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CASE STUDY

Case report of nasal pseudotumor – a rare presentation in severe haemophilia A with high titre inhibitors

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Haemophilia patients with inhibitors suffer from increased morbidity and mortality due to the ineffectiveness of factor VIII replacement. Pseudotumors are rare but dangerous complications in these patients, and nasal pseudotumors are even rarer. Here, we present the case of a young child with severe haemophilia A with high titre inhibitors who developed a nasal pseudotumor. When immune tolerance therapy was not possible due to financial constraints, he was treated with FEIBA prophylaxis and rituximab. The pseudotumor was managed with surgical excision. We conclude that epistaxis in haemophiliacs can be due to an underlying nasal pseudotumor, and highlight the use of rituximab for the eradication of inhibitors.

Keywords: *haemophilia with inhibitors, rituximab, nasal pseudotumor, surgical removal, case report*

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A case report from Kolkata, India, highlights the possibility of treating a high titre inhibitor with rituximab, and the identification of a pseudotumor as the cause of epistaxis.

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Haemophilia A is an inherited coagulation disorder of factor VIII (FVIII) deficiency. Replacement of FVIII with clotting factor concentrate (CFC) is the standard of care [1]. Approximately 30% of haemophilia A patients develop anti-FVIII alloantibodies (inhibitors), rendering factor VIII replacement ineffective and resulting in increased morbidity and mortality [2,3]. People with haemophilia (PwH), with or without inhibitors, usually present with frequent bleeding episodes, especially in the joints, leading to arthropathy and compromised quality of life [4]. Occasionally, repeated bleeds can lead to development of a pseudotumor, most commonly

involving the femur, tibia and pelvic bones. The occurrence of nasal haemophilic pseudotumor is extremely rare and there are limited case reports in the literature [5]. Here, we present the case of a child with severe haemophilia A with high titre inhibitor, further complicated by pseudotumor in the nasal cavity, presenting at Nil Ratan Sircar Medical College and Hospital, Kolkata.

CASE SUMMARY

A three-month-old baby developed a large muscle haematoma following vaccination. The haematoma was managed locally with supportive treatment and fresh frozen plasma, but not evaluated further. Nine months later, he again presented with episodes of spontaneous ecchymosis and was diagnosed with severe haemophilia A (factor VIII activity=0.6%) at the age of one year. He did not have any family history of haemophilia. He was started on low dose prophylaxis with long-acting recombinant factor VIII (Eloctate) at 10 IU/kg/dose twice weekly [6]. His inhibitor status after five exposure days (EDs) and 10 EDs was <0.5 Bethesda units (BU).

Two months later, he presented with swelling at the root of the nose and forehead after a fall (Figure 1-A). He was treated with CFC for five days and supportive care, and then again put on regular prophylaxis. The forehead swelling gradually resolved, however the nasal swelling persisted and gradually started increasing in size (Figure 1-B). Thirty-five days after the trauma, the child had sudden episodes of uncontrolled epistaxis for which he was hospitalised. He was managed conservatively with tranexamic acid, both intravenous and local application; CFC was also continued in therapeutic doses according to World Federation of Hemophilia (WFH) guidelines [3]. A high titre inhibitor (50 BU) was detected, CFC was discontinued immediately, and FEIBA anti-inhibitor coagulant complex was started at 50 units/kg twice daily. However, repeat tests after four weeks revealed an inhibitor level of 250 BU. Immune tolerance induction (ITI) therapy was planned, but was not feasible for financial reasons. The child was subsequently treated with FEIBA prophylaxis to prevent recurrent nose bleeds and given rituximab 375mg/m2 weekly for four doses. A repeat inhibitor assay after one month from first dose and the last dose of rituximab revealed inhibitor levels of 20 BU and 2.5 BU respectively.

The nasal swelling persisted, and the child continued to experience nose bleeds. A CT scan showed a lobular expansile swelling in the anterior nasal cavity and radiological diagnosis of angioma was made

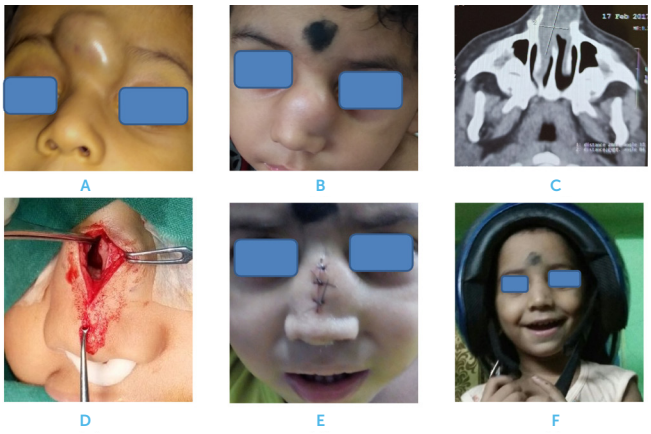

Figure 1
A. Swelling at the root of nose and forehead after trauma due to fall; B. Nasal swelling persisted and gradually started increasing in size; C. CT scan showing a lobulated expansile soft tissue mass in the bilateral anterior nasal space; D. The soft tissue mass was excised –grossly there were only old clots inside; E. Day seven post-operatively, the child did not have any further bleeding episodes; F. The child has been under regular follow-up for the last three years and is on continued prophylaxis.

