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Case Report

Multifocal eosinophilic granuloma with femoral epiphyseal lesion mimicking an aneurysmal bone cyst☆,☆☆,★

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ABSTRACT

Eosinophilic granuloma (EG) is a rare benign tumor-like disorder characterized by abnormal proliferation Langerhans cells. EG frequently presents as a solitary lesion in the axial skeleton and diaphysis long bones. Here we present the case of a 14-year-old male with multifocal EG with a lesion located in the femoral epiphysis mimicking an aneurysmal bone cyst that presented a diagnostic challenge. While the initial presentation of EG patients may appear uncommon, its overlapping features with other benign and malignant etiologies highlight the importance of increased awareness of this condition, as well as the need for an experienced multidisciplinary team in its diagnosis and treatment.

Introduction

Eosinophilic granuloma (EG) is a benign tumor-like disorder characterized by abnormal proliferation of antigen-presenting cells of myeloid dendritic origin known as Langerhans cells [1]. Along with Hand-Schuller-Christian disease and Letterer-Siwe disease, they compose the Langerhans cell histiocytosis; eosinophilic granuloma being the mildest and most common subtype [2,3]. EG frequently presents as a solitary lesion; even though a polyostotic form has been described. It involves the axial skeleton and diaphysis long bones as well as the soft tissues adjacent to the bone causing localized bone pain and tender soft tissue swelling [4]. It has a slight male predominance most commonly affecting the children and young adults; however, it can rarely be seen in adults [5–7].

Imaging studies such as radiographs, MRI and CT scans show a wide variation of nonspecific findings including bone destruction, cortical changes, periosteal reaction, ossification, as well as soft tissue inflammation and edema [8].

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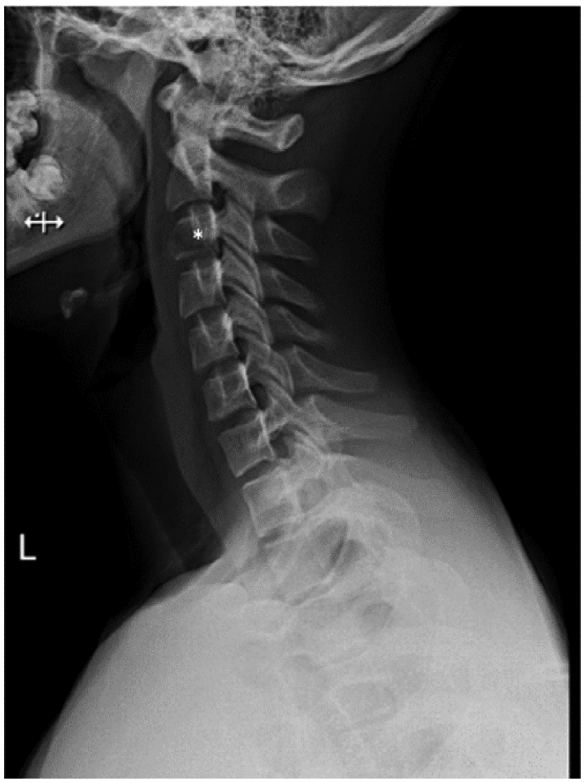

Fig. 1 – Lateral Radiograph of the cervical spine demonstrating a lytic lesion on the anterior cortex of the C3 vertebral body (*) with an associated prevertebral soft tissue swelling.

Therefore, the diagnosis must be confirmed histopathologically and immunohistochemically with a biopsy. The sample obtained is characterized by the presence of clonal proliferation of myeloid dendritic cells with Langerhans cell morphology with surrounding small lymphocytes, eosinophils, and histiocytes [7,9].

