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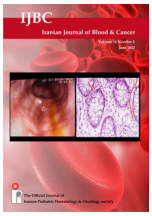

Case Report

Hemophilic Pseudotumor in the Jawbone: A Case Report and Literature Review

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Abstract

Background: Hemophilic pseudotumor is a rare lesion that is progressive and expansile by nature. It is a hematoma or a blood cyst surrounded by a fibrous capsule.

Case report: A 7-years-old boy was referred with a painless swelling in the mandible, bleeding and problem in mastication. Due to a late diagnosis, the patient went untreated for almost a year. After detailed examination and taking medical history as well as paraclinical investigations, including panoramic X-ray, CT (computed tomography), cone-beam CT, and angiography along with laboratory tests, a hemophilic pseudotumor was diagnosed. Treatment plan was set to curettage, coagulation factor injection and regular follow-up. The prognosis was satisfactory and the patient made a full recovery within a year.

Conclusion: A hemophilic pseudotumor is very rare in the jaw and can be diagnosed as a benign or malignant tumor due to its nonspecific radiographic features. Invasive treatment may result in severe bleeding or even death. Therefore, knowledge of the lesion is a prerequisite for careful diagnosis and treatment.

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1. Introduction:

Hemophilia is a genetic disorder of homeostasis at the site of tissue damage due to a deficiency in coagulation factors. A deficiency in coagulation factor VIII (antihemophilic factor) leads to hemophilia A, while that in coagulation factor IX (plasma thromboplastin component) leads to hemophilia B, the so-called “Christmas” disease. Both types have X-linked recessive inheritance and are more common carriers. With regard to the severity of the disease and based on the coagulation factor, the patients are divided into three groups, namely mild: >5% factor VIII, moderate; 1-5%, and severe; <1% [1].

One of the most common problems in patients with hemophilia A is bleeding in the joints, muscles and bones, which occurs as a result of minor trauma. This may lead to a destructive and potentially expansile

lesion known as a HPT (hemophilic pseudotumor) or pseudocyst [2]. The prevalence of HPT in patients with severe hemophilia is 1-2% [3]. Although the lesion also occurs in other long bones or in the jawbone, it is more common in the femur. HPT is very rare in the mandible or maxilla; only 50 cases have been reported since 1968. It is common in younger individuals, with an average age of 11.5 years. The patient's medical history usually includes painless swelling from a month to several years, and eventually sudden changes such as bleeding or perforation that require urgent treatment [4]. Definitive diagnosis is based on medical history, imaging, and FNAB (fine needle aspiration biopsy). An incisional biopsy is initially not recommended due to the risk of bleeding and infection [5].

Bone malignancies are included in the differential diagnosis of the HPT. Misdiagnosis and aggressive treatments can result in mortality and morbidity due to bleeding. In addition, since most of the hemophilic patients with HPT are under the age of 12, accurate diagnosis and prompt treatment are important to avoid further problems in skeletal development, and aesthetics.

In this article, we report on a patient with a mandibular hemophilic pseudotumor who underwent multiple diagnoses and therapeutic difficulties.

2. Case report

A 7-years-old boy with hemophilia A was referred to the Department of Oral and Maxillofacial Diseases of the Faculty of Dentistry at Mashhad University of Medical Sciences, Iran, with complaint of swelling and bleeding in the posterior mandible and problem in mastication. The patient's medical history only included hemophilia, which had been diagnosed when the patient was one year old. The coagulation factor VIII was 2%, indicating moderate hemophilia. The patient's psychological condition was normal. The mother was a hemophilia carrier and the father was healthy.

According to the medical history, the patient had suffered trauma to the left side of mandible a year earlier and thereafter a blood cyst had developed around the mandible of the left second permanent molar with spontaneous blood drainage in the cyst area. Coagulation factor VIII had been prescribed by a hematologist and the patient had appeared to improve. However, the swelling had relapsed after 9 months and subsequent two doses of amoxicillin had not improved the swelling at all. The patient had further received two monthly doses of 250 units of factor VIII for a year without improvement and an incisional biopsy had been suggested by a hematologist.

