

Clinical Communications

Factitious angioedema: a mimic of refractory “angioedema”

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Clinical Implication

- Factitious angioedema is likely underrecognized. A diagnosis of factitious angioedema should be considered in any case of refractory “angioedema,” when hereditary angioedema with a normal C1 inhibitor level is being considered, or in any atypical presentation of “angioedema.”

TO THE EDITOR:

Angioedema can be broadly categorized as (1) allergic, (2) idiopathic, (3) angiotensin-converting enzyme inhibitor associated, (4) hereditary, or (5) acquired. Factitious disorder imposed on self, also known as Münchausen syndrome, is characterized by a deceptive report, or an active falsification, of signs or symptoms with the aim of presenting one’s self in the sick role in the absence of other obvious external rewards (ie, malingering).¹ We describe 4 cases of factitious angioedema with objective findings.

CASE 1

A 34-year-old man was hospitalized with recurrent isolated tongue “swelling.” He reported a several-year history of these attacks, with a prior tracheostomy and multiple prior intubations and hospitalizations. He noted no family history of swelling. Prior community management included placement of a peripherally inserted central venous catheter for self-administration of diphenhydramine 100 mg intravenous every 2 hours and methylprednisolone 20 mg intravenous every 12 hours. Past therapies included doxepin, ranitidine, montelukast, prednisone, dapsone, and cyclosporine, none of which improved the attack frequency or severity. During an acute “swelling” episode, results of a physical examination revealed normal vital signs. His tongue was dusky purple and protruding outside of the oral cavity, although the tongue was normal on palpation and without edema or thickening. No other “swelling” was noted on examination. Total tryptase, C4, and C1 esterase inhibitor levels and function were normal. A urine drug screen result was negative. Intra-attack fiberoptic laryngoscopy examination results were normal. We then manually replaced his tongue into his mouth, and he was instructed to keep his mouth closed. Within a few minutes he was able to open his mouth with resolution of the “swelling.” Inpatient psychiatric evaluation commenced, and somatoform disorder was suspected. The patient did not continue outpatient psychiatric evaluation, and he has subsequently presented to other emergency departments in the area with the same tongue “swelling” complaint.

CASE 2

An 11-year-old boy was hospitalized with a 3-month history of recurrent tongue “swelling” and slurred speech. Intramuscular injection of epinephrine (sometimes 2 or 3 injections in a row) would transiently improve these episodes. Multiple courses of prednisone, high-dose cetirizine, montelukast, and ranitidine were unsuccessful in both treatment and prevention of attacks. During an acute episode, results of a physical examination demonstrated normal vital signs, with his tongue protruding from his mouth without apparent distress. Tongue palpation revealed no edema or thickening. A neurologic examination was normal. Total tryptase, C4, C1 esterase inhibitor levels and function, and C1q values were all normal. Intra-attack facial magnetic resonance imaging was normal. Subsequent evaluations revealed that the patient intermittently spontaneously retracted his tongue back into the mouth while talking. Inpatient psychiatric evaluation commenced, and conversion disorder was suspected. The patient and his family were receptive to psychiatric intervention, and he did follow up on an outpatient basis for several therapy sessions, with some improvement. He has not required further evaluation at our center for acute tongue “swelling” since his outpatient psychiatric sessions.

CASE 3

An 18-year-old woman presented to the clinic with recurrent tongue and lip “swelling.” She reported a several-year history of at least monthly mild lip swelling. At a prior hospitalization for a severe “waxing and waning” episode of tongue swelling, an extensive evaluation, including total tryptase, CH50, C4, C3, and C1 inhibitor levels and function, magnetic resonance imaging of the tongue, and lip and tongue biopsy results, was normal. Prior failed therapies included multiple courses of corticosteroids, high-dose antihistamines, epsilon aminocaproic acid, and cyclosporine. She also was treated with danazol and had been diagnosed with hereditary angioedema with a normal C1 inhibitor level. Analysis for factor XII mutations was negative. During a subsequent acute attack while in our clinic, results of a physical examination revealed normal vital signs, no distress, and a clenched jaw with her tongue slightly protruding but not edematous (Figure 1). Palpation of her tongue revealed soft, pliable tissue without edema or thickening. Her jaw was able to be loosened by gentle manipulation and her tongue retracted back into her mouth upon gagging. A presumptive diagnosis of factitious angioedema was made, and formal psychiatric evaluation was recommended. Psychiatric evaluation was not pursued by the patient.

CASE 4

An 18-year-old woman presented with a 2-year history of daily musculoskeletal pain and nausea associated with swelling of her lip, tongue, and lower back (Figure 2). These episodes typically lasted 10 minutes at a time. A prior workup included negative evaluations for occult infection, vasculitis, mastocytosis, auto-inflammatory, and periodic fever syndromes, and for both hereditary and acquired angioedema. Prior failed therapies included H1 and H2 antagonists, montelukast, corticosteroids, omalizumab, dapsone, hydroxychloroquine, sulfasalazine, cyclosporine, and androgens. Progesterone-induced angioedema and hereditary

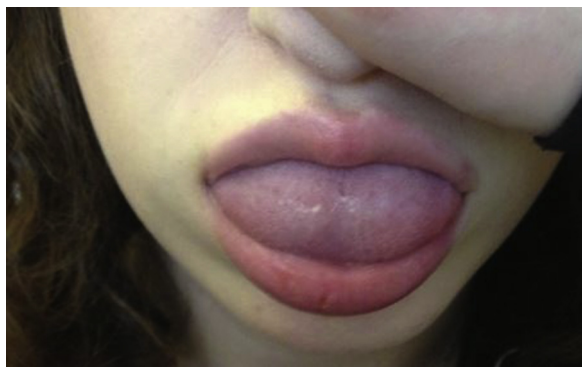


FIGURE 1. The patient in case 3 during an acute “angioedema” attack. No angioedema was palpable, and the tongue spontaneously retracted to normal via a gag maneuver. The tongue was also easily manually replaced in the mouth.