Treatment options may vary depending on the localization and extent of the disease. In unifocal eosinophilic granuloma, close observation of the patient as well as surgical excision, radiotherapy, intralesional administration of corticosteroid and chemotherapeutic agents like vinblastine and etoposide might be considered [7,10,11]. In some cases, spontaneous regression of the lesion has been reported [11]. Patients with extensive disease and visceral organs involvement should undergo systemic chemotherapy [12]. The paucity of this disease, with a limited number of cases described in the literature, and unspecific radiologic findings, can make its correct identification challenging for the treating physician. Here we describe a case of a patient with polyostotic eosinophilic granuloma that presented with a lesion in the femoral epiphysis simulating an aneurysmal bone cyst.

Case report

A 14-year-old male, previously healthy, presented to the emergency department due to a complaint of posterior neck pain. Per the patient the pain started 2 weeks prior, without any trauma, and was aggravated that morning. Additionally, the patient commented on a remote history of left hip pain which was intermittent and mild however fully improved in the last 3 months. He denied any neurological deficits, unintentional weight loss, fevers or any other constitutional symptoms. A cervical spine radiograph was taken and reported as having a nondisplaced anterior cortex fracture at the level of C3 along prevertebral soft tissue swelling (Fig. 1). Following a CT scan without contrast was obtained showing a lytic lesion in C3 with cortical disruption and a soft tissue extension (Fig. 2). At this point, the patient was placed on a cervical collar and an MRI with and without contrast was requested. The exam demonstrated an enhancing marrow alteration in C3 with anterior cortex breakthrough and an area of enhancing soft tissue prevertebral which extended longitudinally over C2 and C4 (Fig. 3). No pathological compression fracture was noted, and no canal involvement was present. Additionally, a radiographic skeletal survey was obtained searching for polyostotic compromise. Besides the cervical lesion, a multilocular cystic lesion was noted within the left femoral head with the dif-

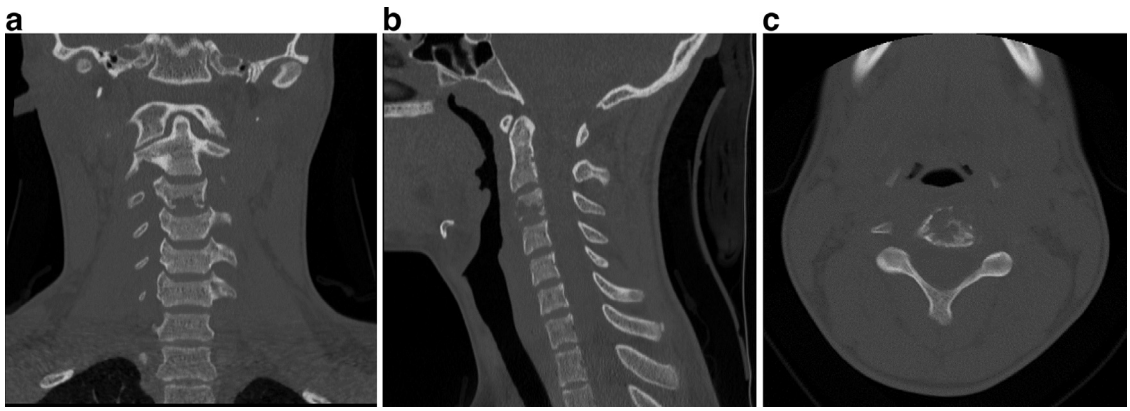

Fig. 2 – CT scan without contrast with coronal (A), sagittal (B), and axial (C) views showing a lytic destructive lesion involving the C3 vertebral body with cortical disruption and a prevertebral soft tissue component.

