CASE REPORT

Acquired Angioedema of the Glottis, Larynx and Neck in a Patient Affected by SLE: Case Report

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Acquired angioedema is a rare complication of systemic lupus erythematosus (SLE). It is generally secondary to C1 inhibitor deficiency due to antibody formation directed against the C1 inhibitor molecule. Face, mouth, tongue, lips, extremities and genitalia are generally involved but also respiratory and gastrointestinal mucosa may be affected. We report a case of a young woman with SLE who presented a severe airway obstruction caused by angioedema. We discuss her diagnostic and therapeutic management including a review of the literature.

Keywords: Angioedema; Lupus; Case report

Introduction

SLE is an autoimmune disease of unknown etiology characterized by a variable course and prognosis with clinical and laboratory manifestation that can involve any organ system (Wallace & Metzger 1997). Angioedema, secondary to C1 inhibitor deficiency, has rarely been reported to be associated with SLE (Habibagahi et al. 2015).

Case report

We describe a 27-year old woman who came from the Internal Medicine Unit of another hospital where she was diagnosed with SLE. She suffered from headaches, migratory arthritis, fever, diarrhea episodes and rectal bleeding. ANA, anti-DNA antibodies and the direct Coombs test were positive (ANA = 1/1280; anti-DNA = 1/10; IgG = 1/30). She had pancytopenia (WC = 3.4 \( \times \) 10\(^3\)/ml; Hb = 9.5 mg/ml; thrombocytes = 109 \( \times \) 10\(^3\)/ml) and complement consuming (C3 = 53 mg/dl and C4 = 7 mg/dl). AMA and ASMA were negative. A 24 h urine collection did not show signs of nephropathy. The ecocardiography did not reveal any pericardial effusion and the chest X-ray was negative for any focal pleuroparenchymal lesions. She was dismissed with a steroid prescription.

A month later, she was admitted to our ICU. She presented a remarkable swelling of the right parotid and submandibular region, extending progressively towards the basal region of the neck; it was non-pruritic, non-pitting and slightly erythematous. She was awake, space and time oriented and in spontaneous breathing with a Venturi Mask. Peripheral saturation was normal and there were no respiratory gas alterations (pH 7.47; pO\(_2\) 126 mmHg; pCO\(_2\) 37 mmHg; Lac 1.2; SaO\(_2\) 99%; HCO\(_3\)\(^{-}\) 26.9 mmol/L), but she had progressive dysphagia and dyspnea. A rhinolaryngoscopy revealed a massive edema involving glottis, pharynx and arynetoid which could compromise respiratory function at any moment. So, in order to avoid airway obstruction, the patient, after her consent, was intubated awake through fiberoptic guided laryngoscopy, after that she was sedated and mechanically ventilated. Steroids and antibiotic therapies were started suspecting infection as a possible cause. An urgent TC-scan (Figure 1) revealed prevalent edema in the right region of the neck involving the soft tissues, tongue and jugulodigastric nodules, with oropharyngeal and ipopharyngeal mucosal edema and remarkable imbibition of contralateral subcutaneous tissues with no evidence of pulmonary disease. Under suspicion of acquired angioedema secondary to SLE, 1500 UI of C1-INH was administered. In the following day, a bed chest x-ray scan confirmed that lungs were clean. However, after three days, a control TC-scan revealed the reduction of edema but the presence of multiple lung parenchymal spots so she remained on steroids and antibiotics. In the following days, the clinical conditions improved until the airway obstruction was resolved; she was extubated in safety conditions with the help of a Frova endotracheal introducer used as guide for a possible emergency intubation, dismissed from the ICU and moved to the Internal Medicine Unit. The patient remained on steroids and antibiotics until the complete resolution of clinical pattern and finally she was dismissed.
SLE is an autoimmune disease more frequent in women causing multiple manifestations in different organ systems including the skin, kidneys, joints, nervous system and blood cells (Crispín et al. 2010). In literature the association between SLE and angioedema secondary to C1 inhibitor deficiency has been rarely described (Koide et al. 2002). In few cases of patients with SLE, acquired angioedema caused upper airway obstruction requiring oro-tracheal intubation and admission in ICU (Markovic et al. 2000; Lahiri & Lim 2007). Mechanical ventilation has been reported to be necessary in lupus patients (Ko et al. 2006; Thong et al. 2001). Protective ventilation is a good choice for such patients (Zhang et al. 2015). Severe respiratory tract infection may be a trigger for angioedema episodes (Cacoub et al. 2001). Although unusual, angioedema may occur as a single episode or as a remitting-relapsing form in relation with the course of the disease or not (Ko et al. 2006; Cacoub et al. 2001).

