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CSU, CHA and CSU-AE

Comment on: Demographic and clinical characteristics of chronic histaminergic angioedema and chronic urticaria with angioedema: a multicenter Italian experience - doi: 10.23822/EurAnnACI.1764-1489.411

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We read with great interest the article by Sartorio *et al.* (1). Despite finding clear clinical and demographic differences between mast cell-mediated angioedema (CHA) and chronic spontaneous urticaria with angioedema (CSU-AE), CHA is considered to be a subtype of CSU, mostly based on shared treatment options, rather than true clinical equivalence. This classification persists even as evidence accumulates supporting their separation as distinct conditions.

Very few studies compare mast cell mediated angioedema with CSU-AE; the present paper confirms the differences found except for a similar male/female distribution. One possible reason is the sample size of 78 patients since previous studies include larger samples with a M/F ratio from 0.56 (2), 0.65 (3) and 0.78 (4) with patient samples of 131, 254 and 3,698, respectively.

All other features also highlighted in this study confirm that CHA and CSU-AE differ in several aspects: CHA typically presents at an older age and shows a higher frequency of tongue angioedema and limb involvement, while eyelid and perioral involvement is less frequent compared to CSU-AE. There is a lower frequency of attacks with a longer duration of episodes and less impairment in quality of life when CHA is compared to CSU-AE (4, 5). Regarding treatment, CHA responds especially well to high-dose H1-antihistamines and omalizumab (a fact sometimes used to justify grouping with CSU), even though the pathophysiological profiles differ. Cold urticaria, for example, is also mediated by mast cell activation and is responsive to antihistamines and omalizumab; however, it is clearly a separate condition.

There is also pathophysiological evidence of differences, CHA and CSU-AE are also distinguished by one key difference which is the absence of IgG anti FceRI receptor in CHA with a 34% incidence in CSU-AE. Basopenia is common in CSU-AE but there is no basopenia in CHA (3). There is a large difference between CHA and CSU-AE in autoimmunity comorbidities (4) also found in the present study.

Classifying CHA as an urticaria subtype risks confusing patients and non-specialist providers – especially when it presents without hives. This confusion can delay the critical recognition and proper management of bradykinin-mediated *versus* mast cell-mediated angioedema. Calling a condition "urticaria" without hives is problematic, as it means defining a disease by a key symptom that is missing.

The conclusion that CSU-AE and CHA are part of a "protean" urticaria spectrum does not address their fundamental differences. Robust evidence now supports considering these as separate entities given their clinical, immunologic and physiologic differences. More focused research, revised guidelines, and refined diagnostic criteria are urgently required to improve clarity for clinicians, and – most importantly – to ensure optimal patient care. In summary, while CHA and CSU-AE share similar treatments, their clinical behavior, comorbidity profiles, and pathophysiology are distinct enough that continuing to consider CHA merely as a urticaria subtype is neither clinically nor scientifically justified.

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Contributions

Both authors contributed equally to the work.

Conflict of interests

The authors declare that they have no conflict of interests.

References

1. Sartorio S, Rivolta F, Tedeschi A, Manzotti G, Piantanida M, Marra AM, et al. Demographic and clinical characteristics of chronic histaminergic angioedema and chronic urticaria with angioedema: a multicenter Italian experience. Eur Ann Allergy Clin Immunol. 2026;58(4):173-179. doi: 10.23822/EurAnnACI.1764-1489.411.
2. Zingale LC, Beltrami L, Zanichelli A, Maggioni L, Pappalardo E, Cicardi B, et al. Angioedema without urticaria: a large clinical survey. CMAJ. 2006;175(9):1065-70. doi: 10.1503/cmaj.060535.
3. Sabaté-Brescó M, Rodriguez-Garijo N, Azofra J, Baeza ML, Donado CD, Gaig P, et al. A Comparative Study of Sex Distribution, Autoimmunity, Blood, and Inflammatory Parameters in Chronic Spontaneous Urticaria with Angioedema and Chronic Histaminergic Angioedema. J Allergy Clin Immunol Pract. 2021;9(6):2284-2292. doi: 10.1016/j.jaip.2021.03.038.
4. Buttgereit T, Vera C, Aulenbacher F, Church MK, Hawro T, Asero R, et al. Patients With Chronic Spontaneous Urticaria Who Have Wheals, Angioedema, or Both, Differ Demographically, Clinically, and in Response to Treatment-Results From CURE. J Allergy Clin Immunol Pract. 2023;11(11):3515-3525.e4. doi: 10.1016/j.jaip.2023.08.020.
5. Rodríguez-Garijo N, Sabaté-Brescó M, Azofra J, Baeza ML, Donado CD, Gaig P, et al. Angioedema severity and impact on quality of life: Chronic histaminergic angioedema versus chronic spontaneous urticaria. J Allergy Clin Immunol Pract. 2022;10(11):3039-3043.e3. doi: 10.1016/j.jaip.2022.07.011.