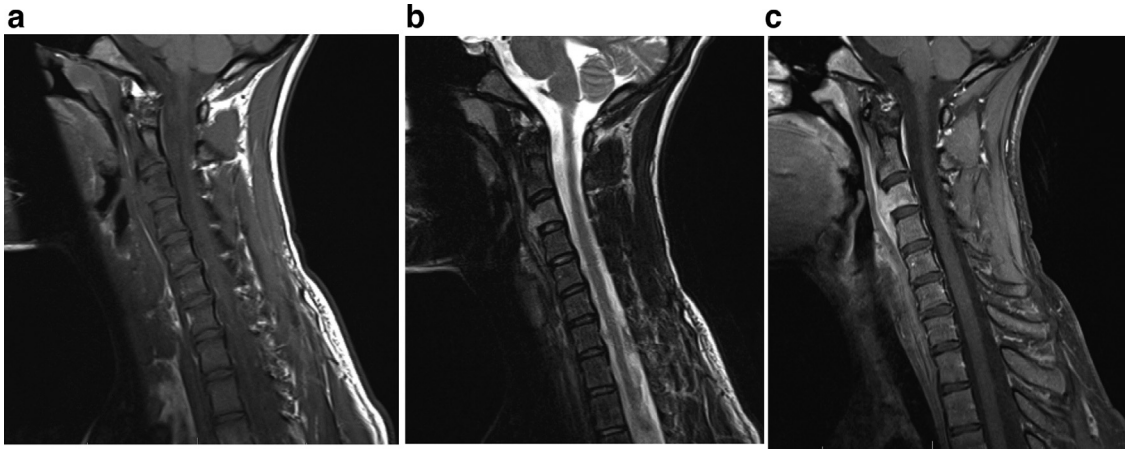

Fig. 3 – MRI with and without Gadolinium enhancement with TSE T1 (A), T2 Dixon (B), and T1 Dixon postcontrast (C) sequences. There is enhancement marrow signal alteration in the C3 vertebral body with breakthrough into the prevertebral space. No canal involvement is noted.

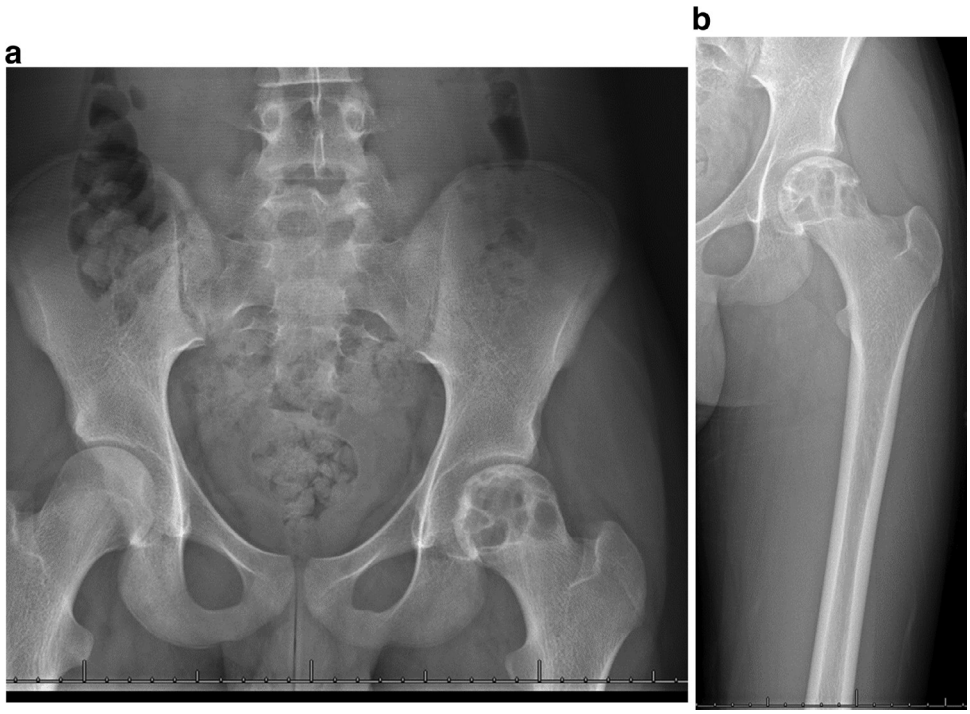

Fig. 4 – Skeletal survey study, here depicting a pelvis AP (A) and femur AP (B) radiograph demonstrating a multilocular cystic lesion involving the proximal left femur epiphysis with internal septations noted.