Different types of acquired angioedema have been identified: idiopathic histaminergic acquired angioedema (IH-AAE), idiopathic non-histaminergic acquired angioedema, acquired angioedema related to angiotensin-converting enzyme inhibitors (ACEI-AAE) and acquired angioedema with C1 inhibitor deficiency (C1-INH-AAE) (Cicardi et al. 2014). The latter form can be caused by autoantibodies neutralizing C1-INH activity (Jackson et al. 1882). Quincke was the first to describe angioedema in 1882 which was considered an independent and hereditary entity until 1973 when Caldwell reported the first case of acquired angioedema in a patient with lymphoma (Quinke 1982; Osler 1888; Caldwell et al. 1972). Even though in literature the association between C1-INH deficiency due to autoantibodies and lymphoproliferative diseases was proved so that it should be considered as the same disease (Branellec et al. 2012; Cicardi et al. 1996; Zingale et al. 2006), other conditions such as infections, SLE and different neoplasias may be associated with acquired angioedema (Nettis et al. 2005; Cicardi et al. 1985). In case of a patient affected by SLE, C1-INH-AAE presents as a syndrome associated with variable potential manifestations (Zingale et al. 2006). In women affected by angioedema, familiar anamnesis is always negative. Generally face, limbs, tongue, pharynx and larynx swell when an episode occurs even if cutaneous and mucosal tissues in any part of the body may be involved (Cicardi & Zanichelli 2010; Bouillet-Claveyrolas et al. 2003). Angioedema suddenly appears as a non-pitting swelling which could be barely pruritic or erythematosus and doesn’t last more than three days (Kaplan & Allen 2008).

In our case, acute clinical symptoms and presentation, upper airway involvement and the presence of SLE in her medical history oriented the diagnosis towards suspected acquired angioedema. Because of the worsening of dyspnea, guided fiber optic intubation was performed as the first step in order to assess respiratory function. A dose of C1-INH was administered with consequent improvement of clinical conditions. Our patient remained anyway on steroids and antibiotics on one hand to treat SLE correlated inflammatory state which cause neck lymphadenopathy and on the other to prevent any possible infective complication. A control TC-scan demonstrated the progressive regression of edema. As soon as the upper airway anatomy was restored, the patient was safely extubated in our ICU. After being admitted to the Internal Medicine Unit, the swelling in the neck region reduced progressively and clinical symptoms resolved completely. In our case the patient had a non-pitting and

**Figure 1:** A CT scan of head and neck showing soft tissue swelling and airway obstruction.
non-pruritic swelling with a severe progression of dysphagia and dyspnea, for this reason intubation is mandatory to ensure airway patency in this kind of patients. Even though in differential diagnosis we need to evaluate any potential pathological cause of airway obstruction, the increasing rapidity of swelling and negative instrumental data obtained by CT-scan and chest X-ray excluding possible disease involving salivary glands or lungs may help in diagnostic process. Patient’s clinical history, correlation between SLE and acquired angioedema, typical acute presentation of the swelling made necessary to administer C1-INH rapidly. Severe presentation of symptoms suggested drug administration without waiting the results of laboratory tests to avoid eventual fatal consequences. The regression of symptoms after drug administration confirmed the diagnosis. Awake intubation, rapid clinical diagnosis and treatment, safety extubation with the help of intubating devices were mandatory in patients affected by angioedema.

Conclusion
Life-threatening airway involvement requiring orotracheal intubation in patients affected by SLE is rare but potentially fatal. Acquired angioedema is a possible cause in this kind of patients. Early airway management and therapeutic treatment are essential for a positive resolution of the disease.

Ethics and Consent
Consent for the publication of this case report and any additional related information was taken from the patient involved in the study.

Competing Interests
The authors have no competing interests to declare.

References


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