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Case Report

Von Willebrand Disease type 2B: A diagnostic dilemma

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Abstract. A young female was presented with isolated chronic unilateral intractable epistaxis with non healing granular mass in the left nasal cavity. Histopathological examination was reported as acute and chronic non specific inflammation which did not respond to antibiotics or steroid. After ten years follow up she was finally diagnosed to have Von Willebrand disease type 2B. This is the first case report of von Willebrand disease presenting with intermittent epistaxis as its sole disease manifestation. Although epistaxis is a common complaint in Otorhinolaryngology clinics, this case posed a diagnostic dilemma.

Key words: Type 2 von Willebrand Disease, epistaxis, isolated, Wegener's Granulomatosis

1. Introduction

Von Willebrand disease (VWD) is an inherited bleeding disorder due to deficient or defective Von Willebrand factor (VWF). It should be suspected in people with excessive mucocutaneous bleeding (1). Rarely, it presents with isolated unilateral epistaxis and non healing granulation in the nasal cavity.

2. Case report

A 32 years old woman was referred for intermittent left epistaxis requiring frequent blood transfusions. She had easy bruising but no menorrhagia, no childhood bleeding and no family history of bleeding disorder. She progressed to have few episode of hematuria which was treated as chronic cystitis. There was history of several turbinate surgeries and grommet insertions since she was 14 years old and multiple biopsies from the left nasal cavity which was performed prior to referral. Examination of the left nasal cavity revealed a granular lesion in left middle meatus. Coagulation profiles were within normal range. We proceeded with endoscopic sinus surgery with excision of the granular mass and osteitic lateral wall of nasal cavity (Figure 1). As before, the histopathological reports consistently reported acute on chronic inflammatory granulation tissue (Figure 2a and 2b). Repeated investigations including C-ANCA and P-ANCA did not support chronic granulomatous disease which was strongly suspected. She remained a diagnostic dilemma for ten years where the granular lesion persisted despite numerous courses of antibiotics

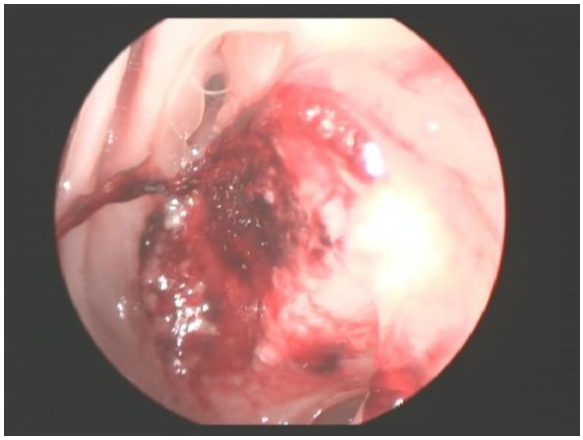

Fig. 1. Nasal endoscopic view of the left nasal cavity with evidence of ethmoidectomy. Granular lesion seen on lateral wall involved the lamina papyricae and lacrimal bone.

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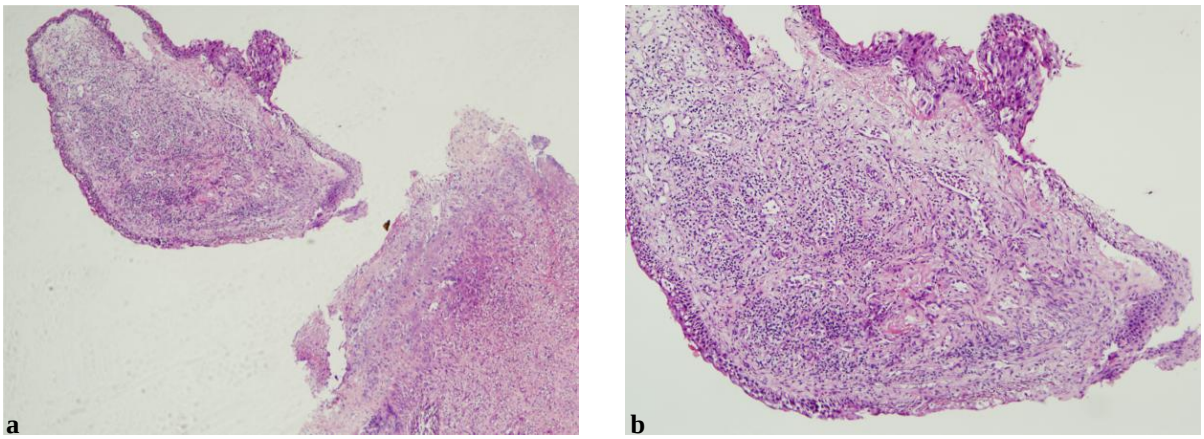