ferential diagnoses of aneurysmal bone cyst or giant cell tumor with secondary aneurysmal degeneration (Fig. 4). Following an MRI with and without contrast of the left femur was obtained showing a cystic lesion with fluid-fluid levels within the proximal femur epiphysis, an image again consistent with an aneurysmal bone cyst or a giant cell tumor with secondary aneurysmal degeneration (Fig. 5). The patient underwent an open biopsy of the cervical spine lesion which confirmed the diagnosis of eosinophilic granuloma (Fig. 6). A few days later the patient also had a percutaneous biopsy of the femoral head lesion given the radiologic images aiming at a different diagnosis. In this case the biopsy showed only focal reactive changes and ruled out an aneurysmal bone cyst and a giant cell tumor, and even though with the sample obtained a confirmation of eosinophilic granuloma could not be achieved, after thorough multidisciplinary discussion a decision was made to treat the patient as a polyostotic eosinophilic granuloma. The patient was then placed on 12 months of a combination of vinblastine and prednisone. At the end of treatment, 3 months from the initial diagnosis, a cervical MRI with and without contrast was obtained showing complete resolution of the initial lesion (Fig. 7). Radiographs of the left fe-

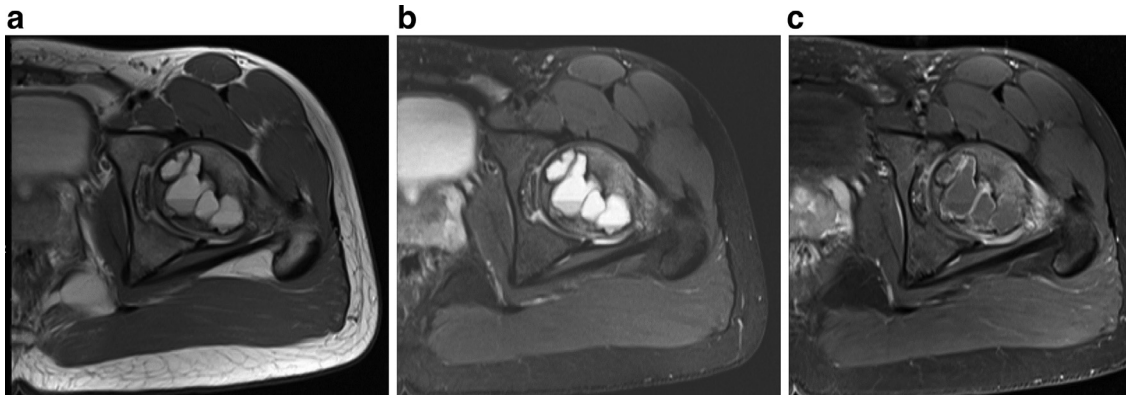

Fig. 5 – MRI with and without gadolinium enhancement. Axial views of PD (A), stir (B) and FS postcontrast (C) sequences depicting a femoral head multi-cystic lesion with narrow zone of transition, irregular margins, fluid-fluid levels and peripheral enhancement.

