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Case Report

Acquired Hemophilia A: A Rare Presentation with Buccal Bleeding: A Case Report

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Abstract

Introduction: Acquired Hemophilia A (AHA) is a rare but potentially life-threatening bleeding disorder characterized by autoantibodies for coagulation factor VIII. Awareness of AHA different presentations may save patients' lives. However, there is diverse presentation of AHA reported in medical literature.

Aim: To report AHA case with rare presentation of buccal bleeding and raise awareness of a such condition.

Case: We reported a case of AHA in a patient with chronic medical condition that presented with buccal mucosal bleed. Despite referral to multiple medical specialties and multiple reviews, the diagnosis was not picked up until the patient had heavy vaginal bleeding and was admitted in tertiary center. The patient was treated eventually and recovered.

Conclusion: AHA could present with buccal mucosa bleeding. It is important to remember this diagnosis when treating a chronically ill and symptomatic patient. An early diagnosis could reduce patient's suffering and medical investigations. The treatment is possible with blood transfusion, steroids, DDAVP, activated factor VII and immunosuppressant.

Keywords: Acquired Hemophilia A; AHA; Factor VIII; Bleeding; United Arab Emirates

Case Presentation

A 54-year-old female, who is known case of chronic respiratory failure on chronic mechanical ventilator and carcinoma of breast, presented with spontaneous buccal mucosal bleeding with localized hematoma formation. Preliminary investigations did not raise any serious suspicion as patient's CBC showed platelets and hemoglobin within normal ranges, confirming no major bleeding. Further, the coagulation profile revealed only mildly elevated APTT of 42.9 with no any escalation in the subsequent results and normal values of INR and PT. Patient was on Enoxaparin for DVT prophylaxis. The bleeding did not resolve with discontinuation of Enoxaparin.

Later on, the case was consulted with a dentist. The management in the form of dental guard and teeth filling was not helpful. A hematology consultation was requested but no particular treatment was advised at the beginning.

Patient was closely observed until developed heavy spontaneous vaginal bleeding along with persistent mucosal hematomas, and was eventually transferred to a tertiary hospital. During her stay, the patient was symptomatically treated with blood transfusion. Further, investigation revealed aPTT of 76 seconds, which was increasing, factor VIII level was significantly low and factor VIII inhibitor level was significantly high. The patient was diagnosed with AHA and was managed with blood transfusion, recombinant activated factor VIIa, IV Steroids, Rituximab and PCC. After treatment the levels of factor VIII were increasing and factor VIII inhibitor were trending down, and all the levels were in physiological ranges in nearly 4 months period. Eventually patient's steroids were tapered off and patient did not show further bleed.

Discussion

In comparison to congenital hemophilia, that has an incidence of one case in 5000 males; AHA is uncommon with incidence of 0.2-1.0 per 1 million persons per year [1,2]. Acquired anti-FVIII inhibitors are distributed equally between sexes and have typically biphasic age distribution, with a small peak between 20 and 30 years (mainly post-partum inhibitors) and a larger peak in patients aged 70-80 years old [3,4].

The etiology in the majority of cases is idiopathic, in approx. more than 50% [1,8,10,11]. There are several risk factors attributed to the development of AHA, including autoimmune conditions, antibiotics, infections and malignancy [4,5,10,12,13]. Malignancies as risk factors for AHA are attributed to only 10% of cases, which commonly include hematologic malignancies (commonly myeloproliferative disorders) and solid tumors (most commonly reported in pancreatic cancer followed by lung and other malignancies including Gastric Cancer, Hepatocellular Carcinoma etc.) [3,14-16]. Among solid tumors, breast cancers are rarely reported as strong predisposing factor for AHA, which we found in our case.

