

CASE REPORT OF A PATIENT WITH EWING'S SARCOMA

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Abstract. Ewing's sarcoma is the second most common bone tumor in childhood and adolescence. Its incidence varies significantly among races, but is relatively rare among black children and the Chinese population. Patients with Ewing sarcoma exhibit local symptoms characterized by tumor mass formation, pain, swelling, venous dilatation, and hyperemia. Pathological fractures due to bone metastases with progressive neurological deficit to paralysis may occur. In cases where Ewing's sarcoma originates in the chest wall, pleural infiltration combined with carcinomatous pleuritis is often presented. We present the case of a 40-year-old patient initially diagnosed with a Baker's cyst in the left popliteal fossa. After consultation with an orthopedic surgeon, the patient was referred for surgical removal of the formation. An extirpation was performed, but the histological result did not confirm the diagnosis and characterized the finding as „cystic lobular capillary hemangioma“. A re-excision was performed in November 2018 due to recurrence of the formation. Immunohistochemical tests performed subsequently found that immunophenotypically and morphologically the finding correlated most highly with Ewing's extraskeletal sarcoma. Two months after excision, PT/CT was performed, which showed no recurrence and no secondary dissemination. One year later, due to arthralgias in the right shoulder joint, the patient underwent MRI and CT. The result of imaging studies revealed tumor recurrence in the diaphysis of the right humerus with secondary intrapulmonary dissemination. The patient started chemotherapy with good clinical response.

Key words: Ewing's sarcoma, therapeutic approach, chronic pain syndrome

INTRODUCTION

Familial Ewing sarcomas (FES) represent a group of malignant tumors of bone and soft tissue. It includes classical Ewing sarcoma, extraosseous (extraskeletal) Ewing sarcoma, pPNET and Askin's tumor [1].

The condition was first described in 1921 when the American pathologist James Ewing examined curetted material from a bone tumor of a 14-year-old girl, which differed from both the typical microscopic picture of osteosarcoma and the familiar forms of myeloma tumors [2]. FES predominantly affect children and adolescents with a peak incidence in the second decade around the age of 15 years, but although less common, is also seen in adults >30 years of age [3, 4, 9]. The incidence in the population ranges between 2.3-3 cases per 1,000,000 population with a slight male preponderance of 1.2-1.5:1 [3, 4, 5]. The individual nosological entities of the Ewing family of sarcomas share some very similar histological, immunohistochemical and genetic features, and are therefore grouped together. Histologically, they present as small round blue cells with sparse cytoplasm and rounded nuclei [6]. It has been shown by chromosomal analyses that approximately 85% of cases are genetic abnormalities, consisting of a

reciprocal translocation between the EWSR1 and FLI1 genes t(11;22)(q24;q12), ultimately resulting in an EWSR1-FLI1 fusion gene [7, 8].

Classical Ewing sarcoma is the second most common bone tumor in children and adolescents after osteosarcoma [3, 4, 9]. Much less common is Ewing's extraskeletal sarcoma, which originates in soft tissue and has an incidence between 6- 47% of all FES [10].

Our case report concerns a 40-year-old patient with Ewing's extraskeletal sarcoma in the popliteal region.

CLINICAL CASE DESCRIPTION

We present a 40-year-old man who reported swelling and pain in his left knee in the area of popliteal fossa at the end of 2017. Subsequently, the patient complained of restriction of movement in the left knee and was hospitalized in an orthopedic clinic in July 2018. The patient was found to have a suspected Baker's cyst measuring 7.4/4 cm. An extirpation was performed, but the histological result did not confirm the diagnosis and characterized the finding as „cystic lobular capillary hemangioma“. A re-excision was performed in November 2018 due to recurrence of the formation. Immunohistochemical study performed

subsequently found that immunophenotypically and morphologically the finding correlated most highly with Ewing's extraskeletal sarcoma. Two months after excision, PT/CT was performed, which showed no recurrence and no secondary dissemination.

