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Learning Point of the Article:
Histiocytoses are rarely encountered in daily orthopedic practice; but synovial involvement is possible and appropriate care must be taken to avoid misdiagnosis.

Abstract

Introduction: Histiocytoses are rare disorders and most orthopedic surgeons are unfamiliar with this diagnosis. We report a case of synovial non-Langerhans cell histiocytosis (LCH) located in the shoulder, which has not been reported in the literature previously.

Case Report: A 24-year-old female patient presented to our clinic with shoulder pain and decreased range of motion. MRI results suggested pigmented villonodular synovitis. Arthroscopic synovial debridement and biopsy were performed. Histologic examination came back as non-LCH of the shoulder. Hematology/oncology evaluation indicated localized disease and no further treatment was necessary. At the 6th month follow-up, the patient gained full shoulder motion and is symptom free.

Conclusion: This case represents a rare diagnosis of synovial non-LCH which should be considered in the differential diagnosis of synovial diseases. A misdiagnosis could result in inadequate treatment, and coordination with the hematology/oncology department is of utmost importance in the treatment of this neoplastic disease.

Keywords: Shoulder, synovitis, pigmented villonodular, histiocytosis.

Introduction

The histiocytoses are rare neoplastic disorders, which are characterized by proliferation of accessory cells of the immune system such as dendritic cells or macrophages. This wide spectrum of diseases has more than 100 subtypes, and the most recent classification system includes five different main groups [1]. Langerhans cell histiocytosis (LCH) is the main subtype that includes the majority of these cases and is defined by the presence of Langerhans cells with characteristic morphologic and immunophenotypic features [2]. Non-Langerhans cell histiocytoses (non-LCHs) are a heterogeneous group of disorders with various clinical presentations, both benign and malignant [3, 4]. Since LCH has many orthopedic manifestations such as the “eosinophilic granuloma,” orthopedic surgeons are relatively familiar with this disease [5]. Among the wide range of clinical presentations of non-LCH, musculoskeletal findings are rare. They are limited to certain subtypes, such as multicentric reticulohistiocytosis [6] and Erdheim-Chester disease [7]. This work presents a unique case of synovial non-LCH of the right shoulder, which mimicked pigmented villonodular synovitis (PVNS). The clinical presentation and radiographic findings will be discussed along with a review of the literature on this subject.

Case Report

A 24-year-old female patient presented to clinic with right shoulder pain and decreased range of motion (ROM). Her symptoms began 1 year before presentation, but significantly worsened over the last month. She used nonsteroidal anti-inflammatory drugs which alleviated the pain at the beginning but failed to do so in the last couple of months. Her history was...
negative for any traumatic events, fever, chills, and skin lesions. She did not report any other musculoskeletal symptoms. Her previous medical history and family history were noncontributory.

On physical examination, the patient’s active and passive right shoulder motion was markedly decreased with abduction to 45°, forward flexion to 45°, and abducted internal/external rotation each 30°. The joint was mildly tender on palpation, and the pain was mainly motion related. There was no swelling or erythema of the joint. Her distal pulses were palpable and neurological examination was normal. Detailed orthopedic examination of the axial and appendicular skeleton did not reveal any other findings.

Her initial right shoulder X-rays revealed joint space narrowing and marginal osteophytes, resembling primary glenohumeral osteoarthritis (Fig. 1). An MRI was ordered to reveal the cause of the significant loss of ROM and arthritic changes. Shoulder MRI (with i.v. gadolinium contrast) was reported as “extensive capsulitis and synovitis, synovial thickening/proliferation zones suggestive of PVNS, and a localized nodular component with a diameter of 12 mm. Glenoid cartilage erosion and marginal osteophyte formation” (Fig. 2).