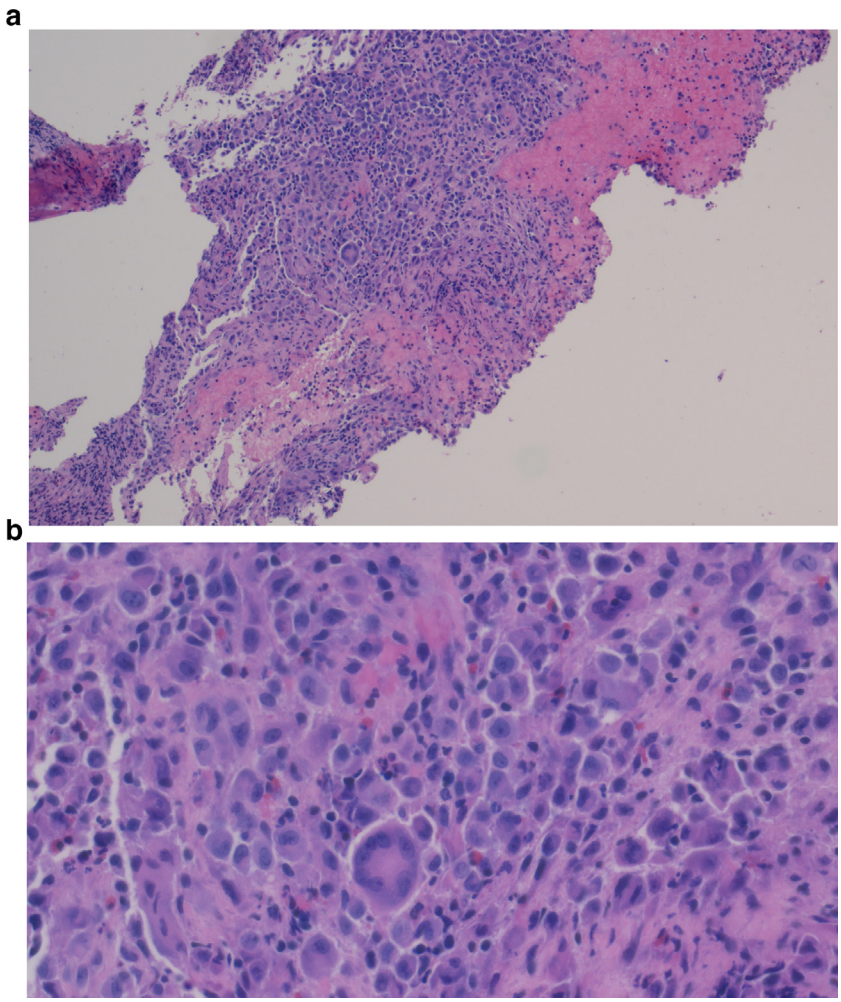

Fig. 6 – Biopsy sample from the C3 vertebral body demonstrating at H&E x10 (A) and H&E x40 (B) a clonal neoplastic process involving the bone. The cells contain large vesicular nuclei with eosinophilic cytoplasm. The background consists of small lymphocytes and eosinophils.

