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SUPERIOR VENA CAVA SYNDROME MIMICKING AN ALLERGIC ANGIOEDEMA: A DIAGNOSTIC ODYSSEY FROM ALLERGIC REACTION TO MEDIASTINAL B-CELL LYMPHOMA

Simone Burgener-Enderli[1], Andreas Schmitt[2], Stefano Bassetti[1], Mark Kirsch[1]

[1] Division of Internal Medicine, University Hospital of Basel, Basel, Switzerland
[2] Division of Medical Oncology, University Hospital of Basel, Basel, Switzerland

Corresponding author's e-mail: sim.burgener@gmail.com

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ABSTRACT

An 18-year-old woman presented to her general practitioner with a history of non-itching facial swelling, erythematous skin rash and a slightly coarse voice for a few days. She denied dyspnoea, B-symptoms and pain. Physical examination revealed generalized facial and neck swelling not involving the tongue or the oral mucous membranes. There was no lymphadenopathy. These findings resulted in the diagnosis of allergic angioedema and in oral treatment with corticosteroids and antihistamines. The swelling responded partially but reoccurred with dose reduction of the corticosteroids. Outpatient referrals to a dermatologist, an endocrinologist and a rheumatologist resulted in confirmation of the diagnosis of allergic angioedema, suspected iatrogenic Cushing syndrome and possible connective tissue disease, respectively.

Three months after the first outpatient presentation the patient was admitted to our hospital with severe fatigue and left-sided chest pain. The clinical examination showed the known facial and neck swelling- and a sinus tachycardia (120 bpm) without any fever. Furthermore, the neck swelling seemed to be slightly asymmetrical. This was accompanied by leucocytosis, elevated C-reactive protein, and lactate dehydrogenase. An electrocardiogram showed sinus tachycardia (120/min) with a S1Q3-type. An ultrasound of the neck showed thrombosis of the left jugular vein. Subsequent computed tomography scan of the chest revealed a large mediastinal mass causing acute superior vena cava syndrome. Mediastinal large B-cell lymphoma was confirmed by biopsy. The patient underwent six cycles of DA-R-EPOCH (rituximab, etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin). Treatment resulted in complete response.

KEYWORDS

Facial swelling, superior vena cava syndrome, anchoring bias, primary mediastinal B-cell lymphoma

LEARNING POINTS

- Vena cava superior syndrome is caused in over 60% of the cases by malignancies (bronchogenic carcinoma, lymphoma, germ cell tumour).
- Facial swelling, plethora of the upper chest without itchiness and hoarseness are classical symptoms of thoracic central venous obstruction.
- At every patient visit open-minded clinical reasoning should be used to avoid anchoring bias.

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INTRODUCTION/BACKGROUND

In an 18-year-old woman, the classic symptoms of superior vena cava syndrome (SVCS) were mistakenly interpreted as an allergic angioedema. Symptoms such as facial swelling, erythema, and hoarseness occur in both SVCS and allergic angioedema[1]. The key distinguishing factor is that erythema in allergic angioedema is histamine-mediated, localized and is associated with urticaria and pruritus. In contrast, SVCS does not involve histaminergic symptoms such as pruritus, urticaria, or diarrhoea. Instead, hallmark manifestations include neck swelling and dyspnoea. The possible accompanying redness, indicative of plethora, appears in a generalized manner rather than being confined to localized areas of the body[2]. The clinical picture was further confounded by the incorrect assumption of a bradykinin-induced angioedema, which, while also not associated with urticaria, typically does not present with erythema. Diagnostic uncertainty was exacerbated by the patient's positive response to corticosteroid therapy. However, an important learning point is that the primary components of allergic angioedema treatment consist of corticosteroids and antihistamines, but if there is no response to these treatments, the working hypothesis should be reconsidered.

CASE DESCRIPTION

A previously healthy 18-year-old woman presented to her general practitioner with ongoing bilateral neck and facial swelling, hoarseness and erythematous non itching skin of the upper chest. The emergency department physicians and the general practitioner interpreted the signs and symptoms as an allergic reaction and prescribed antihistamines and low dose of corticosteroids (prednisone 10 mg/d). Partial improvement and a dermatologist referral resulted in increasing the dose of corticosteroids to 50 mg/d. This resulted in a significant improvement of facial swelling *(Fig. 1)*, disappearance of upper chest redness and hoarseness. However, tapering of the corticosteroid dose resulted in a flare-up of the initial symptoms. Therefore, an endocrinologist suspected iatrogenic Cushing syndrome and strongly recommended tapering the corticosteroid dose. A referral to a rheumatologist resulted in the differential diagnosis of collagenosis and furthermore, testing for antinuclear antibody, C3, C4, and various myositis-specific antibodies was initiated.

