Intra-articular epithelioid sarcoma of the knee: a diagnostic challenge

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ACTA REUMATOL PORT. 2018;43:151-153

ABSTRACT

Epithelioid sarcoma is a rare mesenchymal neoplasm characterized by aggregates of epithelioid cells. Intra-articular occurrence is exceedingly rare with only few reports described in the literature. A 22 year-old man presented a progressive mechanical knee pain. Initially, the investigation revealed a non-infectious unspecific synovitis. The patient gradually presented increasing knee enlargement and functional impairment. Intra-articular nodular proliferation with bone invasion was later observed on magnetic resonance imaging reevaluation. Pigmented villonodular synovitis hypothesis was considered. The biopsy ultimately revealed nodules of epithelioid cells with an immunoprofile compatible with epithelioid sarcoma diagnosis. The patient underwent neoadjuvant chemotherapy and radiotherapy and an above-knee amputation was performed.

Keywords: Knee; Neoplasm; Pigmented villonodular synovitis; Epithelioid sarcoma.

Epithelioid sarcoma (ES) is an uncommon mesenchymal neoplasm of unknown lineage mainly affecting young adults and characterized by nodular proliferation of epithelioid cells with a distinct immunoprofile[1-4]. ES may occur in any soft tissue location, but intra-articular involvement is extremely rare[5-8].

We report a case of a 22 year-old man, smoker, with no other previous medical history. On November 2015, he was referred to the orthopedic consultation due to increasing mechanical pain on his left knee lasting for one year. He presented pain on medial palpation of the knee and limitation of the extension range. The radiographs were unremarkable and the magnetic resonance imaging (MRI) revealed minimal joint effusion, a Baker cyst and a chondral fissure of the patella (Figure 1A). He was therefore referred to a musculoskeletal rehabilitation program.

On October 2016, due to increasing knee enlargement, the patient underwent knee arthroscopy, which revealed extensive macroscopic synovial inflammation. The histology from partial synovectomy demonstrated an unspecific synovitis without granulomas; bacteriological and mycobacteriological studies were negative. The patient was then referred to the rheumatology department. He presented exuberant global knee enlargement, hotness and frank rigidity. He had no other joints involved nor associated systemic symptoms. Except for slight elevation of erythrocyte sedimentation rate and C-reactive protein, there were no other relevant analytical findings. Knee radiograph revealed frank periarticular osteopenia and joint space narrowing (Figure 1B). The MRI demonstrated an exuberant intra-articular nodular proliferation with heterogeneous signal, lobular contours and invasion into femoral and tibial bones. There was also a hemorrhagic popliteal lymph node (Figure 1C). Ultrasound guided synovial biopsy revealed discrete synovitis with mononuclear predominance and few hemosiderin deposits; the microbiological synovial studies were negative once more. Due to high-suspicion of malignancy, he was referred to the oncology institute where a review of previous biopsies was performed. Microscopically, small foci of neoplastic cells with broad and eosinophilic cytoplasm, round and vesicular nucleus and prominent nucleolus was identified. Immunohistochemistry demonstrated diffuse positivity to vimentin and cytokeratin (CAM 5.2), focal expression of Epithelial Membrane Antigen (EMA), negative expression of S100 and complete loss of INI1 (Figure 1D-F). These findings allowed a diagnosis of malignant mesenchymal neoplasm compatible with ES. The positron emission tomography revealed

