

A 72-year-old woman with periorbital swelling

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ABSTRACT

As allergists, we are frequently consulted to evaluate patients with swelling presumed to be angioedema. Patients with presumed angioedema can have multiple possible underlying triggers. We present the case of a hospitalized 72-year-old woman with a history of hypertension and metastatic chordoma who developed marked periorbital swelling that precluded eye opening 2 days after a neurosurgical operation (chordoma resection and T10-11 hardware repair). After a detailed evaluation of her swelling, a broad differential diagnosis was made; she did not respond to high-dose antihistamines, systemic steroids, icatibant and angiotensin-converting enzyme inhibitor cessation. Ultimately, computed tomography imaging confirmed a specific diagnosis. The differential diagnosis for swelling is complex, and this case illustrated the importance of considering alternative causes of swelling when evaluating cases of possible angioedema.

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CHIEF CONCERN

Postoperative periorbital swelling.

History of Present Illness

A 72-year-old woman with a history of hypertension (on enalapril for multiple years) and metastatic chordoma that involved the spine, chest wall, and tibia was admitted to the neurosurgical service for chordoma resection and T10-11 hardware repair. Before surgery, she was treated with dexamethasone (4 mg intravenous every 8 hours), which was continued in the postoperative period. Her postoperative pain was managed with scheduled oxycodone and as-needed hydromorphone. Due to perioperative blood loss and decline in hemoglobin (12.0 g/dL on admission, to a nadir of 8.5 g/dL 2 days after surgery), she received a transfusion of 5 units of packed red blood cells. Thirty minutes after initiation of the blood transfusion, the patient became hypotensive (90/64 mm Hg), which resolved within 30 minutes without intervention. However, 4 hours after completion of the blood transfusion, she developed mild periorbital swelling. Over the next 48 hours, her facial swelling

progressed to severe periorbital swelling, without rash, that precluded eye opening.

The patient's primary service contacted the Allergy/Immunology consult service for evaluation of ongoing facial swelling. The patient had no history of blood transfusion reactions, facial angioedema, or anaphylaxis. The patient's chronic antihypertensive medications included atenolol and enalapril, with hydralazine added 1 month before presentation. On review of systems, the patient stated no tongue or lip swelling, dyspnea, dysphagia, pruritus, rash, wheezing, abdominal pain, vomiting, or diarrhea. She stated that she had no family history of angioedema.

Physical Examination

Vital signs were within normal limits. Examination was only remarkable for severe bilateral periorbital swelling precluding eye opening (Fig. 1). The oral mucosa was moist, without evidence of lip, tongue, or uvular swelling, or of oral lesions. Results of a cardiac examination revealed a normal rate, regular rhythm, and no murmurs. The lungs were clear bilaterally. The abdomen was soft and nontender. The extremities were not edematous. There was no rash on skin examination.

Laboratory Findings

Results of a laboratory evaluation, including C4 complement level, C1 esterase inhibitor quantity and function, C1q level, and immunoglobulin A level, were normal (Table 1).

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Figure 1. Photograph of the patient, demonstrating marked bilateral periorbital swelling that precluded eye opening.

Table 1 Laboratory results

	Results	Reference Range
C4, mg/dL	33	16–38
C1 esterase inhibitor, mg/dL	51	21–39
C1 esterase inhibitor activity, %	>100	>68
C1q, mg/dL	6.3	5–8.6
Immunoglobulin A, mg/dL	117	82–453

Clinical Course

The patient's enalapril was discontinued. Given the progressive nature of her facial swelling, empiric icatibant (30 mg subcutaneous) was administered. She was also initiated on cetirizine 10 mg and famotidine 20 mg, both twice daily, and montelukast 10 mg nightly. She was transitioned from intravenous dexamethasone to oral prednisone 40 mg twice daily. The patient did not demonstrate significant improvement in her swelling after icatibant administration. She was continued on prednisone, histamine H1 and H2 receptor antagonists (H1/H2 blockers), and montelukast without improvement over the following 4 days. Her periorbital swelling persisted, and she remained unable to open her eyes. She also developed waxing and waning bilateral swelling of the hands that intermittently improved when she was in the upright position. Because she did not show clinical improvement with these therapies, the Allergy/Immunology consult team recommended discontinuation of H1/H2 blockers and montelukast, and initiation of prednisone taper over 72 hours. Given a concern for volume overload causing dependent

edema, she was administered 2 doses of furosemide without improvement. An ophthalmologist was consulted and noted normal bilateral visual acuity and had no further recommendations. Seven days after surgery, in addition to continued periorbital swelling, the Allergy/Immunology consult team noted crepitus of the bilateral upper extremities on examination.

QUESTIONS

1. What Is the Differential Diagnosis?

- Angiotensin-converting enzyme (ACE) inhibitor induced angioedema
- Opiate-associated angioedema
- Angioedema secondary to a transfusion reaction (symptom onset in close temporal proximity to blood transfusion and hypotension during transfusion)
- Acquired angioedema (active diagnosis of metastatic chordoma)
- Idiopathic angioedema