Upon referral of the patient and on extraoral examination by an oral and maxillofacial specialist, an asymmetry was found in the left cheek. The swelling had a firm consistency, and the skin was normal. An intraoral examination revealed a hard swelling in the buccal and lingual parts of the left mandible from the primary canine in the left side to the left vertical ramus. The lingual plate in the posterior mandible was completely destroyed and the first permanent mandibular molar had a grade 3 luxation. In addition, a bleeding 1x1 cm ulcer with fibrinolytic membrane was observed in the region of left second permanent molar of the mandible (**Fig. 1**). No active bleeding in the mouth or pumping was observed during the examination and no bruising, swelling or abnormality were found in other areas (**Fig. 1**).

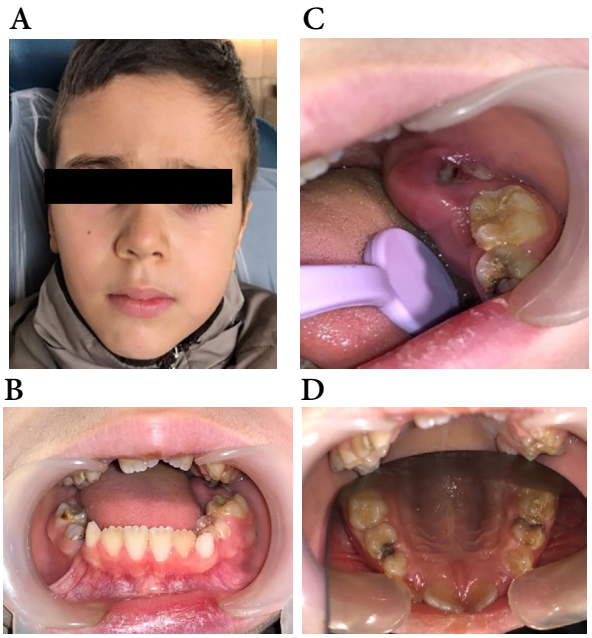

Figure 1: Extraoral appearance of the swelling in the left cheek (**A**). Swelling and expansion of the lesion on the left side of the mandible (**B, C**). The maxilla is normal (**D**).

After examination and taking medical history and upon primarily suspecting a hemophilic pseudotumor or a central giant cell granuloma with aneurysmal

bone cyst, panoramic radiography and CBCT (cone beam computed tomography) of the posterior mandible were prescribed. Panoramic radiograph and CBCT revealed an expansile multilocular radiolucent lesion with wispy septa that extended from the second primary molar of left side of the mandible to the sigmoid notch. The lesion caused the bud of the second permanent molar to be displaced downwards and the first permanent mandibular molar to be displaced upwards, together with a destruction of the mandibular cortex, thinning of the mandibular lower border, and downward displacement of the inferior alveolar nerve canal **(Fig. 2)**.

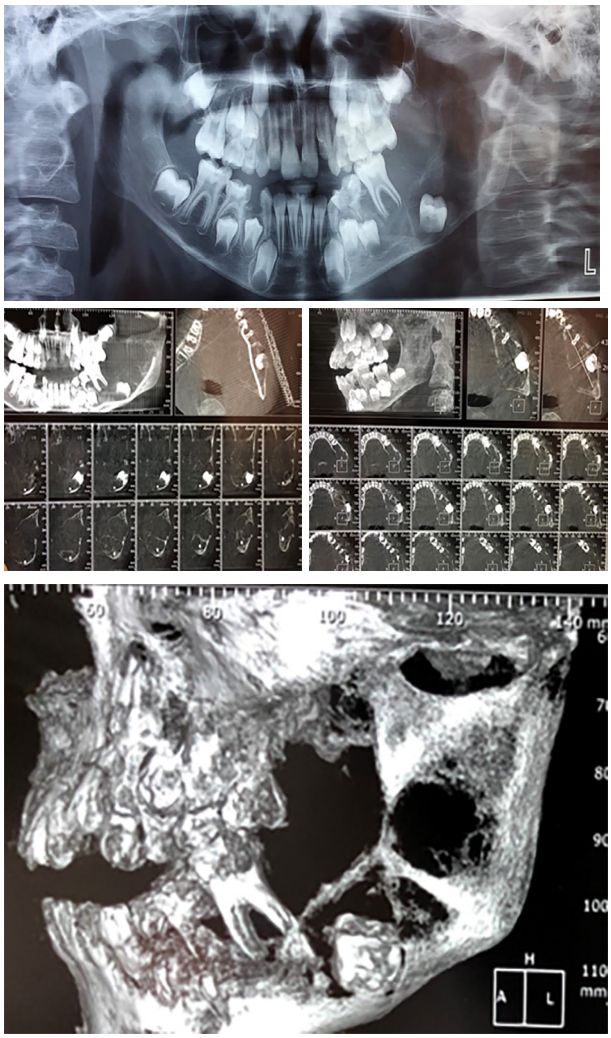

Figure 2: Panoramic radiographic view and CBCT. A multicellular radiolucent lesion with a wispy septum in the left posterior mandible extending from the second primary molar of left side of the mandible to the sigmoid notch, displacing the bud of the permanent second left mandibular molar.