Finally, the patient was admitted to our hospital with severe fatigue and left-sided chest and neck pain. In addition to the earlier described facial and neck swelling we found a significant unexplained sinus tachycardia (120 bpm) in the afebrile patient. Furthermore, the neck swelling seemed to be slightly asymmetrical. This was accompanied by elevated C-reactive protein (42.9 mg/l), leukocytosis (14.11 g/l) and lactate dehydrogenase (LDH) (512 U/l). Liver function tests, coagulation panel, creatinine, electrolytes and cardiac markers were normal. An electrocardiogram (ECG) showed a sinus tachycardia with a S1Q3-type. The asymmetrical neck swelling resulted in our next diagnostic step, an ultrasound of the neck. Here we identified thrombosis of the left jugular vein. This finding on top of sinus tachycardia, S1Q3 type in ECG and elevated LDH resulted in a computed tomography (CT) scan of the chest to search for pulmonary embolism or acute SVCS. The CT scan revealed a large mediastinal mass causing acute SVCS *(Fig. 2)*.

Mediastinal large B-cell lymphoma was confirmed by biopsy. Our patient underwent six cycles of DA-R-EPOCH (rituximab, etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin) resulting in complete response.

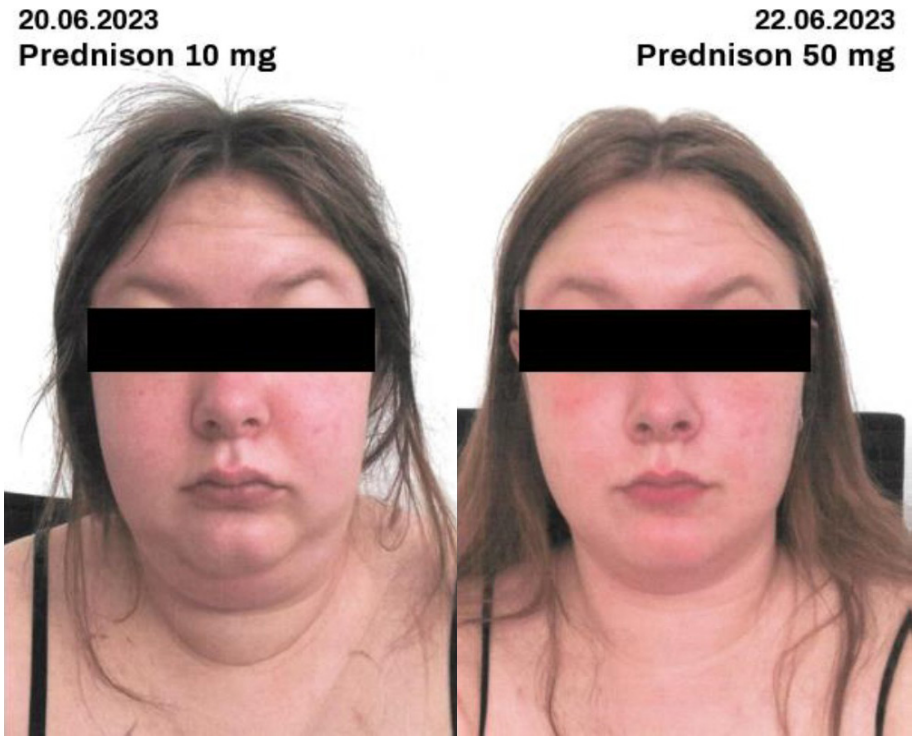


Figure 1. Rapid clinical response to higher dosage of corticosteroids.

