Journal of Chemical Health Risks

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JCHR (2024) 14(5), 48-54 | ISSN:2251-6727

Case Report: Angioneurotic Edema Mimicking a Skull Base Lesion

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(**Received**: 14 June 2024 **Revised**: 01 July 2024 **Accepted**: 18 August 2024)

KEYWORDS
diagnostic, angioedema
Angioneurotic edema
subcutaneous

ABSTRACT:

Angioneurotic edema, also known as angioedema, is a condition characterized by rapid localized swelling due to fluid accumulation in the deep dermal and subcutaneous tissues. It is typically associated with allergic reactions, hereditary factors, or medication side effects. Skull base lesions, on the other hand, are rare but distinct pathological entities that are usually identified through imaging or biopsy. The overlap between these two conditions is exceedingly rare, leading to diagnostic challenges.

We present a rare case of angioneurotic edema clinically mimicking a skull base lesion. A 51-year-old male presented with acute onset swelling of the soft palate, initially suspected to be a skull base lesion based on clinical findings. Despite typical characteristics of angioneurotic edema, the presentation was atypical, leading to significant diagnostic uncertainty. Detailed clinical history, laboratory investigations, and imaging studies were utilized to differentiate between these conditions.

Clinicians should be aware of the potential for angioneurotic edema to mimic skull base lesions. Comprehensive evaluation, including detailed patient history, laboratory tests, and imaging, is essential for accurate diagnosis and appropriate management. This case underscores the need for heightened awareness and consideration of rare mimickers in differential diagnoses to prevent mismanagement and ensure optimal patient outcomes.

Introduction

Angioneurotic edema, now more commonly referred to as angioedema, is a condition characterized by sudden and rapid swelling of the deeper layers of the skin and mucous membranes. It is a relatively common presentation in the emergency department (ED), where it often manifests as unpredictable, recurrent episodes of edema affecting the cutaneous and mucosal tissues, including the lips, eyes, oral cavity, larynx, and gastrointestinal system. Angioedema can occur in conjunction with urticaria (hives) as part of a spectrum of allergic symptoms or can arise independently from non-allergic causes. Notably, laryngeal edema is a severe form of angioedema that can lead to airway obstruction and potentially fatal outcomes if not promptly diagnosed and treated [1].

Historically, angioneurotic edema was referred to by various terms, such as "ephemeral cutaneous nodosities," "ephemeral congestive tumors of the skin," "wandering edema," and "giant hives." However, since 2007, the condition has been consistently referred to as angioedema in medical literature [2]. Angioedema can be classified into several types based on its underlying causes, including allergic, hereditary, and acquired forms. Allergic angioedema is typically triggered by immune system overreactions to allergens, such as certain foods, medications, or insect stings, leading to the release of histamine and other inflammatory mediators that cause tissue swelling. Hereditary angioedema (HAE), a genetic condition, results from a deficiency or dysfunction of the C1-inhibitor, a protein that regulates inflammatory and clotting pathways. Acquired angioedema can occur due to various factors, including medications like ACE inhibitors, autoimmune disorders, or underlying diseases such as lymphoproliferative disorders, often mimicking hereditary angioedema in its pathophysiology [3].

The majority of angioneurotic edema cases are allergic in origin, triggered by a Type 1 hypersensitivity reaction that rapidly induces swelling through histamine-mediated activation of mast cells and basophils. In contrast, non-allergic forms, particularly those mediated by bradykinin, can develop more insidiously and are not responsive to typical antihistamine treatments. In hereditary and some acquired forms of angioedema, the overproduction of bradykinin, due to the deficiency of the C1-inhibitor, plays a central role in the pathophysiology, leading to vasodilation, increased vascular permeability, and mucosal swelling. This can result in severe clinical manifestations, including life-threatening airway obstruction if the swelling involves the larynx [4,5,6].

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JCHR (2024) 14(5), 48-54 | ISSN:2251-6727

Differentiating angioneurotic edema from other serious conditions, such as skull base lesions, can be challenging due to overlapping clinical features. Skull base lesions are rare but potentially serious pathological entities that often require different diagnostic and therapeutic approaches. Imaging studies, particularly CT and MRI, are essential tools in distinguishing between these conditions. Angioedema typically presents as diffuse soft tissue swelling without a distinct mass, whereas skull base lesions are usually well-defined and may show specific patterns of enhancement with contrast agents on imaging. In cases where the clinical history and imaging are inconclusive, endoscopy and biopsy may be necessary to rule out malignancy or other serious conditions [7].