The radiographic differential diagnosis included hemophilic pseudotumor, CGCG (central giant-cell granuloma) and osteosarcoma.

Before the biopsy, a CT angiography was prescribed to rule out vascular abnormalities. In addition, several laboratory tests were also prescribed prior to CT angiography; CBC (Cell Blood Count), PT (Prothrombin Time), PTT (Partial Thromboplastin Time), INR (International Normalized Ratio) were used to assess the risk of bleeding after contrast agent injection. Urea and creatinine were determined to assess renal function during contrast agent clearance. Calcium, Phosphorus, ALP (Alkaline Phosphatase) and PTH (Para¬Thyroid Hormone) were used to rule out secondary hyperparathyroidism due to renal osteodystrophy. The test results were normal.

Because of a high aPTT (activated Partial Thromboplastin Time) (63.5), the hematologist recommended administration of 500 units of coagulation factor VIII half an hour before each CT angiography. After injection of contrast agent into the cubital vein, CT angiography of the face was performed with standard technique and 3D reconstruction. We observed a multilocular expansile lesion with cortical destruction and displacement of the lower left second molar, while no hemangiomas or vascular flushing were observable. The lesion caused displacement of the thyroid and the left labial of external carotid arteries **(Fig. 3)**.

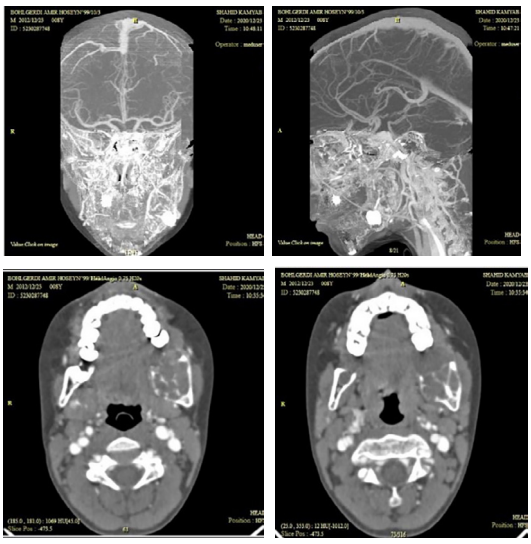

Figure 3: Images of CT angiography; the presence of a multilocular lesion with destruction of the left mandibular cortex is visible. No blushing or hemangioma is present.

According to the decision of surgeon and hematologist, the treatment plan was set to curettage and factor therapy; two 500 units of factor VIII one hour before the biopsy and two 500 units 8 hours after and two 500 units in the next 12 hours together with 250 mg tranexamic acid capsule every 8 hours from two days before the biopsy until two days after were prescribed. The curettage was performed by an oral and maxillofacial specialist with a local infiltration injection of 2% lidocaine and 1:80000 epinephrine for anesthesia and homeostasis. The retromolar incision and curettage were performed with a spoon curette. The cavity was then filled through local hemostatic surgery and the lesion sample was sent to the laboratory for pathological evaluation. In the histopathological images, cyst-like spaces without epithelial lining (pseudocysts) and new and old bleeding sites (hemosiderin pigment), blood cells consisting of eosinophils, lymphocytes, plasma cells and odontogenic epithelial debris with cylindrical (ameloblastic) and stellate lining cells were observable. The diagnosis was a pseudocyst with excessive hemorrhage (**Fig. 4**).