The patient underwent arthroscopic debridement and synovial biopsy of the shoulder with PVNS as a pre-diagnosis. During the surgery, the extensive hypertrophied synovial tissue was debrided, and samples were taken from the nodular portion of the thickened synovium which was also clearly seen on the MRI (Fig. 3). Articular cartilage was also found to be injured, with delaminated areas on both humeral and glenoid surfaces. Early post-operative physical therapy was initiated, and the patient was kept in a sling for 3 weeks.

Histologic examination of the synovial tissue unexpectedly came back as non-LCH of the synovium (Fig. 4). Microscopic appearance was not suggestive of malignant behavior. The tumor had both lymphoid and histiocytic proliferations in a fibroadipose tissue, with the histiocytic component showing significant pleomorphism and occasional giant cells. Immunohistochemical staining of the neoplastic histiocytic cells was positive for CD163 and CD68 (Fig. 5); negative for CD1a, S100, Langerin, fascin, CD33, CD30, HMB45, pankeratin, and MPO. Following these results, the patient was worked up and staged by the hematology/oncology service. Further radiographic examinations including a PET scan and cranial MRI were normal. No further medical therapy was needed.

The patient’s post-operative clinical course was unremarkable. She was pain-free 1 month after surgery, with a significantly better ROM. On her post-operative 3rd month examination, she had pain-free abduction and flexion to 160, internal and external rotation to 75 (Fig. 6). Her latest follow-up visit was at...
The typical scenario faced by the orthopedic surgeon is symmetric diaphyseal osteosclerosis in the long bones of the lower extremity; femur, tibia, and fibula are the most frequently affected bones. Synovial involvement, similar to our case, is extremely rare and only one case report has come to our attention [15], with the difference of coexisting systemic findings. Biopsy sampling and pathological examination is necessary for the diagnosis. CT scan of the chest, abdomen, and pelvis, PET scan, and MRI of the brain and heart recommended for every patient after the diagnosis has been made [13]. Chemotherapy is the main treatment modality for this disease and IFN- is the first choice in the majority of the patients [14]. Recent studies reported that up to 68% of the patients have the BRAF V600E mutation [13], therefore, vemurafenib is utilized as an option of targeted therapy with very promising results [16]. Surgical treatment is not frequently applied; although patients with cranial and retro-orbital lesions may benefit from debulking. The case reported by Aouba et al. [15] described a patient with synovial involvement of the hip joint and was treated with systemic chemotherapy and regression of the symptoms was reported. No surgical intervention was performed.

Multicentric reticulohistiocytosis is another subtype which is extremely rare and causes destructive arthritis and skin lesions, accompanied by multiple systemic manifestations, including underlying possible malignancies [3, 4, 17]. Most of the patients are elderly females, and the majority of the cases present with arthritis, skin lesions appear later [4]. The destructive polyarthritis may be confusing, resembling rheumatoid arthritis, and delaying the diagnosis. Accurate diagnosis and rapid onset of chemotherapy is very important; because 40–50% of the cases progress to a severely destructive arthritis mutilans if not treated properly [18]. The main focus of therapy is to prevent joint destruction with chemotherapeutic agents [4], and if this fails, different surgical options may be considered [19, 20].

Sinus histiocytosis with massive lymphadenopathy, also called the Rosai-Dorfman Disease, is another group of non-Langerhans cell histiocytoses that can affect the musculoskeletal system [4]. The most common presentation is a patient with bilateral cervical lymphadenopathies accompanied by systemic symptoms such as fever, night sweats, and weight loss. Around 8% of the cases have bone involvement, which is rarely isolated [21]. Treatment method is determined on a case-by-case basis. A case located in the talus which also mimicked PVNS has been reported in the literature [22], similarly treated with arthroscopic-assisted surgery. Spinal involvement has also been reported with severe neurologic involvement that required surgical decompression [23].

