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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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 iliopectoral mass and associated radiculo-patellar, 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-hemophilic patient, highlighting the rarity of this case and the associated diagnostic dilemma.

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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 repairation 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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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 pseudotu-
mors 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 hem-
orrhage. These findings are not specific to pseudotumors; however,
and are also seen in malignant tumors with hemorrhagic compo-
nents [8]. Without prior knowledge of a patient’s hematological
condition, it is unlikely that hemorrhagic pseudotumor will rank
highly in the differential diagnosis for this radiological presenta-
tion. 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 pro-
gressively 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 ilio-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 pre-
viously, 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 fibrovas-
cular tissue, and were negative for malignancy.

Physical examination demonstrated a 6-cm, tender mass palpa-
table 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 × 10^9/L |
| Prothrombin time           | 145 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 µg/dL | 5.8–11.8 µg/dL    |
| 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 mus-
cle ventrally, located within one centimeter of the left internal
iliac artery. Posteriorly, it extended into the subcutaneous tissue
(Figs. 1b & 2a). Increased metabolic activity was noted on PET/CT
with a standardized uptake value of 1.8 (Fig. 2b). CT guided biopsy
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).

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

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-hemophilic 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
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 ant platelet/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-hemophilic 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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