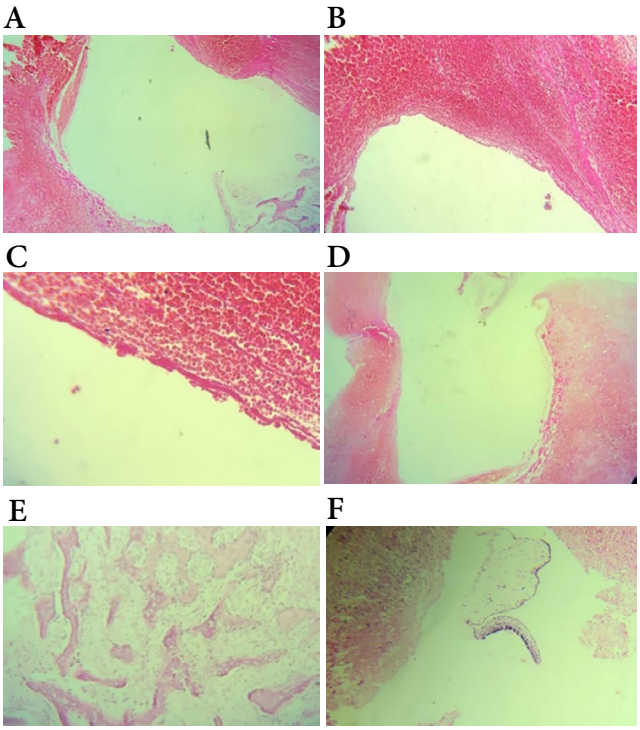

Figure 4: Histopathological images of the lesion; Cyst-like space without epithelial lining (**A, B, C, D**). Sections of normal bone trabeculae with an osteoblastic rim border (**E**). Odontogenic cysts with cylindrical cells corresponding to the second molar follicle (**F**).

For the first three months after the biopsy, 500 units of factor VIII were injected twice weekly, followed by weekly injection of 500 units of factor VIII for three months. Regular visits to adjust factor dose based on tolerability of therapy were also prescribed. There was no recurrence of swelling or bleeding at the surgical site or elsewhere within 12 months after therapy and no allergy to the injected factors was noted (**Fig. 2**).

3. Discussion

The exact pathophysiology of HPT (hemophilic pseudotumor) has not yet been elucidated, although several hypotheses have been put forward, including osteonecrosis with hemorrhage, subperiosteal hemorrhage or soft tissue necrosis and bone destruction, and formation of a cystic lesion with bone destruction and hemorrhage [4].

Starker et al. reported in 1918 the first case of HPT in a 14-year-old boy with hemophilia and swelling in the right femur with a recent history of trauma. Cortical degradation and reduction in periosteal thickness were observed in radiographs diagnosed as osteosarcoma. Upon probing the lesion, 750 ml of blood was lost and the patient died of fever and anemia after 4 days [6]. The first case of a mandibular PTH was reported in 1968 by Lazarovits et al. in an 11-year-old boy with mild hemophilia, who was treated with radiation therapy and eventually recovered [7]. Several cases of unknown pseudotumors were reported by 1975 and mortality and morbidity were high due to lack of diagnosis and inadequate treatment. However, significant improvements have been made in treatment with factor therapy in combination with surgery [2, 8]. Intraosseous radiographs show an osteolytic lesion with distinct and irregular geography-like and often expansile borders that extend into the soft tissue [1]. We searched the Google Scholar, Scopus and PubMed databases and found fewer than 50 cases of mandibular PTH [2, 3], of which about 70% had hemophilia A and 20% had hemophilia B (**Table 1**). Most patients were male. In addition, about 40% of patients had moderate and 10% had severe hemophilia. The age range was between 5 months and 34 years with a mean age of 11.5 years. Most cases involved the posterior mandible and in eight cases a history of trauma was reported. The most common signs and symptoms were painless swelling and bleeding in the mandible and problem in mastication. Paresthesia, dysesthesia, and significant nerve involvement were also reported in several cases.

Table 1: Mandibular hemophilic pseudotumor cases in 2020-2021 [3].

Study	Nanda Pai et al., 2020 [3]	Nanda Pai et al., 2020 [3]	Xu Cai, 2020 [10]
Age (years)	11	9	11
Sex	Male	Male	male
Location	Mandible	Mandible	maxilla
Size (cm)	4×4	5×2.1	3×2.5
Clinical presentation	painless swelling	swelling, gingival bleeding	painless swelling
Duration (months)	2	1	6
Trauma	No	Tooth extraction	no
Type of hemophilia	Severe	Severe	mild
Treatment	curettage and factor	curettage and factor VII therapy	right subtotal maxillectomy
Radiographic view	VII therapy	loculated radiolucent	multicystic low-density shadow in
Follow-up	loculated radiolucent	healed, no recurrence	CT scan
	healed, no recurrence (1 year)	(9 months)	healed, no recurrence (5 years)

Radiographs often showed multilocular osteolytic lesions with bone expansion and sometimes a formation of radiopaque specks and reactive bones. Some cases were treated with surgery, including curettage, enucleation, tooth extraction, and even hemimaxillectomy or hemimandibulectomy, with or without coagulation factor replacement. About 25% of the cases were treated with hemophilic factor alone with aminocaproic acid and ethanol embolization.