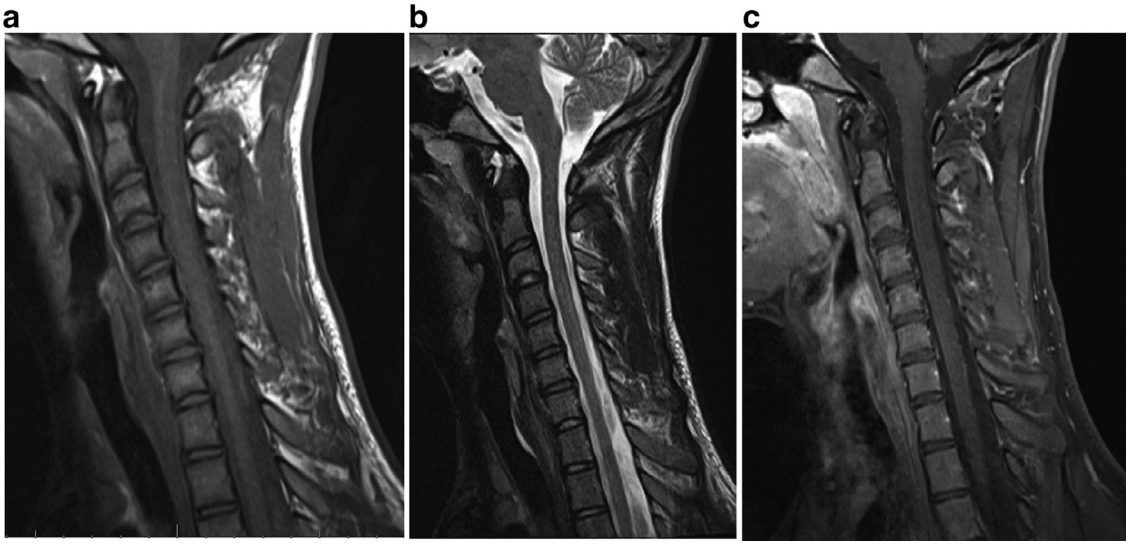

Fig. 7 – Cervical spine MRI with and without Gadolinium enhancement 3 months from diagnosis and post-systemic treatment. TSE T1 (A), T2 Dixon (B), and T1 Dixon postcontrast (C) sequences showing resolution of the initial lesion.

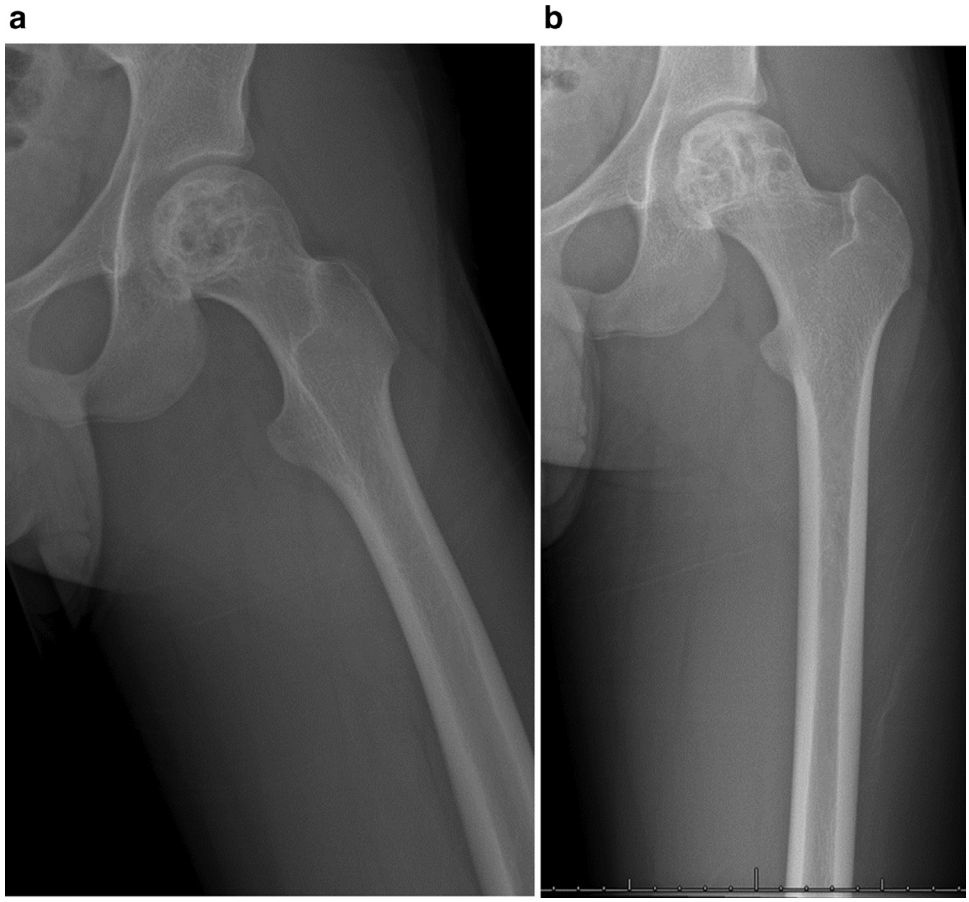

Fig. 8 – Proximal femur AP (A) and lateral (B) radiograph 3 months from diagnosis and postsystemic treatment demonstrating increasing resolution of the previously noted cystic areas within the proximal femoral epiphysis.

mur were also obtained at that point in time, which showed improvement of the area with new bone ingrowth where the cystic lesion was originally noted, confirming a response of the femoral epiphysis lesion to the systemic therapy and corroborating the diagnosis of eosinophilic granuloma in this location as well (Fig. 8). A year after completing treatment the patient is completely asymptomatic.

