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Hemophilic pseudotumor in a non-hemophilic patient treated with a hybrid procedure of preoperative embolization of the feeding arteries followed by surgical resection—A case report

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ABSTRACT

INTRODUCTION: Hemophilic pseudotumor is a rare but well documented complication seen in approximately 1–2% of patients with hemophilia. The incidence continues to decrease, likely because of increasingly sophisticated techniques in managing factor deficiency. We present a case of hemophilic pseudotumor in a patient without hemophilia, an exceptionally rare entity, and outline a hybrid approach to treatment.

PRESENTATION OF CASE: The patient presented with a left sided iliopsoas mass and associated radiculopathy, with a history of a poorly characterized bleeding diathesis and Noonan's syndrome. He had no history of trauma and was not being treated with anti-coagulation. Of note, factors VIII, IX and XI were normal. An open biopsy was consistent with hemophilic pseudotumor. The patient underwent a hybrid procedure of preoperative embolization of the left internal iliac and left deep circumflex arteries followed by surgical debridement and resection, with an excellent outcome.

DISCUSSION: Hemophilic pseudotumor is rarely seen in patients with hemophilia, and even less frequently in patients without. Trauma is often the inciting event. A high index of clinical suspicion is required in order to secure the diagnosis, as the radiographic appearance is non-specific. Our patient had no history of trauma, although we question whether his underlying bleeding diathesis may have predisposed him to developing the pseudotumor. Surgery remains the cornerstone of management in these cases.

CONCLUSION: Within the literature, there are only two other cases of hemophilic pseudotumor occurring in a non-hemophiliac patient, highlighting the rarity of this case and the associated diagnostic dilemma.

1. Introduction

Hemophilic pseudotumors are a well-established yet rare complication affecting between 1 and 2% of individuals with severe Hemophilia A and B [1]. Given more recent improvements in the management of factor deficiency, they are seen even less commonly than this. Pseudotumors grow as a result of recurrent, episodic and intermittent bleeding into soft tissue and osseous regions, causing mass effect and destruction of nearby tissues and structures [2]. They are frequently found at sites of previous trauma, as this provides a focus from which hemorrhage and the reparation process occurs [3]. However, they may be seen in the absence of trauma. They occur most frequently in soft tissue but also in bones such as the femur, pelvis and tibia [4]. They can cause compression and damage to adjacent structures; bones may erode or be replaced and connective tissue may become atrophic and necrotic. Serious sequelae include compartment syndrome or permanent limb contractures with loss of function [5].

The radiologic appearance of a pseudotumor will depend on its' size, location and extent of growth. Pseudotumors may be mistaken for malignant tumors as a result of their clinical presentation and findings on imaging [6]. While the pseudotumor itself is usually painless, compression on local structures and nerves can produce

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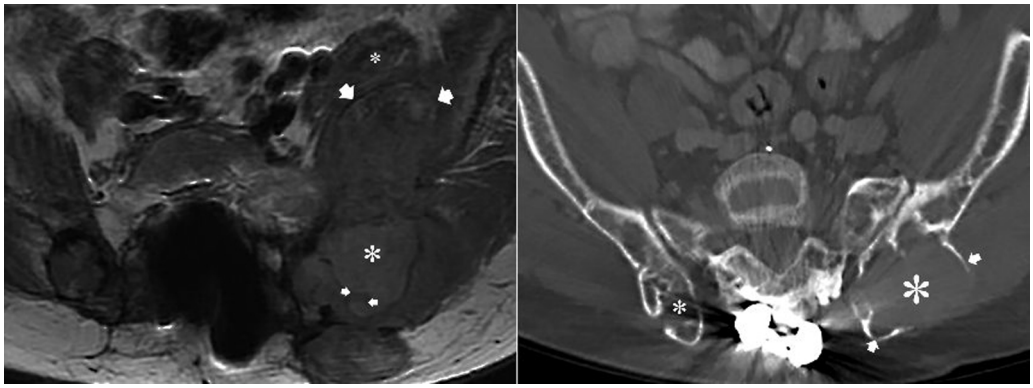

Fig. 1. (a) Axial noncontrast CT of the pelvis shows a large lytic lesion in the posterior left ilium (large asterisk) with prominent expansile remodeling of the ilium (arrows). The lesion is likely at the site of prior bone graft harvesting during prior spinal surgery. Note small similarly located lesion in the contralateral ilium (small asterisk). (b). Axial T1-weighted SE MR image shows the mass extending anteriorly into the iliacus muscle (large arrows), displacing the psoas muscle (small asterisk) anteriorly. The mass shows heterogeneous signal intensity with areas of increased signal (large asterisk) consistent with subacute bleeding. Subtle fluid levels (small arrows) are noted. While not specific for a diagnosis, they are characteristic of prior hemorrhage.