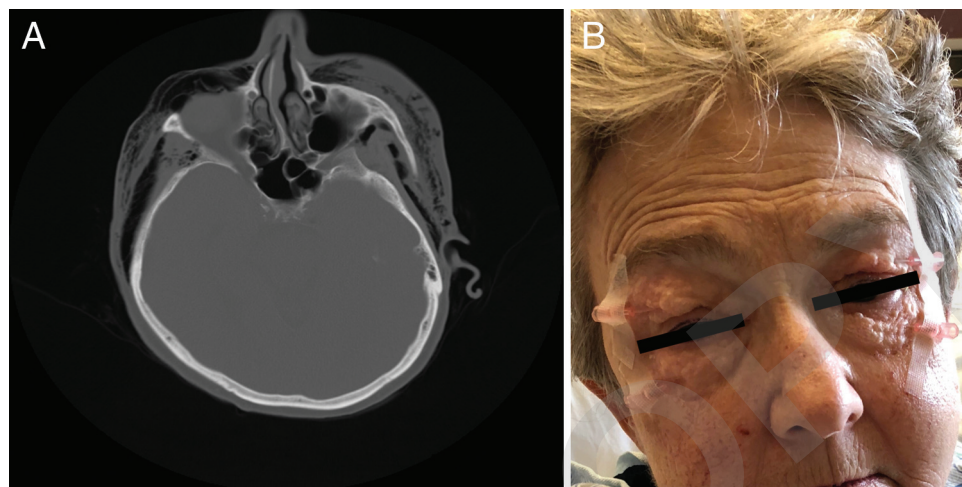
2. What Additional Laboratory Data or Investigations Would Be Helpful in Arriving at a Diagnosis in This Patient?

Given the presence of bilateral upper-extremity crepitus on examination in a postsurgical patient and persistent periorbital swelling, computed tomography (CT) of the chest, head, and neck was the next logical step. CT imaging was obtained and was notable for extensive pneumomediastinum and subcutaneous emphysema throughout the entirety of the anterior and posterior chest wall and throughout the soft-tissue planes of the neck and extending into the periorbital region (Fig. 2A). The Cardiothoracic Surgery team was consulted for management of pneumomediastinum and subcutaneous emphysema. Angiocatheters were placed in the bilateral eyelids and bilateral anterior chest. The patient demonstrated marked improvement in periorbital swelling immediately after this intervention at the bedside, and she was able to open both eyes within hours of catheter placement (Fig. 2B). Angiocatheters were kept in place for 3 days and were then removed without complication.

DISCUSSION

Angioedema is defined as a "vascular reaction of deep dermal/subcutaneous tissues or mucosal/submucosal tissues with localized increased permeability of blood vessels resulting in tissue swelling."¹ Angioedema can be mediated by mast cell-mediators (allergic and idiopathic angioedema) and/or bradykinin (hereditary, acquired, or ACE-inhibitor-induced forms). For suspected bradykinin-induced

Figure 2 (A) Computed tomography of the head, demonstrating extensive subcutaneous emphysema in the bilateral periorbital regions. (B) Photograph of the patient, demonstrating marked improvement in periorbital swelling after placement of angi catheters in bilateral eyelids.



angioedema, laboratory evaluation includes a C4 level and C1-esterase inhibitor level and function.¹ A C1q is obtained for possible acquired angioedema, which should be considered in patients ≥ 40 years of age, with a negative family history for swelling and/or patients with swelling in the setting of underlying conditions, such as monoclonal gammopathy and lymphoma.¹

Mast cell-mediated angioedema is often treated with antihistamines, leukotriene-receptor antagonists, corticosteroids, and epinephrine. Bradykinin-mediated swelling can be treated acutely with C1-inhibitor concentrate or bradykinin-inhibitors, such as ecallantide or icatibant. Mast cell-mediated angioedema is more common than bradykinin-mediated angioedema. Therefore, in patients with acute onset swelling in whom the underlying diagnosis is undetermined, it is appropriate to treat these patients with antihistamines, leukotriene receptor antagonists, and corticosteroids while the diagnostic workup is underway.¹ In cases of presumed ACE-inhibitor-induced angioedema, the ACE inhibitor is discontinued and icatibant has been used acutely.²

In this case, the failure of the above treatments and development of subcutaneous crepitus of the upper extremities in this postoperative patient prompted further radiologic evaluation, which revealed subcutaneous emphysema as the cause of periorbital swelling. Her periorbital swelling was thought to be due to initial pulmonary barotrauma and subsequent tracking subcutaneous emphysema in the setting of her recent neurosurgical procedure.

Periorbital subcutaneous emphysema has been reported as a complication of invasive procedures. There are literature reports of this complication after dental procedures and upper-gastrointestinal endoscopy.^{3,4} Moreover, there is a case report of subcutaneous periorbital and facial emphysema mistaken for angioedema after a dental procedure.⁵ A review of 78 cases of

patients with orbital subcutaneous emphysema from 1900 to 1994 found that the majority (49 cases) were due to blunt trauma, 7 cases were post-surgical, and 6 were due to pulmonary barotrauma.⁶ This literature review indicated that subcutaneous emphysema is a recognized, albeit uncommon, complication of surgical procedures. Timely recognition of this phenomenon can lead to improved patient outcomes, targeted therapeutic intervention, and minimization of unnecessary testing and treatments.

Final Diagnosis

Periorbital subcutaneous emphysema as a postoperative complication.

CONCLUSION

The onset of periorbital or facial swelling in the patient who is hospitalized should prompt allergists to formulate a broad differential diagnosis and consider alternative causes of swelling beyond allergic and bradykinin-mediated angioedema. Normal laboratory evaluation for different causes of angioedema and the lack of response to bradykinin inhibition, steroids, antihistamines, and leukotriene receptor antagonists suggest that the appearance of swelling is not consistent with angioedema.

In this case, the establishment of a broad differential diagnosis and thorough physical examination allowed for consideration of alternative causes of swelling. Ultimately, the finding of crepitus on physical examination led to CT imaging, which demonstrated subcutaneous emphysema as a postoperative complication that caused periorbital swelling. In the evaluation of patients with presumed angioedema, the presence of crepitus in association with postoperative swelling warrants timely radio-

logic imaging for evaluation of possible subcutaneous emphysema.

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