(Figure 1-C). In view of the increasing swelling and recurrent epistaxis, the opinion of an ear, nose and throat (ENT) specialist was taken, who advised surgical excision of the mass under cover of FEIBA. The soft tissue mass was excised (Figure 1-D); grossly only old clots were found inside. The operation was uneventful with minimal intra-operative bleeding. The child was given FEIBA 50 units/kg twice daily for seven days post-operatively. He did not have any further bleeding episodes (Figure 1-E) and was discharged after 10 days with FEIBA prophylaxis as before. Histopathological examination of the excised nasal mass was consistent with pseudotumor.

Inhibitor testing was repeated at two months, three months, and four months from the last dose of rituximab, showing levels of 0.75 BU, <0.5 BU and <0.5 BU respectively. In view of the severity of haemophilia, recurrent spontaneous bleeds and persistent negative inhibitor status, the child was restarted on low dose prophylaxis with CFC, with close monitoring of inhibitor status (levels continued to be <0.5 BU). He has now been on regular follow-up for three years with continued prophylaxis (Figure 1-F).

DISCUSSION

Pseudotumors are a very rare but dangerous complication of haemophilia, occurring in 1–2% of patients with severe forms of the disease [5]. A pseudotumor is a chronic, slowly expanding haematoma, surrounded by thick fibrous capsule, and results from repetitive bleeding. Pseudotumors

usually progress without timely intervention, leading to the slow destruction of adjacent structures through increasing pressure [6]. Invasive techniques such as percutaneous aspiration and needle biopsies are not recommended for diagnosis due to the increased risk of complications [5,7]. High quality CT scanning and/or magnetic resonance imaging (MRI) are excellent tools for the preoperative visualisation of pseudotumors and their effect on surrounding structures [7].

In general, operative removal of the entire mass is a reliable treatment because the pseudotumor will likely reform if it is not completely removed [5,7]. Purkait et al. reported a case of nasal pseudotumor in a patient with haemophilia B successfully treated with radiotherapy [5]. Ogata et al. reported a case of nasal pseudotumor in a patient with haemophilia A along with allergic rhinitis [8]. The pseudotumor was cured by supplementation with recombinant factor VIII concentrates, and medication for allergic rhinitis. They concluded that pseudotumor should always be considered in haemophiliac patients, even in those with only mild deficiency of coagulation factors. In this case, the patient developed a nasal pseudotumor over a period of time, which was managed by operative removal of the mass under prophylaxis of FEIBA.

For patients with inhibitors, bypassing agents such as recombinant factor VIIa (rFVIIa) or FEIBA can be used for the control of acute bleeding [3]. The use of FEIBA prophylactically has also been shown to be an effective and safe method for reducing bleeding events in people with haemophilia A and inhibitors [9]. Immune tolerance induction (ITI) is the recommended therapy for treatment of inhibitors [3]. In view of the high titre inhibitor in the present case, ITI was planned for; however, it was not feasible due to financial constraints. Although no randomised controlled trials exist on the use of rituximab for treating inhibitors in PwH, some case reports have shown promising results. Liu et al. assessed the efficacy and safety of rituximab for treating inhibitors in patients with haemophilia A or B and concluded that meta-analysis of case reports and case series may provide some evidence [10]. The present case of haemophilia A with high titre inhibitors responded well to the standard dose of rituximab therapy.

CONCLUSION

Pseudotumors are a rare but dangerous complication of haemophilia and can occur at unusual sites including the nasal cavity. In the case reported here, epistaxis in a patient with severe haemophilia A was the result of an underlying nasal pseudotumor. The case was further complicated by the presence of high titre inhibitors. When ITI therapy was not possible, use of rituximab was shown to be an effective alternative for the eradication of inhibitors.

AUTHOR CONTRIBUTIONS

PKM designed the study. PKM and UJ were the consultants in charge of the case. UJ performed the surgery. PKM, MG and DG contributed to the manuscript writing, literature search, and manuscript editing. All authors reviewed the manuscript and gave final approval.

ACKNOWLEDGEMENTS

The long acting recombinant FVIII Fc fusion (ELOCTATE) products used for regular prophylaxis in the case reported here was received as Humanitarian Aid from the World Federation of Hemophilia (WFH).

The authors have advised no interests that might be perceived as posing a conflict or bias.

Informed and written consent has been obtained from the legal guardians of the individual reported in this case study.

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HOW TO CITE THIS ARTICLE:
Mandal PK, Garg M, Gantait D, Jana U. Case report of nasal pseudotumor; a rare presentation in severe haemophilia A with high titre inhibitors. *J Haem Pract* 2021; 8(1): 11-14. *https://doi: 10.17225/jhp00172.*