In 2019, the patient was again hospitalized for new-onset mechanical-type pain in the right shoulder and arm. From the imaging studies performed, there was MRI and CT evidence of tumor recurrence in the right humerus diaphysis with secondary intrapulmonary dissemination. Biopsy was performed from the lesion and histological result confirmed recurrence of Ewing sarcoma. The patient was referred to the oncology clinic, where chemotherapy with Episindan and Ifosfamide was started. After two therapeutic courses, the treatment continued according to the VEC/IE regimen.

TESTS

Complete blood count, biochemistry, coagulation status – no deviations from reference values were found.

MRI of the primary finding prior to the first surgical intervention: large depressed complex multinodular Tu formation in the popliteal fossa on the left, reaching a size of 66/59/64 mm, involving the subcutaneous fat and exerting marked compression on the adjacent muscles. The intra-cutaneous texture of the formation is complex: there are cystic (mainly peripherally located) and solid (with variable intensity) components. Perifocal edema is observed in the adjacent adipose tissue. After application of contrast material, there is intense enhancement in the area of the solid components of the formation and peripherally in the cystic components.

Histopathological examination: cystic lobular capillary haemangioma.

Histopathological examination (recurrence): soft tissue tumor of the left popliteal fossa with morphology of small cell sarcoma, with morphology and immunophenotype similar to extraskeletal Ewing sarcoma.

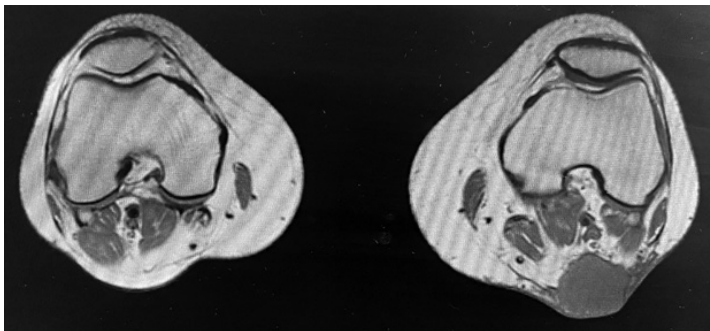


Fig. 1. Extrasosseous Ewing's sarcoma in the left popliteal fossa



Fig. 2. Lung radiograph showing intrapulmonary dissemination of Ewing's sarcoma

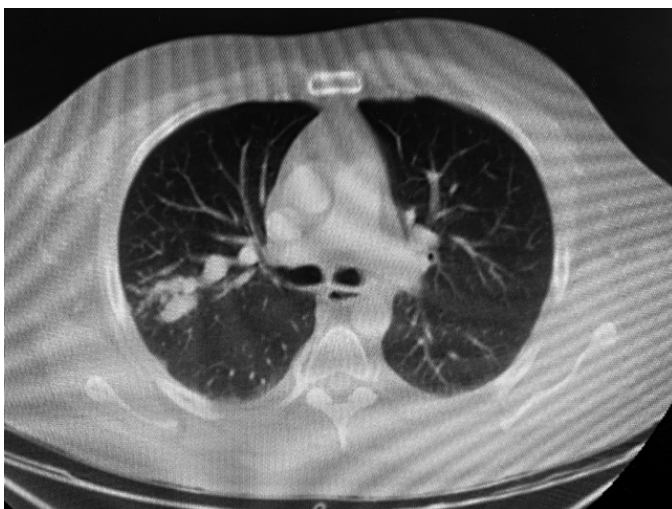


Fig. 3. CT evidence of intrapulmonary dissemination of Ewing's sarcoma

Immunohistochemistry: atypical cells expressed: CD99 (100%), Vimentin, S-100. They do not express: TLE-1, MDM2, HMB45, CK19, MyoD1, CD31, NSE, NF200. FLI1 has not been studied.

Immunohistochemistry of humerus biopsy material (recurrence): bone fragments and soft tissue infiltration from a malignant „small, blue, round cell“ tumor, most likely Ewing sarcoma. Atypical cells express CD99 and Vimentin. Not expressed: Actin, Desmin, CD45, EMA.

