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Short Report

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An uncommon case of difficult to treat acquired angioedema

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Introduction

Acquired angioedema (AEA) with decreased C1 inhibitor is a rare disease, with an estimated prevalence between 1/100,000 and 1/600,000. Frequently begins in the fourth or fifth decade of life, without a family history of angioedema. Clinically, it presents with subcutaneous and submucosal edema that may involve face, tongue, trunk, genitals, gastrointestinal tract, upper respiratory tract, and extremities. This condition is generally associated with autoimmune or neoplastic diseases, where acquired C1 inhibitor deficiency occurs due to the presence of anti-C1 inhibitor autoantibodies or excessive consumption by tumor cells, respectively. Decreased levels of C4 and C1q are also observed in these cases [1-4]. Currently, available treatment options are based on hereditary angioedema treatment [5]. Lanadelumab, a monoclonal antibody that inhibits plasma kallikrein, a prophylactic treatment option for hereditary angioedema, has proven effective in treating these patients [6,7]. We report for the first time in Brazil a rare and serious case of late diagnosis of acquired angioedema in a woman with Monoclonal Gammopathy of Undetermined Significance (MGUS) refractory to second-line medications and responsive to lanadelumab and icatibant.

Report

A 30-year-old Caucasian brazilian woman from Rio de Janeiro, a hairdresser, began experiencing vomiting, abdominal pain, lip and limb edema associated with aspirin, which improved with antihistamines and antibiotics. Three months later, she experienced a new episode of untreated hand (Figure 1) and foot edema. Immediately after this episode, she developed significant lip and facial edema, hospitalized for two days and discharged with partial improvement. She developed new episodes of angioedema associated with shrimp and artificial seasonings. She had been taking ketoprofen and scopolamine in combination with dipyrone recurrently without reaction and denied other triggers. Since then, she has reported several episodes of abdominal pain, vomiting, and facial and limb edema, approximately twice a month (Figures 2). In the emergency room, she was treated with antihistamines, analgesics, corticosteroids, and epinephrine, without improvement. She was treated in one of the visits with 16 injections. She was regularly taking omeprazole, levonorgestrel, and ethinyl estradiol. She presented a reduction in C4 of 1 mg/dL (VR: 10-40 mg/dL), C1q = 10 mg/dL (VR: 118-124 mg/dL), and C1 inhibitor = 20 mg/dL (VR: 21-39 mg/dL), in addition to a reduced functional

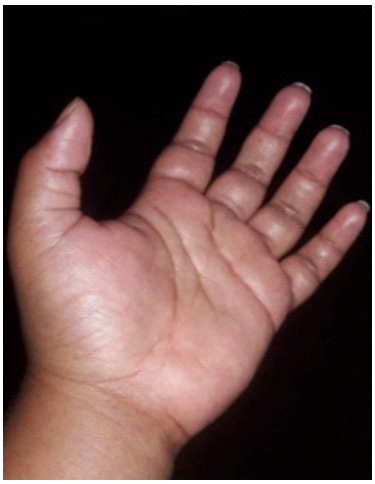

Figure 1: Hand edema.

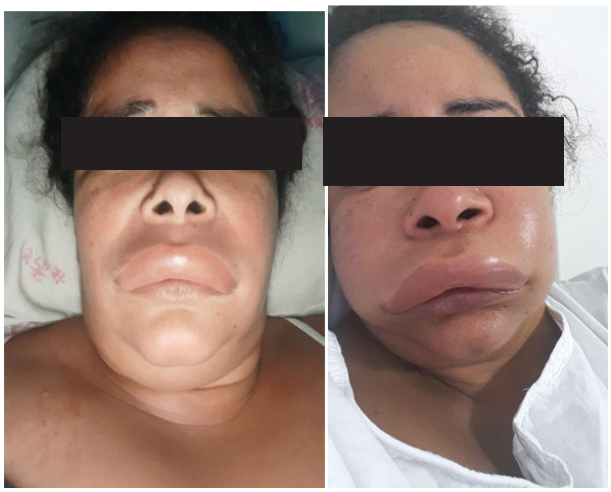

Figure 2: Severe face swelling.

C1 inhibitor of 8% (VR: 70-130%). A monoclonal band was observed against IgG and lambda light chain antisera, consistent with IgG-Lambda monoclonal gammopathy, with a diagnosis of MGUS. She discontinued contraception and had a copper IUD inserted. The SERPING1 mutation was negative. Treatment with tranexamic acid in high dose combined with 200 mg of danazol was started due to increased symptom frequency without improvement. She required transfusions with fresh plasma concentrate on two episodes and intravenous tranexamic acid in many others. She used icatabant getting better within one hour. She is taking psychotropic medications due to anxiety and depression. As the frequency of crises did not improve, we started lanadelumab a year ago, effective control since the first administration.

Reports of acquired angioedema in women are rarer, with 69% of males being affected [8]. Involvement of the face and upper airways is mainly observed in patients with acquired angioedema. A Spanish study reported a high frequency of 91.3% of facial involvement [9]. Although abdominal involvement has been described more frequently in hereditary angioedema, this case shows recurrent symptoms of abdominal pain [8]. Furthermore, hematologic disorders, particularly MGUS in a study of 162 patients with AEA were the most frequent [9].

In this report, the diagnosis was made 2 years after symptom onset, which is considered late when compared to the 12.3-month onset in a Spanish cohort study [8]. Long-term prophylactic treatment, including lanadelumab, danazol, or tranexamic acid were effective in most of patients with acquired angioedema associated with MGUS in a French retrospective study [9]. Lanadelumab has been described as safe and effective in patients with acquired angioedema due to C1Inh deficiency [7]. However, there are still few published data on long-term prophylaxis in acquired angioedema, with most cases described in hereditary angioedema, with response from the first dose [10].

This is the first report of a Brazilian female patient with a late diagnosis of AEA with MGUS, severe symptoms, no response to attenuated androgen-binding antifibrinolytics, but with an effective and safe response to icatibant and lanadelumab since the first dose for long-term prophylaxis.

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