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Case Report

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A rare case of metastatic proximal-type epithelioid sarcoma of the ischioanal fossa: case report and literature review

Abstract

Epithelioid sarcoma (ES) is a rare high-grade sarcoma subtype that constitutes less than 1% of soft tissue sarcomas (STS).There are two types: distal-type epithelioid sarcoma and proximal-type epithelioid sarcoma, based on anatomic location and the histopathological features. The clinical presentation of ES is varied and can lead to a delay in diagnosis. histopathology examination followed by immunohistochemistry will help to establish the diagnosis. The treatment of choice of Localized ES is a radical excision with microscopically radical margins and perioperative radiotherapy. systemic therapies are used in cases of locally advanced or metastatic ES. We describe a case of reoccurring proximal-type epithelioid sarcoma of the ischioanal fossa. A 56-year-old man operated two years ago for a epithelioid sarcoma of the ischioanal fossa. The patient presented with reoccurring mass at the same location, Magnetic resonance imaging (MRI) of the pelvis showed a mass of the ischioanal fossa. computed tomography (CT) of the chest, abdomen, and pelvis showed multiple pulmonary and liver metastasis. Histopathological features and immunohistochemistry were those of proximal type epithelioid sarcoma. He received intravenous doxorubicin with a partial response after 3 cycles of treatment.

Keywords: epithelioid sarcoma, soft tissue sarcomas, proximal type, radiotherapy, chemotherapy

Volume 12 Issue 3 - 2021

Harrak Soukaina, Lemsanes Siham, Razine Sawsan, Benchekroun Khadija, Lkhouyaali Siham, Abahsaine Halima, Boutayeb Saber, Errihani Hassan

Department of Medical Oncology, National Institute of Oncology, Morocco

Correspondence: Harrak Soukaina, Department of Medical Oncology, National Institute of Oncology, 10100, Rabat, Morocco, Tel 00212624459709, Email Soukaina.hrk@gmail.com

Received: June 20, 2021 | **Published:** July 01, 2021

Introduction

Epithelioid sarcoma (ES) is a high grade malignant mesenchymal tumor that exhibits epithelioid cytomorphology and a predominantly epithelial phenotype. It was first described in 1970 by Franz Enzinger.[1] ES is a soft tissue sarcomas (STS) subtype that is recognized in less than 1% of STS patients.[2] It mostly occurs in the deep dermal or subcutaneous areas of the distal portions of the extremities of young adults particularly the hand, yet it can arise in any part of the body, including the penis, vulva, and perineum.[3,4] The tumor occurs in all ages, however, it is most prevalent in individuals aged 20–40 years and is rarely found in children and older individuals.[3] The clinical presentation of ES is usually non specific, it is frequently mis diagnosed as a benign process and this remains a challenge in terms of diagnosis and management. Surgical resection of localized disease has been the mainstay of care with an undefined role for pre or post-operative radiation therapy.[5] Systemic therapy in the metastatic setting with either doxorubicin or gemcitabine based therapies are often given, however, outcomes are poor with a short duration of response.[6,7] Recently tazemetostat demonstrated significant activity in ES. The prognosis of such a disease is dismal with high mortality rates in the recurrent and metastatic cases.[8] In this report, we describe a case of an 56-year-old men with a metastatic proximal epithelioid sarcoma of the ischioanal fossa treated by doxorubicin.

Case report

A 56-year-old man with any medical history was referred to our institution for evaluation of reoccurring mass on the ischioanal fossa. The patient reported a left perianal mass measured to about 5cm, 6 months duration before his first consultation. The patient has already had the mass surgically removed. The basis of the histopathological examination and immunohistochemistry finding, the patient was diagnosed as having a proximal type localized epithelioid sarcoma of the ischioanal fossa. No adjuvant chemotherapy or radiation was recommended. The patient did not attend his schedule follow-up meetings at the hospital. Two years after the surgery, he noticed recurrence of the mass at the same location.

Follow this finding he was referred to our institution for the management. On examination, a a left perianal mass was noted measured to about 4cm, there were no palpable lymph nodes. The rest of the physical exam was unremarkable. A magnetic resonance imaging (MRI) of the pelvis was performed and showed a 54x44x72mm mass of the left ischioanal fossa, infiltrating the levator ani muscle homolaterally without endopelvic extension (Figure 1). CT showed liver and lung metastasis.