In this report, we discuss a rare case of angioneurotic edema that mimicked a skull base lesion. The patient, a 51-year-old male, presented with symptoms that were initially concerning for a skull base lesion, including swelling in the soft palate and associated clinical findings. This case underscores the importance of a thorough differential diagnosis and the need for clinicians to consider atypical presentations of more common conditions, such as angioedema when evaluating patients with unusual or ambiguous symptoms.

Case Presentation

Patient Information:

The patient is a 51-year-old male who presented to the ENT outpatient department (OPD) with a chief complaint of difficulty swallowing (dysphagia) and a sensation of throat blockage. These symptoms had been present for four days prior to presentation and were described as sudden in onset and gradually progressive. The patient did not report any specific aggravating or relieving factors for his symptoms. He also noted a recent change in his voice and had been experiencing intermittent throat pain, which he described as mild and occurring sporadically over the past few weeks.

The patient's medical history was significant for type 2 diabetes mellitus, for which he was on oral hypoglycemic agents. He had no known drug or food allergies, and there was no family history of hereditary angioedema or other similar conditions. Additionally, the patient denied any history of recent infections, trauma, or stress, which could potentially trigger angioedema. He also did not report any symptoms such as fever, weight loss, or loss of appetite, which might suggest a more systemic or malignant process.

Clinical Examination:

During the physical examination, the patient appeared to be in mild distress due to the sensation of throat blockage but was otherwise stable. Vital signs were within normal limits, with no evidence of respiratory distress or hemodynamic instability.

During the local examination of the throat, the patient's lips, gums, and teeth appeared normal, showing no signs of swelling or inflammation. However, the soft palate was notably edematous and congested, with swelling more pronounced on the left side, causing the mucosa to appear erythematous and thickened. This asymmetry raised concerns about potential underlying pathology. The uvula was similarly affected, showing signs of edema and congestion, which contributed to the sensation of throat blockage. The uvula was elongated and slightly deviated to the right, likely due to the significant swelling on the left. The bilateral anterior pillars showed mild congestion but did not present with any significant swelling or masses. Examination of the posterior pharyngeal wall (PPW) was challenging, as the swollen soft palate and uvula partially obstructed the view, limiting the ability to fully assess this area for further abnormalities.

An examination of the ears and nose revealed no abnormalities, with both the tympanic membranes and nasal passages appearing normal. No signs of inflammation, masses, or other lesions were detected in these areas.

Given the significant findings in the oropharynx, particularly the pronounced asymmetry and decreased movement of the soft palate, a more detailed evaluation was warranted. The patient underwent a video laryngoscopy on the day of his OPD visit to further assess the extent of the swelling and to rule out any obstructive lesions in the upper airway.

Video Laryngoscopy Findings (Day 1):

The examination of the base of the tongue revealed normal findings, with no evidence of swelling, masses, or other abnormalities. However, the soft palate was notably edematous and congested, with more pronounced swelling on the left side. The mobility of the soft palate was reduced, especially on the left, where movement was visibly impaired. The bilateral arytenoids and

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JCHR (2024) 14(5), 48-54 | ISSN:2251-6727

aryepiglottic folds appeared normal, showing no signs of edema or congestion, and the bilateral pyriform fossae were also normal, with no detectable pathology. The bilateral vocal cords were observed to be free and mobile, with no evidence of obstruction or abnormality. These clinical and laryngoscopic findings led to a diagnosis of significant oropharyngeal edema, which raised concerns about possible underlying causes, including the potential for a skull base lesion. Due to the diagnostic uncertainty, the patient was admitted for further evaluation and management (Figure 1).

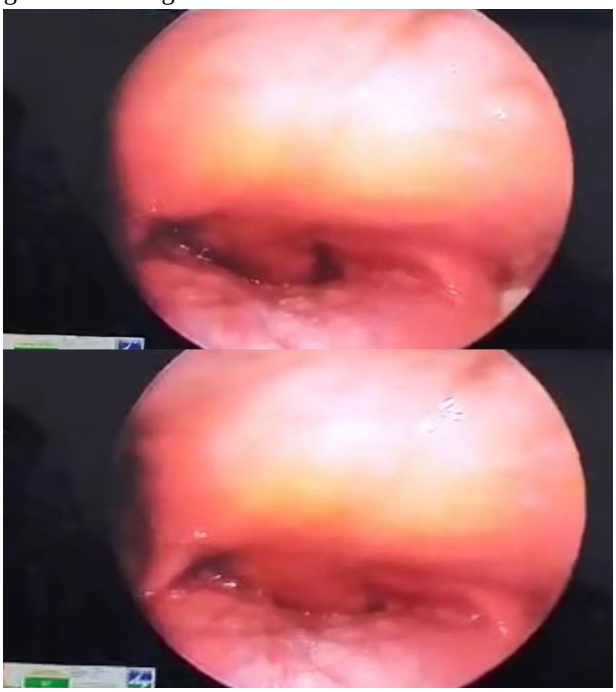

Figure 1. Video Laryngoscopy Findings (Day 1)