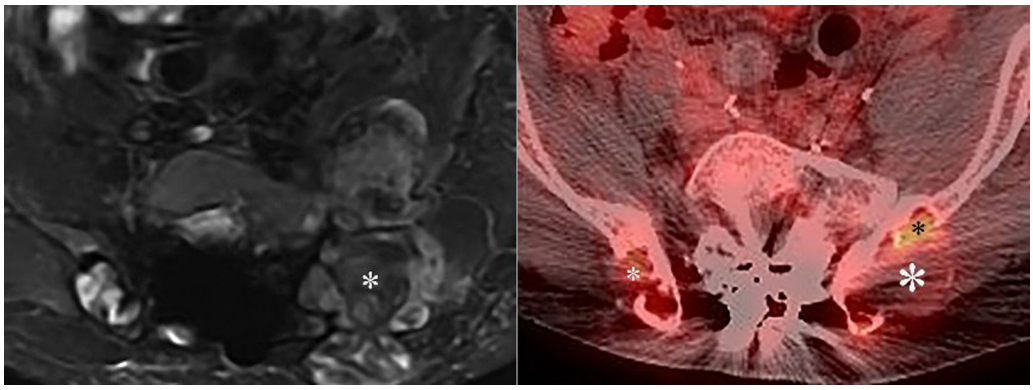

Fig. 2. (a) Corresponding axial inversion recovery image shows the mass to have a complex, relatively intermediate, signal intensity. The small fluid levels seen on the T1-weighted image are not appreciated. (b). Corresponding fused image from PET/CT shows the small lesion in the posterior right ilium (small white asterisk) to have relatively low level metabolic activity. The large lesion on the left (large white asterisk) shows a focus of somewhat greater metabolic activity (black asterisk), reaching that which can be seen with malignancy.

significant pain and neurological deficits [7]. Given its ability to delineate soft tissue structures, magnetic resonance imaging (MRI) is a very useful tool for visualization of hemorrhagic pseudotumors of soft tissue. Computed tomography (CT) imaging is more useful for evaluating pseudotumors that involve bone. The MRI appearance of pseudotumors is relatively consistent, depicting the characteristic time dependent signal changes associated with hemorrhage. These findings are not specific to pseudotumors; however, and are also seen in malignant tumors with hemorrhagic components [8]. Without prior knowledge of a patient's hematological condition, it is unlikely that hemophilic pseudotumor will rank highly in the differential diagnosis for this radiological presentation. In those patients without factor deficiency, the diagnostic challenge is even greater.

2. Presentation of case

A 46 year old male with a history of Noonan's syndrome and surgically corrected congenital heart disease presented with progressively worsening back pain of six months duration. The pain radiated down the left lower leg, suggesting radiculopathy. The patient noticed a small lump located in the left ileo-lumbar region which was increasing in size, with concomitant worsening of his symptoms. He had no history of trauma to this area and was not on anti-platelet medications or anti-coagulations. Two years previously, he was noted to have mild isolated thrombocytopenia and splenomegaly, which can be seen in Noonan's syndrome. Due to a family history of myeloproliferative disorders, he underwent a bone marrow biopsy. Both samples showed necrotic and fibrovascular tissue, and were negative for malignancy.

Physical examination demonstrated a 6-cm, tender mass palpable under the skin of the left lower back. Hip range of motion was preserved bilaterally, flexion of the hip produced pain of the left, and extension was non-tender. Plantar flexion was preserved bilaterally. There was diminished sensation in no particular nerve root distally in the lower extremities. Initial laboratory values are shown below:

Laboratory Test	Value	Reference Range
Hemoglobin	138.0 g/L	140–175 g/L
Platelets	109×10^9 L	$151–355 \times 10^9$ L
Prothrombin time	14 s	11.8–14.2 s
Activated partial thromboplastin time	35.8 s	25.0-35.0 s
International normalized ratio	1.12	0.8–1.1
Fibrinogen	8.41 μmol/L	5.8–11.8 μmol/L
Factor VIII	93%	55–200%
Factor IX	117%	65–140%

Lumbar CT imaging showed a 12 cm left-sided mass located over the iliac bone (Fig. 1a). MR imaging demonstrated extension of the mass into the pelvis with displacement of the left iliopsoas muscle ventrally, located within one centimeter of the left internal iliac artery. Posteriorly, it extended into the subcutaneous tissue (Figs. 1 b & 2 a). Increased metabolic activity was noted on PET/CT with a standardized uptake value of 1.8 (Fig. 2b). CT guided biopsy