The patient had a biopsy of the mass whose Histological examination revealed multinodular pleomorphic proliferation of epithelioid cells with abundant eosinophilic cytoplasm, The tumor cell nuclei were round or oval, hyperchromatic and presenting a low number of mitoses. Immunostaining showed positivity for CD34, epithelial membrane antigen (EMA), and pan-cytokeratin, and negativity for PS100, myogenin and INI1. Ki 67 was 10%. Because of the presence of multiple metastasis, the patient was therefore recommended to undergo chemotherapy, he received first line palliative chemotherapy with doxorubicin 75mg intravenously every 3 weeks.

Reassessment CT scan performed after three cycles of chemotherapy showed a partial response. He has now been treated with 5 cycles of doxorubicin and the chemotherapy cycles were exceedingly well tolerated by the patient. A second evaluation scan will be scheduled after the sixth cycle.

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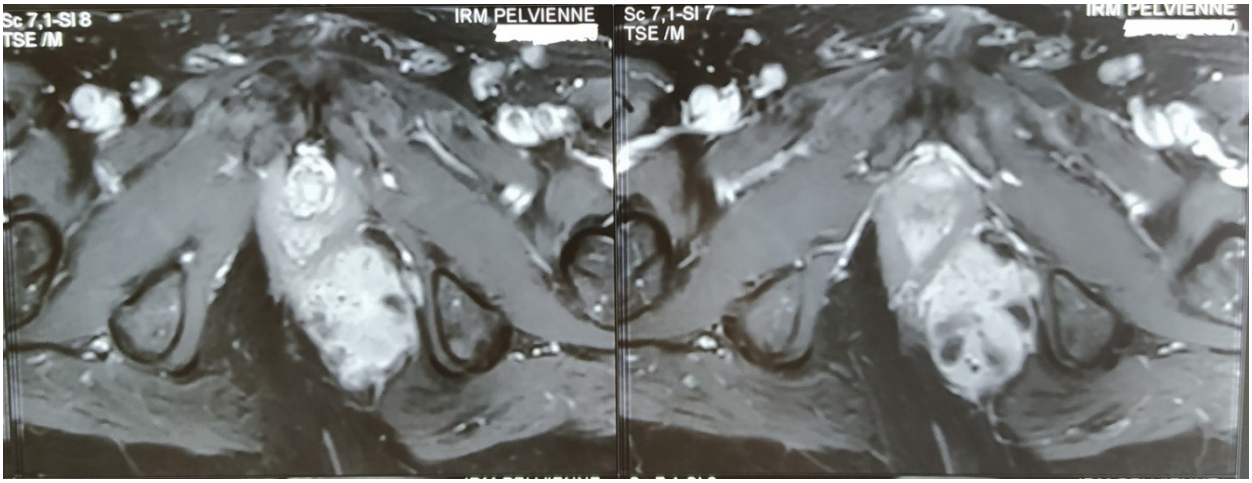

Figure 1 Pelvis MRI axial showing a mass of the left ischioanal fossa, which was measured at about 54x44x72mm.

Discussion

Epithelioid sarcoma (ES) is a rare mesenchymal tumor that occurs mostly in the dermal or subcutaneous area of the distal extremities. Generally, ES is considered as a high-grade soft tissue sarcoma.9 ES occurs in less than 1% of all adult soft-tissue sarcomas and approximately 4%–8% of pediatric non-rhabdomyosarcomatous sarcoma.[10,11] Traditionally, ES is divided in two subtypes: The classic form (distal-type) and the proximal-type. The classic form is seen more in teenagers and young adults. The proximal-type ES is a rarer form, which mainly affects adults and is often presented as a more aggressive and mainly affects adults.[12] Distal-type ES is characterized as afirm, non-tender, slow-growing tumor with predilection towards distal extremities, especially the hands.[13] Different from distal-type, proximal-type ES is characterized by deeper masses infiltrating soft-tissue, commonly with hemorrhage and necrosis, affecting axial proximal regions.[12] Reported sites include the pelvis and perineal region, pubic region, and vulva, buttock, hip, penis, axilla, mediastinum, occiput, and forearm.[12-14]