The clinical picture of acquired hemophilia is typically characterized by bleeding into the skin, muscles, soft tissues and mucous membranes, whereas hemarthroses, a typical manifestation of congenital hemophilia A, are unusual [3,6,17]. Not rarely the hemorrhages in acquired hemophilia are serious or life threatening, as in the case of cerebral hemorrhage or rapidly progressive retroperitoneal hematomas. Among the types of mucosal bleeding,

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patients of AHA presenting with genitourinary, gastrointestinal and nasal bleeding, have been reported [1]. However, there is no report in the established academia of patient presenting with buccal mucosal bleeding and hematoma.

Moreover, mucosal bleeding events are reported with active malignancies or during the treatment of malignancies [8,11]. Unlike, our patient who was in complete remission after several years of treatment of her breast cancer. Although aPTT levels for our patient were only mildly deranged, the discontinuation of Enoxaparin did not affect the intensity of the bleeding [10]. Usually buccal mucosal or gum bleeding is mainly reported in the deficiency of vWB deficiency and not in AHA patients [10]. After period of six months, our patient developed frank vaginal bleeding [12]. During the time of massive bleeding, levels of aPTT were markedly prolonged and the degree of derangement was correlating to severity of bleeding [6].

Clinical management of patients with AHA requires early involvement of hematologist, initial hemodynamic support (blood transfusion if indicated), homeostatic treatment, immunosuppressive agents and follow up investigations to monitor the response [1,10-12,17]. Homeostatic treatment include either direct transfusion of factor VIII or by-passing agent like recombinant factor VII and FEIBA (factor Eight inhibitor bypassing activity) etc., [6,8,11,17]. There are several immunosuppressive agents used for treatment of AHA including Steroids, Cyclophosphamide, Rituximab, Mycophenolate, and Cyclosporine. Also DDVAP has been tried with good results in cases of minor bleeds with the advantage of being readily available and inexpensive [6,8,11,17]. Rituximab is used quite often off the label. However, the rate of successful remission with Rituximab is significant [1,18,19].

After initial blood transfusion and homeostatic treatment with Novo VII, our patient was treated with IV Methylprednisolone and IV Rituximab. Methylprednisolone was eventually tapered to oral Prednisolone and was completely discontinued slowly. Rituximab was commenced on weekly basis for four weeks. During the similar time aPTT, Factor VIII and Factor VIII inhibitor levels were monitored on weekly basis for four months [6,7]. It is worth mentioning that our patient also developed hyperglycemia, which was managed with the insulin (expected due to steroid use).

After normalization of factor VIII and inhibitor levels, aPTT is considered for follow up [1,6]. While, in our case we also continued follow up of factor VIII and inhibitor levels on weekly and then bi-weekly basis initially due to poor correlation of aPTT with initial event of bleeding. After completion of treatment, factor VIII and inhibitor levels were checked every 8 weeks for a year from the establishment of diagnosis. In rare cases following the complete remission, patient may develop hyper-coagulopathy and, in such situations, direct measurement of factor VIII and inhibitor are suggested for proper control of the disease [6,7,12]. After complete remission, patients may be considered for thrombo-prophylxis based on the risk factors and underlying co morbidities [6,7].

Bleeding is the most common clinical presentation of AHA. It is reported in more than 90% of cases [5,20]. However, the literature still suggests under-reporting of AHA cases [1,5]. Through our case, we remind that it is worth considering the acquired hemophilia A as differential diagnosis in elderly patient with no previous or family history of bleeding diathesis in the background of strong risk factors like autoimmune conditions or malignancy [2,20]. If bleeding persists despite discontinuation of anticoagulants and prolonged aPTT, then suspicion of AHA should be considered. Buccal bleeding could be an early presentation of AHA. An early diagnosis could spare the patient from bleeding complication and repeated investigations. As the literature documents that in spite of increase in number of newly diagnosed cases of AHA, mortality was reduced from 42% to 12% due to the practice of early diagnosis and treatment [3,6,21].

Conclusion

To the best of our knowledge, there is no data in the established academia that buccal bleeding per se is a presentation of AHA. Early recognition of this possible condition may save patients' lives and limit suffering. Although AHA is usually idiopathic but other etiologies like drugs, infections, autoimmune disorders and malignancy are to be considered as well.

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