DISCUSSION

Extrasosseous Ewing sarcoma is an aggressive soft tissue neoplasia with high metastatic potential that can affect any anatomical region [11, 12, 13]. Unlike osteosarcoma of bone, the extraskeletal form of the tumor affects older patients, who are diagnosed around the fourth decade [14]. In an Indian cancer hospital and research institute, Sudha S Murthy et al. studied a cohort of 302 patients with FES, followed for a period of about 10 years. Data from the study showed that in 119 (77.7%) of the patients, the tumor was located in the soft tissues, with the most common sites being the buttocks, thorax and paraspinal region. In only two patients of this cohort the tumor was localized in the popliteal region, which appears to be a relatively rare localization, as in the clinical case we presented.

Due to the nonspecific clinical picture, which is mainly expressed by swelling and local pain [15], further radiological, histological and immunohistochemical examinations are needed to establish the diagnosis, respectively after taking biopsy material from the formation.

Radiographic features of this tumor are also nonspecific [16]. A large soft tissue formation, in some cases with calcifications, as well as involvement and erosion of the underlying bone can be seen on radiographs. In a tumor formation of small size, it is possible to have a normal radiographic image of the examined area [17].

Usually, CT imaging in most cases reveals a nonspecific soft tissue tumor formation with reduced attenuation similar to that of muscle [18].

Ultrasound findings visualize a hypoechoic heterogeneous mass with high PWD signal [19]. As a more sensitive imaging modality, MRI with contrast can isolate a pseudocapsule with well-defined edges. Typically, at T1, the soft tissue formation has a heterogeneous signal intensity, whereas at T2, it is mostly elevated [18].

Histological findings in FES are characterized by small round blue cells with scant cytoplasm contain-

ing glycogen and oval nuclei with scattered chromatin [6, 20]. Cells of the Ewing sarcoma family of tumors express 99% CD99 membrane antigen [21], which is, however, also found in other neoplastic cells [22]. FLI1 expression is thought to be most specific for this group of neoplasias [23]. In the clinical case we presented, immunohistochemical study confirmed the expression of CD99 by atypical cells (100%). According to the literature review performed, the expression of other membrane antigens such as NSE, S-100 protein and synaptophysin, is also possible, which is thought to depend on the degree of neuroectodermal differentiation [20]. Although FLI1 was not investigated, NSE was detected in our case, which verified the diagnosis. Radiotherapy was the standard treatment for FES until 1960, and radiotherapy or surgical removal of the tumor were the only treatment modalities until then [26]. Ewing sarcoma currently requires a multidisciplinary approach involving chemotherapy, surgery and radiotherapy. In tumor formations difficult to excise with an adequate margin, preoperative radiotherapy (36-55 Gy) is administered. Similarly, postoperative radiotherapy is administered if the margin achieved by surgery is insufficient for local control. Clinical trials have shown that patients who are found to have pulmonary metastases and undergo radiotherapy have a more favorable prognosis compared with those who do not [27, 28]. In the clinical case we described, chemotherapy was performed when lung metastases were detected, but despite this, a good clinical response and stabilization of the patient's condition was observed.

CONCLUSION

Soft tissue sarcomas in the popliteal region are a rare disease and atypical localization [24]. At the same time, popliteal cyst (Baker's cyst) is relatively common in rheumatologic practice, which represents edema of the bursa gastrocnemius – semimembranosus due to various intra-articular pathology of the knee joint [25]. This was the initial diagnosis in our patient, but thanks to the histopathological studies performed, the rare diagnosis of Ewing's extraskeletal sarcoma was made.

Further imaging studies significantly contributed to the refinement of the diagnosis due to the wide differential diagnostic picture of the pathology in this anatomical region. Life-saving differentiation of benign from malignant processes, with the gold standard in the least suspicion of malignancy being biopsy with immunohistochemical examination of the tissue.

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