Due to the clinical presentation of ES is usually non specific, the painless and indolent nature of the tumour, and it may initially look like benign lesion, ES is frequently mis diagnosed as a benign process and the diagnosis is not made until the tumor has already reached an advanced stage. As it is difficult to diagnose ES clinically, the biopsy with immunohistochemistry plays an important role in confirming the diagnosis. Classic distal-type ES shows characteristic histological features of a nodular growth pattern of plump epithelioid cells with a relatively abundant eosinophilic cytoplasm. Spindled cells can also be seen. The nodules typically contain prominent central necrosis. On the other hand, proximal-type ES is characterized by multinodular distributions and sheets of large polygonal cells with pleomorphic vesicular nuclei and prominent nucleoli. Rhabdoid features are also frequently observed in this form of ES. The nodules sometimes contain central necrosis, but this may be with or without the geographic pattern of necrosis typical of classic ES.[15,16] The histologic type in our case was similar to the proximal type despite the central location of the tumor.

Immunohistochemical staining usually reveals cytoplasmic immunoreactivity for cytokeratin, vimentin, and EMA, where as S-100 and CD31 staining are usually negative. Epithelioid sarcoma commonly displays membranous positivity for EMA, in contrast to other majority of soft tissue sarcomas, which show nonspecific cytoplasmic EMA expression. About 50% of the cases express CD34.[14] Loss of integrase interactor 1 (INI1) function is the most common alteration found in ES, occurring in nearly 90% of cases.[17] This loss of INI-1 protein is related to biallelic inactivation of the tumor suppressor gene SMARCB1/ INI1, which is located at chromosome 22q11.2.[17] ES has an unfavourable prognosis with reported 77% local recurrence and 45% distant metastasis rates, usually to regional lymph nodes, lungs, skin, scalp, bone, brain and other soft tissue parts.[18-20] Factors that are associated with a worse prognosis for ES are proximal and deep location, rhabdoid features, large size, older age, male sex, necrosis, and vascular invasion.[15]

Due to their rare incidence and the absence of dedicated clinical trials, specific recommendations and guidelines on the optimal management of ES are almost inexistent. First, complete surgical resection with optimal margins (R0) remains the mainstay of curative therapy in nonmetastatic, localized ES patients.[4] For localized disease, neoadjuvant or adjuvant radiation therapy is often given to reduce local relapse[21,22] but the role of adjuvant chemotherapy is unclear.[14,23-25] Chemotherapy is widely used in locally advanced or metastatic ES, as in our patient with liver metastasis. The most commonly administered chemotherapy regimens are single-agent anthracycline therapy or the combination of an anthracycline with ifosfamide.[6] A single group reported activity of a regimen combining gemcitabine with docetaxel, but the experience is limited to a small number of patients.[7] Progression free survivals (PFS) reported in the literature are relatively low, with one study reporting a median PFS for gemcitabine-based regimens of 4 months and doxorubicin regimens of 6 months.[26]

Many expectations arose around targeted therapies for ES. Signs of activity in a few cases have also been reported with pazopanib, the only anti-angiogenic compound currently licenced in advanced, pretreated, nonadipocytic, STSs and trabectedin.[27,28] very limited data on the activity of immunotherapy in ES are currently available, with one response ascribed to pembrolizumab.[29] Recently, the Food and Drug Administration (FDA) has approved tazemetostat, an EZH2 inhibitor that has the potential to block this genetic alteration, demonstrated significant activity in several hematological and solid tumors , for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for radical resection. The approval has been granted based on the results of cohort 5 of the phase 2 clinical trial (NCT02601950).[30,31]

Citation: Soukaina H, Siham L, Sawsan R, et al. A rare case of metastatic proximal-type epithelioid sarcoma of the ischioanal fossa: case report and literature review. *J Cancer Prev Curr Res.* 2021;12(3):107–109. DOI: 10.15406/jcpcr.2021.12.00462

Conclusion

Epithelioid sarcoma (ES) is a rare mesenchymal tumor, This tumor has a high risk for local recurrence and distant metastasis. Prognosis, as with most malignancies, is primarily determined by the clinical stage of the disease. Complete resection while is considered as the main treatment. Tazemetostat, has shown promising results in ES patients. Novel therapies, including immunotherapy, are still needed.

Acknowledgments

None.

Conflicts of interest

The authors declare that they have no conflict of interests.

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