Initial Management:

The patient was treated with an intramuscular injection of hydrocortisone, a corticosteroid known for its anti-inflammatory properties, to reduce the swelling. This was done as a precautionary measure while awaiting further diagnostic workup. The patient's symptoms remained stable, and he was closely monitored in the hospital setting.

Further Investigations:

On the second day of hospitalization, a repeat video laryngoscopy was performed to assess the progression of the swelling and to check for any changes in the clinical findings.

Video Laryngoscopy Findings (Day 2):

The base of the tongue remained normal on re-examination, with no new findings. However, the soft palate continued to be edematous and congested, with persistent asymmetry. The swelling on the left side was still prominent, and there was a noticeable decrease in movement in the affected area, raising further concerns about a potential underlying lesion. The bilateral arytenoids and aryepiglottic folds remained normal, as did the bilateral pyriform fossae. The bilateral vocal cords were free and mobile, showing no changes from the previous examination. Due to the persistent asymmetry and reduced movement of the soft palate, particularly on the left side, a neurology consultation was sought to evaluate the possibility of a neurological cause, such as cranial nerve involvement, which could indicate a skull base lesion. Following the neurological assessment, a CT scan of the neck, from the skull base to the mediastinum, was ordered to further investigate the extent of the swelling and rule out any underlying mass or lesion (Figure 2).

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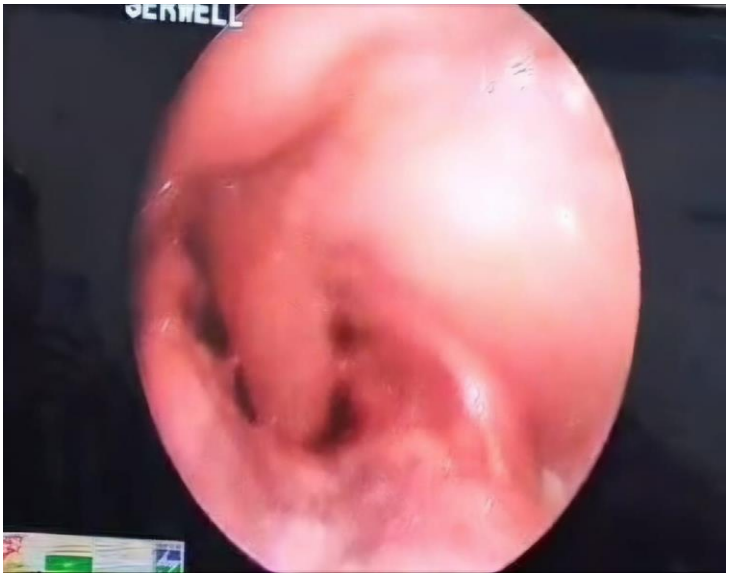

Figure 2. Video Laryngoscopy Findings (Day 2)

CT Neck Findings:

The CT scan revealed edematous changes involving the soft palate and uvula, with several air pockets present in the region. There was a noticeable narrowing of the oropharyngeal airway due to the swelling, but importantly, there was no evidence of a mass lesion, significant lymphadenopathy, or other structural abnormalities that would suggest a skull base lesion. The findings were more consistent with diffuse soft tissue swelling rather than a localized lesion. Despite the reassuring CT findings, an MRI of the neck was performed to provide further detail, particularly regarding the soft tissues, and to exclude any subtle mass lesions that might not be apparent on the CT scan.

MRI Neck Findings:

Impression and Clinical Correlation:

The MRI findings supported the CT results, showing no evidence of a mass lesion but confirming the presence of edematous changes involving the soft palate and uvula. The narrowing of the oropharyngeal airway due to the swelling was consistent with the patient's symptoms of throat blockage and difficulty swallowing (Figure 3).