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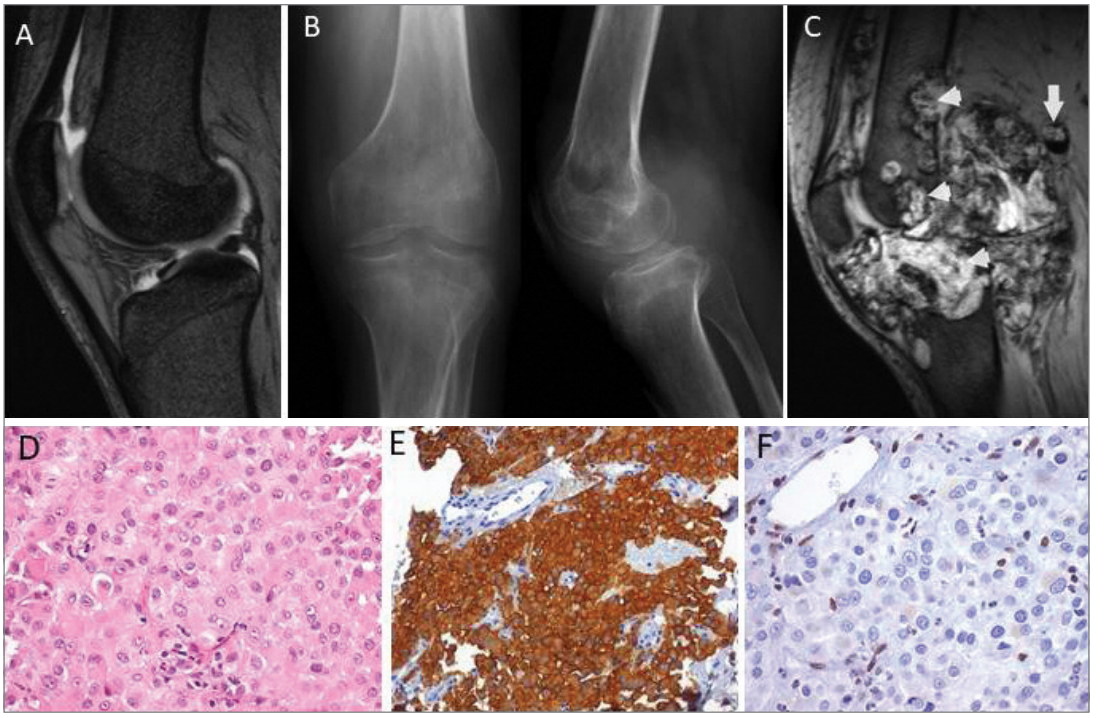

FIGURE 1. **A)** Sagittal gradient echo T2W image of the left knee, performed in 2016, showing a small amount of articular fluid. **B)** Anteroposterior radiograph and lateral radiograph of the left knee acquired in 2017, revealing left knee effusion with soft tissue swelling, periarticular osteopenia, joint space narrowing and erosions. **C)** Sagittal gradient echo T2W image of left knee, obtained in 2017, demonstrating a huge intra-articular lobulated mass, with areas of low signal intensity, more conspicuous in this sequence, representing blooming artifact, suggesting the presence of hemosiderin from prior hemorrhage. There were extensive bone erosions (arrowheads) and a popliteal lymph node (arrow) with blooming artifact. **D)** Hematoxylin and eosin staining (HE), 400x magnification. Cells with broad and eosinophilic cytoplasm, round and vesicular nucleus and prominent nucleolus. **E)** Immunohistochemistry for cytokeratin CK8/18, 200x magnification, showing diffuse positivity to cytokeratins. **F)** Imunohistochemistry for INI1, 400x magnification, showing a complete loss of INI1.

metastasis in the inguinal lymph nodes and left iliac bone. The patient underwent radiotherapy and neo-adjuvant chemotherapy (doxorubicin and ifosfamide) and an above-knee amputation was then performed.

We reported an unusual presentation of ES, initially mistaken for unspecific synovitis. The differential diagnosis included infectious and non-infectious chronic synovitis, as well as mesenchymal neoplasms. Pigmented villonodular synovitis (PVNS) diagnosis was raised due to the anatomic location and apparent synovial nodular proliferation with blooming artifact on MRI. Although these entities can present similar findings, the rapid evolution, extensive bone erosive changes and the presence of a hemorrhagic adenopathy favored an underlying malignancy[8-10]. Subsequent recognition of a multinodular proliferation of atypical epithelioid cells with co-expression of cytokeratin and EMA raised the ES hypothesis. Additionally, complete loss of INI1 reinforced the diagnosis (described in > 90% of the cases)[11].

To the best of our knowledge, only five cases of intra-articular ES were reported. The patients were aged between 19 and 60 years and the knee was involved in all the cases, with symptomatology lasting from 6 months to 6 years[5-8]. Two patients presented intra-articular proliferation, also suggesting PVNS[6, 8]. Three cases presented metastatic disease involving lymph nodes, lungs and disseminated disease, respectively[6-8].

This case highlights the possibility of intra-articular involvement of ES, a slow growing tumor with a high potential to metastasize (30-50%)[3]. A high level of suspicion and a multidisciplinary approach are determinant for the diagnosis of this rare neoplasm.

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