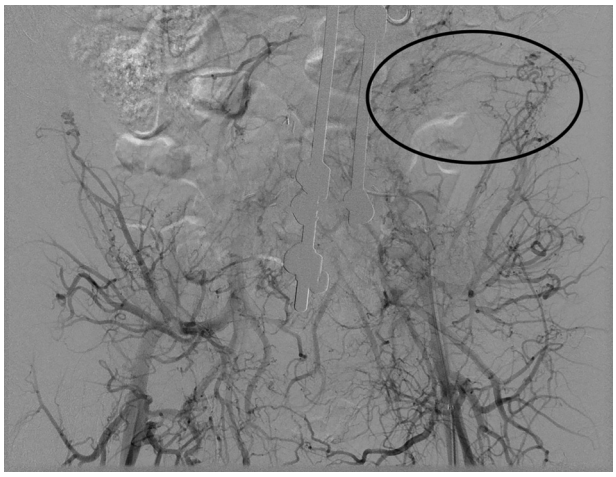

Fig. 3. Late arterial phase image from pre-embolization arteriogram shows areas of prominent vascularity associated with the lesion (oval).

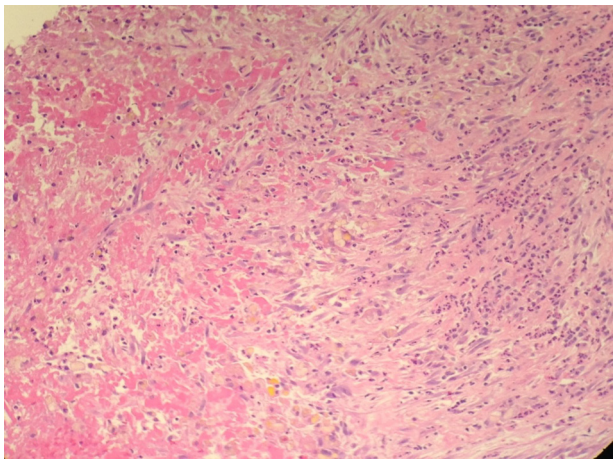

Fig. 5. Pathology slide demonstrating areas of dense fibrosis, chronically inflamed granulation tissue and a fibrin capsule. No areas of malignancy noted.

revealed an "entirely necrotic mass" without a specific diagnosis; hence surgical intervention and tumor debulking was planned.

There was concern regarding the patient's hematological status in the perioperative period, given his mild thrombocytopenia and a prior history of perioperative bleeding. Surgery was anticipated to be extensive and in close proximity to blood vessels so Hematology were consulted for expert opinion. Further laboratory data suggested evidence of disseminated intravascular coagulation (DIC), supported by a markedly elevated soluble fibrin monomer, D-dimer and mild thrombocytopenia. Additional hematological workup suggested a dysfibrinogenemia. Treatment of this condition is not routinely required unless the patient is actively bleeding, in which instance fresh frozen plasma (FFP) or cryoprecipitate can be used. Given the high risk of perioperative blood loss, the patient's hematologic status was optimized using subcutaneous heparin to treat the DIC and FFP immediately prior to surgery.

The patient underwent a hybrid procedure of preoperative embolization of the left internal iliac and left deep circumflex arteries (Fig. 3), followed by surgical debridement and resection. The surgical procedure consisted of an open biopsy and debridement of the tumor bulk (Fig. 4a & b). The lesion extended through the subcutaneous tissue and gluteus maximus and had completely eroded through the ilium posteriorly. The mass, along with the pseudocapsule was removed. Frozen section showed no evidence of malignancy and the pathological findings were consistent with that of hemophilic pseudotumor (Fig. 5).

The patient required a total of three units of FFP for mild bleeding episodes in the perioperative period. The laboratory findings of DIC resolved after the removal of the pseudotumor. His remaining hospital course was uncomplicated and the patient was discharged home on postoperative day five.

3. Discussion

There have been cases of hemophilic pseudotumor reported in the literature for more than a century [9]. Males are almost exclusively affected due to X-linked inheritance patterns. In non-hemophiliac patients, these pseudotumors are very rare, with only two documented cases in the literature to date [10,11]. They are the result of chronic, repeated small volume bleeds creating a slowly expanding heterogeneous hematoma inside a fibrous capsule. A high index of suspicion is required in order to diagnose a hemophilic pseudotumor but is only likely to be considered in patients with known bleeding disorders. On radiologic imaging including CT and MRI, hemosiderin deposition within the pseudotumor results in a dense and heterogeneous appearance, similar to that seen in benign and malignant tumors, infectious processes and abscesses [12]. MRI is the most useful imaging modality for diagnosis but is nonspecific [8]. As a result, they are often initially suspected for malignancy, as was true in this case.