Discussion

Eosinophilic granuloma is a type of benign bone tumor, and the mildest subtype of Langerhans cell histiocytosis. This condition has been described in many different anatomic locations within the human body [2,3,6–8,11,12], and may present either in a single or multiple foci. This disease typically affects the axial skeleton, however, may also affect long bones with the majority of lesions occurring in the diaphysis [1]. Isolated case reports have also described of other less common locations such as the femoral neck [13]. There are also patterns of the disease typically consistent with pediatric versus adult-onset presentation. Pediatric lesions are more commonly encountered in the skull and thoracic spine, [14] while lesions in adults are more commonly found in the mandible and cervical spine [15].

Eosinophilic granuloma presents with a non-specific radiographic appearance. Radiographs can show lytic lesions which may or may not demonstrate periosteal reaction. Cortical involvement varies widely based on location and size of lesion, however, typically demonstrates distinct borders with a "punched-out" appearance. Sequestrum may also be present, representing residual bone within the lesion. Often the physis acts as a barrier, although less commonly the lesion may extend transphyseal. Isolated epiphyseal lesions are described as rare [16]. Cross-sectional imaging such as computed tomography or magnetic resonance imaging can be helpful in further identifying characteristics, to evaluate adjacent soft tissue involvement, and may be especially useful in imaging of the spine and for preprocedural planning. A number of other benign and malignant etiologies demonstrate similar or overlapping radiographic characteristics with eosinophilic granuloma including (but not limited to) osteomyelitis, tuberculosis, multiple myeloma, plasmacytoma, and lymphoma. Lesions are typically seen as areas of increased radiotracer uptake on nuclear medicine bone scintigraphy scans [1,16].

Once a biopsy specimen has been obtained, there are certain histologic stains that can help confirm the diagnosis. As it is a subtype of Langerhans cell histiocytosis, positive staining for Langerhans cells is demonstrated. CD1a is one of the most common positive histologic markers seen in eosinophilic granuloma, however other markers such as S-100 and CD207 (Langerin) are also useful in establishing a diagnosis [1,17]. Electron microscopy may also be performed, demonstrating the pathognomonic tennis-racket shaped Birbeck granules within the Langerhans cells. Treatment of eosinophilic granuloma typically depends on the extent and location of disease and may include surgical treatment such as curettage with bone grafting versus non-surgical treatment such as expectant management, radiation therapy, intralesional injections, or chemotherapy [18].

Conclusion

The patient described here initially presented with a unique combination of findings. To begin with, polyostotic eosinophilic granuloma accounts for an estimated 10% of patients compared to the monostotic form which occurs in ~90% of patients [1]. In addition, as stated above the thoracic spine is more typically affected in pediatric patients rather than the cervical spine which is described here. The lesion in the femur of our patient is also less common as it was located in an epiphyseal location (femoral head) rather than the usual diaphyseal location. This presented a unique challenge in identifying a correct diagnosis for this patient, as the femoral head lesion was initially thought to be either an aneurysmal bone cyst or giant cell tumor and even after obtaining a biopsy specimen of the femoral head lesion the diagnosis remained unclear. Both areas in question responded favorably to the prescribed treatment of vinblastine and prednisone. While the initial presentation of patients with eosinophilic granuloma may appear uncommon or unique, its overlapping features with other benign and malignant etiologies highlight the importance of increased awareness of this condition, as well as the need for a competent multidisciplinary team in its diagnosis and treatment.

Patient consent

Per the local Institutional Review Board consent was exempt due to this being the case of research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimen with the information being recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. Nevertheless, the patient was informed and consented to publication.

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