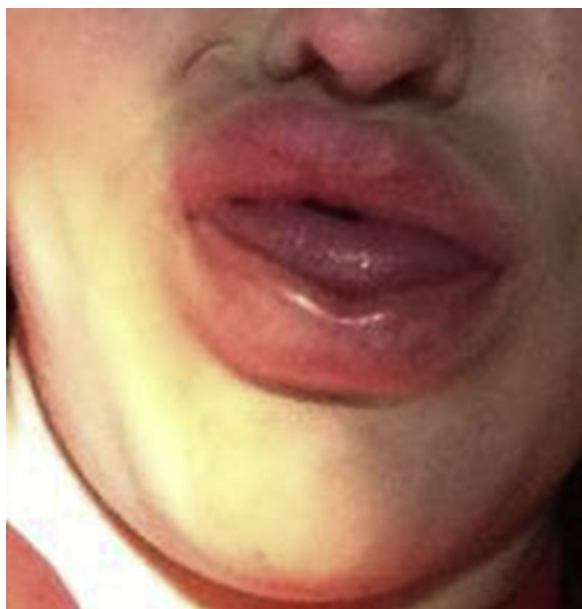


FIGURE 2. The patient in case 4 during an acute “angioedema” attack. Her apparent lip and tongue swelling would resolve spontaneously within 10 minutes. Despite a report of associated throat “swelling,” results of an intra-attack laryngoscopy demonstrated no laryngeal edema but did demonstrate vocal cord dysfunction.

angioedema with normal C1 inhibitor value, were suspected but gonadotropin-releasing hormone agonist injections and C1 esterase replacement therapy, respectively, had no effect. Intra-attack laryngoscopy demonstrated vocal cord adduction and no edema during a sensation of throat “swelling.” All angioedema-specific therapies subsequently were stopped, and, along with hydration and rest, she was started on COX-2 inhibition for pain and antiemetics for nausea. She is currently seeing a psychologist for suspected factitious angioedema.

CONCLUSIONS

We posit that factitious angioedema most accurately describes and unifies these 4 clinical presentations. The *Diagnostic and*

Statistical Manual of Mental Disorders 5th edition criteria provides updated terminology for case 1: factitious disorder imposed on self is a specific subtype of the somatic symptom and related disorders (formerly known as somatoform disorder). Furthermore, no medication-related or work absence—related secondary gain could be identified in case 1, therefore, malingering does not apply. In pediatric patients, factitious disorder imposed by another (also known as Münchausen syndrome by proxy) should be considered, but no supporting evidence for Münchausen syndrome by proxy was uncovered in case 2. In addition, during multiple interactions with our patient in case 2, we noted his contentedness with assuming the sick role. Thus, we favor a diagnosis of factitious disorder imposed on self (intentional sick role) instead of conversion disorder (unintentional sick role with neurologic symptoms).

Angioedema due to surreptitious use of aspirin with a patient with known aspirin sensitivity and angioedema due to ingestion of tree nuts with a patient with known tree nut allergy have been previously reported in the literature.² Other reports have described patients who were referred for evaluation of possible idiopathic anaphylaxis but who presented with various different subjective complaints.³ In our case series, the patients presented in a fundamentally different way than in prior series; our patients were not factitiously precipitating true allergic angioedema nor were they endorsing vague subjective complaints. Rather, all 4 of our patients presented with objective but truly falsified tongue and/or lip angioedema.

In our case series and in another,³ the erroneous diagnosis of angioedema contributed to significant cost expenditures and morbidity. A thorough physical examination, including palpation of pertinent structures, supports or refutes the diagnosis of angioedema. Patient-supplied images may aid in the diagnosis but may also be falsified or deceptive. The total tryptase level was not elevated in all 4 of our patients. An elevated tryptase level is a valuable diagnostic test to confirm systemic mast cell activation and, when present, is extremely useful. Unfortunately, the tryptase level is rarely elevated with patients who present with angioedema in the absence of anaphylaxis and is not different in those with allergic reactions with and without angioedema.⁴ Three of the 4 patients in this series were previously diagnosed with hereditary angioedema with a normal C1 inhibitor value, which is thought to be exceedingly rare.⁵ Factitious disorder may be present in 1% of hospitalized patients.¹ We believe a diagnosis of factitious angioedema should be considered with any case of refractory “angioedema” when hereditary angioedema with a normal C1 inhibitor value is being considered or with any atypical presentation of “angioedema.”

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REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition. Arlington, VA: American Psychiatric Association. Available from: dsm.psychiatryonline.org; 2013. Accessed October 7, 2013.
2. Hendrix S, Sale S, Zeiss CR, Utley J, Patterson R. Factitious Hymenoptera allergic emergency: a report of a new variant of Munchausen's syndrome. *J Allergy Clin Immunol* 1981;67:8-13.
3. Choy AC, Patterson R, Patterson DR, Grammer LC, Greenberger PA, McGrath K, et al. Undifferentiated somatoform idiopathic anaphylaxis: non-organic symptoms mimicking idiopathic anaphylaxis. *J Allergy Clin Immunol* 1995;96:893-900.
4. Lin RY, Schwartz LB, Curry A, Pesola GR, Knight RJ, Lee HS, et al. Histamine and tryptase levels in patients with acute allergic reactions: an emergency department-based study. *Allergy Clin Immunol* 2000;106(Pt 1):65-71.
5. Zuraw BL, Bork K, Binkley KE, Banerji A, Christiansen SC, Castaldo A, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc* 2012;33(Suppl 1):s145-56.