseases being equally rare, we tried to focus on the association of proliferative glomerulonephritis with angioedema-like features in this patient and considered acquired angioedema as the unifying diagnosis.

Keywords

acquired CI esterase inhibitor deficiency, acquired angioedema, acute kidney injury, proliferative glomerulonephritis, hypocomplementemic urticarial vasculitis

To the Editor:

We sincerely thank Dr Andrew Whyte, who keenly reviewed our case report and came up with critical reasoning to justify his thoughts and critique with regard to our published article.

We agree that hypocomplementemic urticarial vasculitis (HUV) can be a close differential to our case. However, with both the diseases being rare and renal manifestation being more strongly associated with angioedema, we feel our diagnosis of acquired angioedema (AA) is more likely.

In order to systematically present our justifications regarding each of the 3 points raised by the esteemed reader, we present our counterarguments:

First, the skin lesions of our patient were papules and were not painful, unlike HUV.¹ The lesions of our patient resolved in <72 hours every time without any residual skin findings and were too transient to require biopsy.² Also, her symptoms were acute and life-threatening with angioedema and rapidly worsening renal failure; skin biopsy was not considered initially. HUV, or McDuffie syndrome, is a rare disease process that typically manifests as chronic, nonpruritic, urticarial vasculitic lesions that persist more than 24 hours or recur at short intervals.³ We apologize for not mentioning the exact duration of the skin lesions in our article, but the lesions were not chronic over >6 months, which is likely in HUV.

Among systemic manifestations, arthralgia, being one of the most frequent presentations of HUV, was absent in our patient. In our case, we tried to highlight the renal aspect more, and this is equally rare in both AA and HUV. We agree that pedal edema is infrequent with angioedema; it can occur with acute kidney injury and with her proliferative glomerulonephritis.

¹Lynchburg Nephrology Physicians, Lynchburg, VA, USA ²Ashland Bellefonte Cancer Center, Ashland, KY, USA ³Miami Valley Hospital, Dayton, OH, USA ⁴Adventist Medical Center, Hanford, CA, USA ⁵Interfaith Medical Center, Brooklyn, NY, USA ⁶The Nephrology Group, Fresno, CA, USA

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Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage). Second, we agree that AA, being a bradykinin-mediated phenomenon, does not generally respond to steroids, and this feature may be a strong point in favor of HUV as described by the author. However, our patient did respond well to steroids, mainly her renal failure completely subsided, and her skin lesions resolved. As rightly pointed out, there is no guideline suggesting the benefit of steroids in AA, but there is anecdotal literature of corticosteroid efficacy on a small subset of patients with AA.⁴ We also want to clarify that patient's allergist advised her to carry EpiPen in case she develops life-threatening acute angioedema.

Third, the clinical tests mentioned were all done, but we did not include in the details due to word constraint and unremarkable values. Serum immunofixation was done; it revealed no abnormal bands. Immunoglobulin (Ig) G was 1127 mg/dL, IgA was 190 mg/dL, and IgM was 165 mg/dL, all necessarily within a normal range. Further complement level testing done 3 months later were also low; the "spurious" remark in the text of the original article was used in error, and we apologize for the confusion it created. In the immunofluorescent findings on kidney biopsy, C1Q, C3 showed 2+ and there was no significant staining for IgM, IgA, or lambda (not kappa) light chain. The immune deposits stained 3+ for IgG1 and trace for IgG2, G3 and none for G4. Due to the constraint of words, we did not elaborate on all these features in the biopsy results, but we did provide the original slide pictures provided by the pathologist. We did mention the anti-C1Q level, which was low at 1.3 mg/dL (normal = 11.8-24.4 mg/dL). Additionally, urticarial vasculitis is commonly associated with positive ANA, which was negative in our patient and may not be typical of HUV.5

In summary, we agree with the author that HUV can be a reasonable contender as a diagnosis in this case. There are indeed some features in this case that do not entirely fit either classic presentation of AA or HUV. Both diseases being equally rare, we tried to focus on the association of proliferative glomerulonephritis with angioedema-like features in this patient and considered AA as the unifying diagnosis.

We again thank the author of the "Letter to the Editor" for a very thoughtful analysis and review.

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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