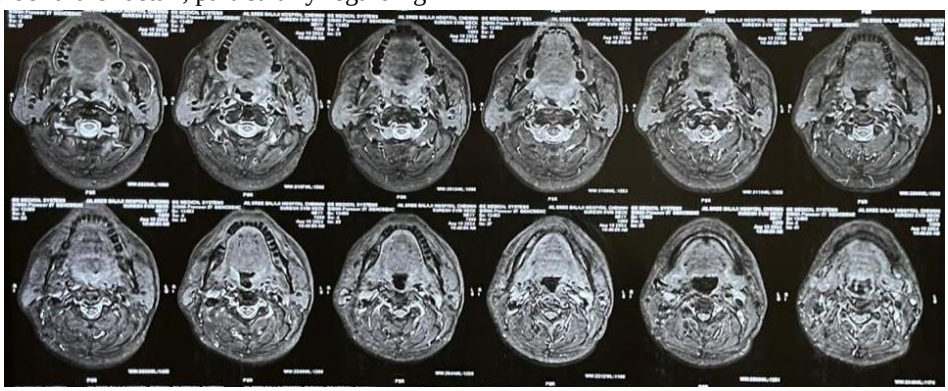

Figure 3. MRI Findings

Post-Treatment Progress:

Five days following the initiation of treatment, the patient showed significant symptomatic improvement. The swelling in the soft palate and uvula had markedly reduced, and the associated symptoms, such as difficulty swallowing and the sensation of throat blockage, had largely resolved. A follow-up examination confirmed the reduction in edema, and a post-treatment image demonstrated clear visual improvement, with the soft palate and uvula appearing less congested and more

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symmetrical (Figure 4). This positive response to therapy underscored the effectiveness of the treatment regimen and supported the diagnosis of angioneurotic edema. The patient continued to recover well, with no further complications observed during this period.

Figure 4. Post treatment progress

Final Diagnosis and Outcome:

Given the imaging findings and the clinical course, the final diagnosis was angioneurotic edema with an atypical presentation, mimicking a skull base lesion. The patient continued to receive corticosteroids, which resulted in a gradual reduction of the edema. Throughout his hospital stay, his symptoms improved significantly, and there were no further episodes of swelling or airway compromise.

The patient was discharged with instructions for follow-up to monitor his condition and to ensure that the edema had completely resolved. He was also advised to avoid potential triggers for angioedema and to seek immediate medical attention if similar symptoms recur.

Follow-Up:

At the follow-up visit, the patient reported complete resolution of his symptoms, and repeat imaging confirmed the absence of any residual edema. The case highlighted the importance of considering angioneurotic edema in the differential diagnosis of patients presenting with atypical oropharyngeal swelling, especially when the initial clinical presentation raises concerns for more serious conditions like skull base lesions.

Discussion

Angioneurotic edema is a complex condition with various underlying causes, each with distinct pathophysiological mechanisms. The condition is broadly categorized into allergic and non-allergic types, with allergic angioedema being the most prevalent. This form of angioedema is mediated by the release of histamine and other inflammatory substances in response to an allergen, leading to the rapid onset of tissue swelling. Common triggers include certain foods, drugs (such as NSAIDs and ACE inhibitors), and insect stings. Hereditary angioedema (HAE) is another well-known form, characterized by its genetic basis involving mutations in the C1-inhibitor gene. The deficiency or dysfunction of the C1 inhibitor leads to uncontrolled activation of the complement and contact systems, resulting in excessive production of bradykinin, a potent vasodilator. Unlike allergic angioedema, HAE does not respond to antihistamines or corticosteroids, making its management more challenging. The episodic nature of HAE, with attacks often triggered by stress, trauma, or infections, further complicates patient care. Acquired angioedema shares similar mechanisms with HAE but occurs in individuals without a genetic predisposition. It is often associated with underlying medical conditions, such as autoimmune disorders or lymphoproliferative diseases, which can lead to the depletion of the C1 inhibitor or the production of autoantibodies against it. Medications, particularly ACE inhibitors, are also a significant cause of acquired angioedema, as they increase bradykinin levels by inhibiting its degradation [8].

