Acquired Factor VIII Inhibitor Presenting as Life Threatening Oral Swelling

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ABSTRACT

Acquired factor VIII inhibitor is a rare hematological disorder that develops more commonly in the elderly. Several risk factors have been reported, including autoimmune disorders, pregnancy, post-partum status, and surgery. In contrast to hemarthrosis associated with congenital hemophilia syndromes, bleeding into subcutaneous tissue is the most common presentation of this disorder. Oral swelling as the initial presentation of acquired factor VIII inhibitor is rare. High clinical suspicion and early diagnosis are crucial.

Keywords: Acquired factor, Autoimmune, Oral swelling, Congenital hemophilia

INTRODUCTION

Acquired factor VIII inhibitor is a rare disease with an incidence of 1 to 4 per million[1]. The incidence increases with age, peaking in patients above 85 years of age, with a reported incidence of 14 cases per million[2]. This disease is associated with life-threatening bleeding, with subcutaneous tissue being the most common site of bleeding[3]. However, acquired factor VIII inhibitor presenting as tongue swelling has been reported a few times in the literature[4-7].

CASE PRESENTATION

A 62-year-old male presented with severe abdominal pain and was found to have bowel obstruction secondary to incarcerated hernia. The patient was admitted to the hospital and underwent exploratory laparotomy, right hemicolectomy with terminal ileum resection, Meckel's diverticulectomy, and repair of inguinal hernia with allograft and temporary abdominal closure. The patient was retaken to the operating room for a second look laparotomy, primary ileal-transverse colon anastomosis, and closure of the abdomen. On day 8 of the admission, a CT scan of the abdomen and pelvis was performed due to persistent leukocytosis, and the patient was found to have multiple intra-abdominal abscesses. He subsequently underwent subcutaneous drainage of the largest abscess. During the course of his hospitalization, the patient had been on different antibiotics. The patient significantly improved and was planned for discharge.

Before discharge, the patient complained of mild sore throat and chest tightness. Subsequently, he developed minor swelling on the left side of the neck that continued to enlarge and threaten his airway. The surgical team evaluated the patient and decided to take him emergently to the operating room for evacuation of the suspected sublingual hematoma. Intra-operatively, the patient was found to have continuous oozing of blood from the oral mucosa without an obvious source. The patient was intubated and continued to have oozing blood from his mouth and nose. Within a few hours, the patient developed significant tongue and neck swelling. He remained intubated and was admitted to the surgical intensive care unit. The patient has a past medical history significant for peptic ulcer disease and severe aortic stenosis; status-post surgical aortic valve replacement. The patient had no history of cancer or bleeding disorders. He had multiple surgical interventions in the past, including this admission, and bleeding was not an issue peri-operatively.

After intubation, the patient was in mild distress but able to follow commands. Heart rate was 110 BPM, apart from hypotension (90/72 mmHg), Temp: 36.4 C. An oral exam revealed a protruding and swollen tongue with purple discoloration. Continuous slow oozing of blood from the mouth was noted. The neck was grossly swollen but without palpable lymph nodes.

Complete blood count, metabolic panel, and liver function tests were all within normal limits. However, the coagulation profile was significant for prolonged activated partial thromboplastin time (aPTT, 84.2 seconds) and elevated international normalized ratio (INR, 1.3). Further coagulation work-up revealed a positive mixing study consistent with the presence of an inhibitor. Factor VIII was very low with Bethesda titer of 172 units. Thromboelastography was performed initially, which showed a flat line concerning for severe coagulopathy. CT scan with contrast of the neck showed marked swelling and enlargement of the tongue with extensive stranding of the soft tissues of the neck and effacement of the left pharyngeal mucosa. Based on these findings, the patient was diagnosed with acquired factor VIII deficiency superimposed with bleeding and tongue swelling.

Initially, the surgical team decided to transfuse the patient with various blood products before the hematology team was involved in the patient's care. The acute bleeding was treated with recombinant factor VII every 4 to 6 hours. Although immunosuppression with 1 mg/kg of steroids was initiated, the patient continued to bleed intermittently, and thus frequent administrations of factor VII were required to achieve hemostasis. The neck and tongue swelling gradually decreased, and the patient was successfully extubated to room air. Rituximab 375 mg/m^2 weekly was added to the steroid regimen. Unfortunately, after two cycles of therapy, the patient continued to require intermittent blood and factor VII transfusions. Oral cyclophosphamide 100 mg twice daily was then added. The frequency of the bleeding and blood transfusion decreased gradually over a week. The patient's bleeding resolved, and the patient was discharged home on prednisone and cyclophosphamide after completing four cycles of rituximab. The patient returned to the hematology clinic after about six months in good condition with a normal coagulation profile.

DISCUSSION

In contrast to hemarthrosis in congenital hemophilia, subcutaneous soft tissue and muscles are the most common bleeding sites in acquired

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factor VIII deficiency. However, acquired factor VIII inhibitor presenting as bleeding causing life-threatening airway compromise is reported few times in the literature. Furthermore, it is less reported with tongue swelling as the initial presentation[7-9].

Diagnosis is usually made by the findings of a prolonged aPTT, positive mixing studies, and low factors level. The goal of factor VIII inhibitor treatment is to control acute bleeding and provide adequate immunosuppression to counteract and eradicate the action of circulating inhibitors[10]. In case of tongue swelling or bleeding causing airway compromise, early consult of airway experts is critical since the bleeding can be insidious and fatal, as noted in all the reported cases of airway involvement[4,5,7,8,11,12]. This case supports the findings of the European Acquired Hemophilia Registry (EACH2) that among different treatment regimens, a combination of steroid and cyclophosphamide is more likely to achieve remission and bleeding control[13].

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