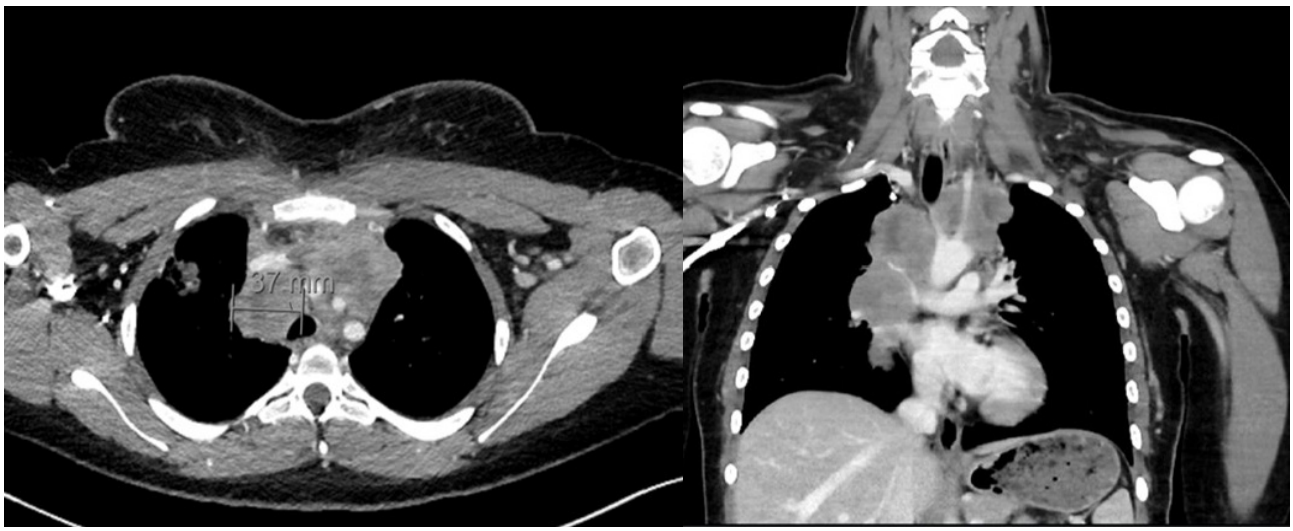


Figure 2. Initial computed tomography scan of the chest on the day of admission showing a large mediastinal mass.

DD facial swelling	Prevalence/incidence	Key findings
Angioedema (histaminergic, hereditary, idiopathic)	10-20% of population[4] (allergic, worldwide) Prevalence: 2/100'000 (hereditary, CH)[5]	• Onset: min-hours, resolution hours-days • Distribution: face, lips, larynx, bowels, • Asymmetric, non-pitting • Accompanying features: ±urticaria[1]
Hypothyroid myxoedema	Incidence: 262.2/100'000/y[6] (hypothyroid dysfunction, EU)	• Onset: days • Distribution: face, legs • Symmetric, non-pitting[4] • Accompanying features: bradycardia, depression, weight gain dry skin, intolerance to cold, obstipation
Connective tissue disease lupus (SLE), dermatomyositis (DM)	Prevalence DM: 13/100,000[7] (US) Prevalence SLE: 30/100'000[8] (CH)	• Onset: days-weeks (SLE, DM) • Distribution: hands (Gottron's papules, DM), periorbital (DM), malar distribution cheeks and nose, sparing nasolabial folds (SLE) • Symmetric, erythematous • Accompanying features: weakness, fatigue, weight loss (DM, SLE), appears after sun exposure (SLE)[8]
Cushing syndrome/disease	Incidence: 0.2/100'000/y[8] (DE)	• Onset: days-weeks • Distribution: head, neck, between shoulders • Accompanying features: weight gain, easy bruising, thin arms and legs, abdominal purple stretch marks[8]
Malignancy-related vena cava superior syndrome	Incidence: 15,000 cases/y[9] (US)	• Onset: days-weeks • Distribution: head, neck, arms • Accompanying features: B-symptoms, hoarseness, dyspnoea and dysphagia[9]
Mononucleosis	Seroprevalence 90-95%[3] (worldwide)	• Onset: early transient • Distribution: upper eyelid, oral • Accompanying features: B-symptoms, lymph node swelling, fever[3]
Other rare diseases: Morbihan disease, Gleich syndrome, Melkersson-Rosenthal syndrome, Chagas® disease...		

Abbreviations: DD, Differential diagnosis; CH, Switzerland; EU, European Union; US, United States; DE, Germany.

Table 1. Differential diagnosis of facial swelling.

DISCUSSION

Chest pain, asymmetrical neck and facial swelling, sinus tachycardia, and elevated inflammatory markers and LDH levels strongly support the diagnosis of acute SVCS, often reflecting an underlying mediastinal malignancy. Among malignancies causing central venous obstruction, bronchogenic carcinomas are most common, while lymphomas rank third[2].

This case underscores the diagnostic challenge of differentiating SVCS from angioedema. Certain clinical features can aid in avoiding misdiagnosis. For instance, allergic angioedema typically shows a rapid response – within hours to a few days – to corticosteroids and antihistamines, whereas bradykinin-mediated angioedema generally follows a more protracted course without clinical improvement under steroid therapy[3]. Similarly, a delayed or absent response to corticosteroids may also be observed when SVCS is the underlying cause, as in the case of a mediastinal B-cell lymphoma, such as in our patient. This symptomatic overlap can further obscure a clear diagnosis. In the present case, asymmetrical facial swelling, thoracic pressure, sinus tachycardia, and, most notably, plethora – a diffuse facial redness – were key clinical signs pointing toward SVCS.

We provide a useful mnemonic for recognizing SVCS: FACE SVC - **F**acial swelling, **A**rm swelling, **C**yanosis, **E**ngorged neck veins, **S**hortness of breath, **V**enous distention, **C**ough/chest discomfort.

Accurate identification of facial swelling requires a comprehensive medical history, including symptom onset, duration, and associated features such as fever, dyspnoea, dizziness, or headache. An objective assessment of the swelling – its symmetry, localization, and extent – is also essential. Following history and examination, visualizing key differential diagnoses can guide further evaluation. *Table 1* supports this process by correlating symptoms with their respective prevalence and incidence. Finally, it is vital to continuously assess treatment responses and monitor the progression of clinical signs to avoid diagnostic fixation – known as anchoring bias – and ensure appropriate clinical reasoning throughout the patient's course.

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