Management differs depending on the site and size of the pseudotumor, although the literature suggests that surgical excision is the preferred treatment in most cases [13]. If surgery is not a feasible option, alternative treatment strategies including arterial

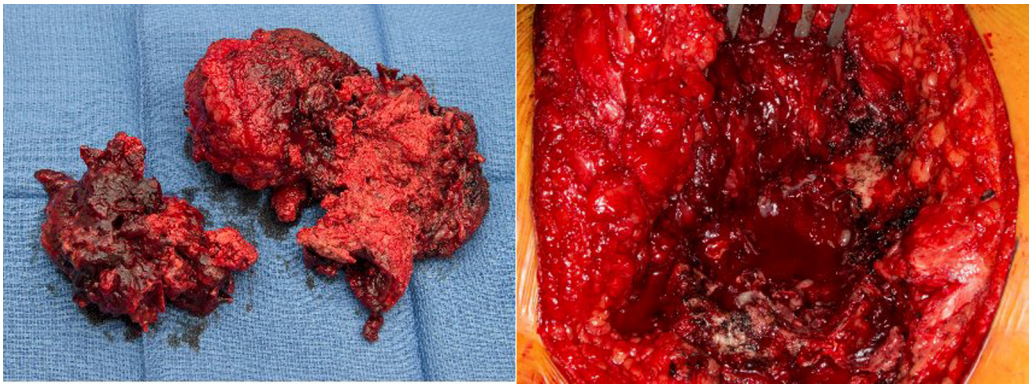

Fig. 4. (a) & (b) Intraoperative images showing two necrotic masses that were dissected out from the surrounding tissue. The mass on the left measured approximately 2.5 × 2.0 × 0.3 cm while the one on the right measured approximately 10.0 × 6.0 × 5.0 cm.

embolization and radiotherapy have been employed with some success. In this case, a hybrid approach of feeding 'culprit vessel' arterial embolization was utilized as an adjunct to surgery in order to minimize intraoperative bleeding, with good results. Choosing when to operate depends on several factors including lesion size, site, associated symptoms, impact on daily functioning, comorbid conditions and hematological status. A multidisciplinary team approach is paramount in ensuring best outcomes for these patients.

There are approximately thirty five cases of hemophilic pseudotumor documented in the literature over the past ten years. Two of these occurred in non-hemophilic patients. Stevenson and Keast [10] discussed a case in a patient who was anticoagulated with warfarin and developed a nasal pseudotumor resulting in epistaxis. This lesion was treated with radiotherapy with good response. Gouse et al. [11] described the case of a pelvic hemorrhagic pseudotumor treated with surgical excision with good recovery. Our patient had no history of trauma and was not on any medications that could cause or exacerbate bleeding. He did, however, have an undefined bleeding diathesis characterized by mild thrombocytopenia, an elevated soluble fibrin monomer and an elevated D-dimer. Factor levels were all within normal limits. Bleeding was managed with the administration of FFP as needed in the perioperative period. He was treated preoperatively with subcutaneous heparin to address the laboratory evidence of DIC. Interestingly, this resolved following surgical removal of the pseudotumor.

Is it possible that our patients' bleeding diathesis put him at increased risk of developing a pseudotumor? Perhaps other conditions aside from hemophilia increase a patient's risk? Given the burden of bleeding disorders along with the use of antiplatelet/anticoagulant medications in the population, it would be expected however, that these pseudotumors would be seen more frequently. There is no evidence to support this theory within the literature, but in the absence of other known precipitating factors in our patient's history, it is worth considering.

4. Conclusion

To the best of our knowledge, this report represents one of three cases in the literature of hemophilic pseudotumor in a non-hemophiliac patient [10,11]. It highlights the diagnostic and therapeutic challenges associated with hemophilic pseudotumors, and raises the question as to whether our patient's unspecified bleeding diathesis put him at increased risk. This case was managed with a hybrid procedure of coil embolization and surgical resection, with excellent results.

Declaration

This manuscript had been reported in line with the CARE criteria of 2013 [14].

Conflicts of interest

None.

Funding

None.

Ethical approval

Ethical exemption was obtained prior to undertaking this case report from the Mayo Clinic Institutional Review Board.

Consent

Informed consent was obtained from all participating parties involved within this case report. All personal information was anonymized where applicable.

Author contribution

Sorcha Allen collected the data regarding the case and drafted the manuscript.

Craig Reeder provided expert Hematology input and reviewed the paper.

Mark Kransdorf selected the radiology images, provided the figure legends and reviewed the paper.

Christopher Beauchamp provided intra-operative images and expert commentary regarding the surgical aspect of the case.

Matthew Zarka: Provided the pathological specimen images and expert input along with review.

Farouk Mookadam supervised the project, designed the format and modified the manuscript.

Guarantor

Guarantor #1: Sorcha Allen.

Guarantor #2: Farouk Mookadam.

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