The differential diagnosis of PTH includes osteolytic lesions with irregular borders that involve the periosteum and can result in bone formation. These have been discussed in the literature and include osteomyelitis, giant cell tumor, osteitis deformans, cystica fibrosa, solitary plasmacytoma, reticular cell sarcoma, metastasizing and osteogenic sarcoma [1].

Several strategies have been proposed to limit or treat the lesions. One possible treatment is low-dose radiotherapy (2-23 Gray) with or without additional coagulation factor VIII and has shown the best results. Radiation destroys small blood vessels and replaces them with fibroblastic and calcified tissue after four weeks, with a healing time of 8-12 weeks. During this time, due to bleeding, coagulation factor VIII is recommended to compensate for the factor deficiency. A less invasive method is immobilization with factor injection, while resection, drainage or curettage with cavity filling has been suggested for the surgery [4, 9]. Some studies have recommended that patients with facial asymmetry, especially children, receive prompt medical intervention to allow calcification and bone regeneration, thus allowing the jaw to continue growing to reduce the likelihood of asymmetry, deformities and cosmetic problems. Early detection and intervention of PTH are also important. A key issue in the diagnosis and treatment of PTH is the collaboration of specialists, i.e. hematologists, oral surgeons, maxillofacial pathologists and radiologists.

4. Conclusion

Because hemophilic pseudotumor is rare, demographic information, careful examination, and radiography play an important role in correct diagnosis, otherwise it can be misdiagnosed as a bone tumor, which can lead to unnecessary aggressive interventions and serious consequences. The primary goal of treatment is control of bleeding and homeostasis, although long-term plasma transfusion is sometimes required. However, therapeutic interventions should be done early to prevent infection, jaw fracture, deformity, and cosmetic problems, as their treatment can become difficult over time.

Ethical considerations

The patient's parents signed an informed consent form, provided that the patient's name would be excluded.

Conflict of interest

None.

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References

1. Prasad, R.K., et al., Self healing hemophilic pseudotumor of the mandible in a 5-year-old boy, an interesting and rare finding: Case report and review. Journal of Indian Society of Pedodontics and Preventive Dentistry, 2016. 34(1): p. 82.
2. Throndson, R.R., et al., Pseudotumor of hemophilia in the mandible of a patient with hemophilia A. Oral surgery, oral medicine, oral pathology and oral radiology, 2012. 113(2): p. 229-233.
3. Pai, N., et al., Pseudotumour of haemophilia in jawbones: A systematic review and report of two cases managed conservatively. Haemophilia, 2020. 26(3): p. 409-421.
4. Chattopadhyay, P.K., et al., Hemophilic pseudotumor of the mandible in a patient with hemophilia B. Oral and maxillofacial surgery, 2017. 21(4): p. 467-469.
5. Lima, G.S., et al., Maxillary hemophilic pseudotumor in a patient with mild hemophilia A. Journal of pediatric hematology/oncology, 2008. 30(8): p. 605-607.
6. Starker, L., Knochenusur durch ein hamophiles, subperiostales Hamatom. Mitt Grenzgeb Med Chir, 1918. 31: p. 381-415.
7. Lazarovits, P. and M.L. Griem, Radiotherapy of hemophilia pseudotumors. Radiology, 1968. 91(5): p. 1026-1027.
8. Ahlberg, A., On the natural history of hemophilic pseudotumor. The Journal of bone and joint surgery. American volume, 1975. 57(8): p. 1133-1136.
9. Rodriguez, M.E.C., Hemophilic Pseudotumors: Diagnosis and Management (CURRENT CONCEPTS REVIEW). 2020.
10. Cai, X., et al., Intraosseous venous malformation of the maxilla after enucleation of a hemophilic pseudotumor: A case report. World Journal of Clinical Cases, 2020. 8(19): p. 4644.