Diagnostic Challenges: The clinical overlap between angioedema and other pathological entities, such as skull base lesions, is rare but can lead to significant diagnostic

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confusion. Skull base lesions encompass a wide spectrum of conditions, ranging from benign cysts and tumors to malignant neoplasms, each with its own clinical course and management requirements. The presentation of these lesions can vary widely, but they often include symptoms related to cranial nerve compression, headache, and facial swelling, depending on the lesion's size and location [9]. In this case, the patient's presentation with soft palate swelling and unilateral involvement initially suggested the possibility of a skull base lesion. The clinical findings, including decreased movement on one side of the soft palate, further raised concerns for a neurological or structural pathology involving the skull base. However, the lack of a definitive mass lesion on imaging and the patient's rapid response to corticosteroids eventually pointed toward a diagnosis of angioneurotic edema.

Role of Imaging: Imaging studies play a crucial role in differentiating angioedema from skull base lesions. CT and MRI are particularly valuable in evaluating patients with suspected skull base pathology [10]. Angioedema typically presents on imaging as diffuse swelling of soft tissues without a discrete mass, whereas skull base lesions are usually well-defined and may show characteristic patterns of enhancement with contrast agents. The absence of a mass on imaging, combined with the diffuse nature of the swelling in this case, supported the diagnosis of angioneurotic edema. However, imaging alone is not always definitive, especially in cases where the clinical presentation is atypical. In such instances, a thorough clinical history and physical examination are critical. The presence of a history of allergies, hereditary angioedema, or use of medications known to cause angioedema can provide important clues that support the diagnosis [11].

Pathophysiology Insights: The pathophysiology of angioedema, particularly in cases involving hereditary or acquired forms, is complex and involves multiple pathways of inflammation and vascular regulation. The key mediator in non-allergic angioedema is bradykinin, which leads to vasodilation and increased vascular permeability, resulting in the characteristic swelling. In hereditary angioedema, the lack of functional C1-inhibitor leads to uncontrolled activation of the kallikrein-kinin system, resulting in excessive bradykinin production. This explains why patients with HAE do not respond to conventional treatments for allergic angioedema, such as antihistamines or corticosteroids, and instead require targeted therapies like C1-inhibitor concentrates or bradykinin receptor antagonists. The overlap of these mechanisms in acquired forms of angioedema, particularly those induced by medications such as ACE inhibitors, highlights the importance of recognizing medication history as part of the diagnostic process. ACE inhibitors prevent the breakdown of bradykinin, leading to its accumulation and the onset of angioedema in susceptible individuals. This mechanism is distinct from the allergic pathway and underscores the need for tailored treatment approaches depending on the underlying cause.

Clinical Management and Outcomes: The management of angioedema depends on its etiology. For allergic angioedema, treatment typically involves the use of antihistamines, corticosteroids, and in severe cases, epinephrine. In contrast, the management of hereditary and acquired angioedema requires more specific interventions that target the underlying pathophysiology. For hereditary angioedema, this includes C1-inhibitor replacement therapy, bradykinin receptor antagonists, and in some cases, prophylactic treatment to prevent recurrent attacks [12,13].

In this case, the patient responded well to corticosteroids, indicating that the angioedema was likely histamine-mediated. The resolution of symptoms and the absence of further episodes following treatment confirmed the diagnosis and highlighted the effectiveness of the therapeutic approach used.

Conclusion and Implications for Practice: This case underscores the importance of considering angioedema in the differential diagnosis of patients presenting with atypical swelling, particularly when the clinical presentation suggests a more serious underlying pathology, such as a skull base lesion. The overlap in symptoms between these conditions can lead to diagnostic uncertainty and potential mismanagement if the correct diagnosis is not made promptly. Clinicians must maintain a high index of suspicion for angioedema, even in cases where the presentation is not classic. A comprehensive evaluation, including detailed history-taking, physical examination, and appropriate imaging studies, is essential to avoid misdiagnosis. Early recognition and appropriate management are crucial to prevent complications and ensure optimal patient outcomes. This case also highlights the need for further research and awareness of rare presentations of common conditions like angioedema. By understanding the full spectrum of clinical manifestations and the underlying pathophysiological mechanisms, clinicians can improve their diagnostic accuracy and

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JCHR (2024) 14(5), 48-54 | ISSN:2251-6727

provide better care for patients with complex presentations.

Conclusion

This case highlights the importance of considering angioneurotic edema in the differential diagnosis of patients presenting with atypical swelling, particularly when the clinical presentation mimics more serious conditions such as skull base lesions. A thorough clinical evaluation, including detailed history, physical examination, and appropriate imaging studies, is essential for accurate diagnosis and management. Clinicians should be aware of the potential for angioneurotic edema to present in unusual ways, leading to diagnostic uncertainty. Early recognition and appropriate treatment are crucial to prevent complications and ensure optimal patient outcomes.

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