Discussion

Histiocytic neoplasms are rarely seen in an orthopedic surgery practice, with most of the cases belonging in the LCH [5, 8] group. LCH, formerly referred to as histiocytosis-X, is primarily a disease of the pediatric age group, with majority of the cases being diagnosed between the ages of 1 and 15 [9]. The disease can present itself in monostotic (eosinophilic granuloma), polyostotic or multisystemic forms [5]. When confined to the skeleton, either in the monostotic or polyostotic form, it has a very good prognosis, although multidisciplinary approach together with the hematology/oncology department is always necessary. Treatment options are various and include observation/NSAIDs, corticosteroids, bisphosphonates, and radiotherapy [5]; chemotherapy is usually reserved for patients with systemic disease [10]. Surgical treatment should be decided on a case by case basis; biopsy and curettage either with or without grafting are the frequently applied methods. Spinal disease may result in neurologic deterioration and require surgical decompression [11], so close follow-up is necessary.

Non-LCH is an even more infrequent entity, some subtypes are typically related to the musculoskeletal system. Erdheim-Chester disease is a non-LCH disorder that almost always involves long bones, in the form of multifocal sclerotic lesions [7, 12, 13]. It mainly affects adult male patients in the 5th decade of life [14]. Immunohistochemically, neoplastic histiocytes in this disorder are positive for CD68, CD163, and F XIIIa, negative for CD1a, CD207, and SI100. Skeletal involvement is present in up to 96% of the patients followed by cardiovascular involvement in 77% and central nervous system involvement in 51% [14]. Skin lesions are also present in the form of xanthelasma, and multiple other organ systems are involved. The typical scenario faced by the orthopedic surgeon is symmetric diaphyseal osteosclerosis in the long bones of the lower extremity; femur, tibia, and fibula are the most frequently affected bones. Synovial involvement, similar to our case, is extremely rare and only one case report has come to our attention [15], with the difference of coexisting systemic findings. Biopsy sampling and pathological examination is necessary for the diagnosis. CT scan of the chest, abdomen, and pelvis, PET scan, and MRI of the brain and heart recommended for every patient after the diagnosis has been made [13]. Chemotherapy is the main treatment modality for this disease and IFN- is the first choice in the majority of the patients [14]. Recent studies reported that up to 68% of the patients have the BRAF V600E mutation [13], therefore, vemurafenib is utilized as an option of targeted therapy with very promising results [16]. Surgical treatment is not frequently applied; although patients with cranial and retro-orbital lesions may benefit from debulking. The case reported by Aouba et al. [15] described a patient with synovial involvement of the hip joint and was treated with systemic chemotherapy and regression of the symptoms was reported. No surgical intervention was performed.

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In the above case, the disease involves a single joint without any other musculoskeletal or systemic manifestations. To the best of our knowledge, there is no report on non-LCH with such limited involvement. This presentation is also atypical for LCH, although there are reports in the literature regarding synovial involvement of the disease, mimicking PVNS such as in this case [24, 25]. Furthermore, the immunohistochemical characteristics of this case do not match with any of the well-described subtypes of non-LCH [1, 3, 4].

Non-Langerhans cell histiocytoses are a group of disorders with very different characteristics, both benign and malignant. Therefore, the diagnosis of non-LCH does not guide the physician toward a clear treatment strategy or give a clue about the prognosis. In this case, arthroscopic debridement resolved all the symptoms and further medical treatment was not initiated by the hematology/oncology service. The patient has been examined every 3 months throughout the 1st year and yearly thereafter.

Conclusion

For the practicing clinician, this can be valuable information to contribute to the literature. The presentation of this non-LCH mimics PVNS. Treating it as PVNS without confirmation could have potentially led to inadequate or incomplete treatment. Appropriate due diligence should be exercised during surgery by obtaining appropriate biopsies and tissue samples.

Clinical Message

Non-LCH can affect the synovial tissue and present itself like a case of PVNS. Histologic evaluation can be the only way to reach a correct diagnosis, so biopsies should be acquired properly, and the treatment should be carried out in coordination with other departments.

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