Fig. 2. a) Low power view of the tissue sampled from the lateral nasal wall show ulcerated surface epithelium with underlying granulation tissue, inflammatory cells infiltration and areas of hemorrhage (Hematoxylin & eosin, 40x magnification). b) Proliferating blood vessels are more obviously seen within the granulation tissue but no evidence of granuloma, dysplasia or malignant changes (Hematoxylin & eosin, 100x magnification).

and steroids. Left sphenopalatine artery ligation was performed which reduced her episodes of epistaxis and blood transfusion. Finally, haemostatic workup showed abnormally increased ristocetin-induced platelet aggregation at low level of ristocetin (26 Ohm at 0.5mg/mL and 44Ohm at 1mg/mL ristocetin). VWF antigen and factor VIII levels were not low at 126% and 190% respectively. In view of history of bruising, hematuria and intractable epistaxis in the presence of platelet hyper aggregation with low dose ristocetin, she was diagnosed to have Von Willebrand disease type 2B.

3. Discussion

Epistaxis is a common rhinologic emergency. It is thought as intractable when it is resistant to conservative therapeutic measures including posterior nasal packing (2). A patient with intractable epistaxis may be treated conservatively if there is no obvious underlying source of bleeding (idiopathic). As this patient had unilateral epistaxis with granulations in the nasal cavity, chronic granulomatous disease or neoplastic lesion need to be ruled out. Several differentials entertained were chronic granulomatous disease (local nasal Wegener's granulomatosis (WG), sarcoidosis, *tuberculosis*, rhinosporidiasis), inflammatory pseudotumour, *leischmaniasis*, arteriovenous malformation and carotid aneurysm. This patient was diagnosed with VWD type 2B. VWD will generally present with mucosal bleed commonly epistaxis and menorrhagia. There have been two other reports of systemic bleeding disorder with isolated epistaxis (3,4). To our knowledge, this is the first reported case of VWD presenting with isolated unilateral epistaxis. Early diagnosis of this condition would have saved her from the repeated attempts of biopsy and its complications. In retrospect, the granular mass may be the result from previous surgeries leading to chronic osteitis and inflammation.

Von Willebrand disease is the most common inherited bleeding disorder due to deficient or abnormal von Willebrand factor. It is generally divided into three types. Type 1 VWD is when there is mild to moderate decrease in VWF which may lead to mild bleeding tendencies. Type 2 is associated with abnormal function VWF and is further divided into 2A, 2B, 2M and 2N subtypes. Type 2A is due to selective decrease in high molecular weight multimer VWF, type 2B is caused by increased affinity for platelet which leads to depletion of large functional VWF multimers. Type 2B is differentiated from type 2A by finding abnormally increased ristocetin induced platelet aggregation at low concentrations of ristocetin (5). The rare type 3 is due to very low or undetectable VWF and is associated with severe bleeding diathesis (6). VWD is diagnosed by history of abnormal bleeding and diagnostic laboratory result. Screening tests such as activated partial prothrombin time (APTT), prothrombin time and bleeding time is non- specific and may be normal especially in type 2 VWD. The APTT may only be prolonged in VWD type 1 and type 3 due to associated decrease of factor VIII, the VWF carrier protein. This patient had unilateral epistaxis which began in her 3rd decade of life. Acquired VWD is possible as it occurs in individuals with no personal or family history of bleeding disorder. Acquired VWD is also more

commonly type 2 on laboratory analysis (7). However, it is a rare complication with only more than 300 cases reported. It may be secondary to myeloproliferative or autoimmune disease and have also been associated with hypothyroidism (8). In our patient, there is no underlying disease that may cause acquired VWD except the non healing chronic inflammation in the nasal cavity which had only served as a red herring in this case.

It is important to realize that in spite of the underlying cause, the main problem in this patient is the intractable epistaxis. In order to control the epistaxis, Sphenoplatine artery ligation was done in order to decrease the necessity of her blood transfusion. There had been reports of superselective embolization which may be effective for uncontrolled epistaxis due to systemic bleeding disorder (9). This would be an option to consider for her in the future when the epistaxis worsen.

4. Conclusion

Unilateral intractable epistaxis may present as a diagnostic dilemma. However, clinician should be aware of systemic bleeding disorders which may manifest as isolated epistaxis whereby prompt diagnosis, can save time, money and avoid unnecessary investigation.

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