PEComa of soft tissues can mimic lymph node relapse in patients with history of testicular seminoma

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Abstract

Perivascular Epithelioid Cell tumour (PEComa) is rare. We describe a 39-year-old man who underwent a left radical orchidectomy and adjuvant radiation therapy for a stage IA classical testicular seminoma. He was diagnosed with a mass lateral to the right common iliac artery that was considered suspicious for late lymph node relapse after 3 years of follow-up. Due to the unusual location of the mass and the equivocal findings of percutaneous biopsy, a laparoscopic pelvic lymphadenectomy was performed. Final pathology revealed PEComa of soft tissue. The patient is disease-free after 38 months of follow-up without adjuvant treatment. The presence of rare soft-tissue neoplasm should be considered in differential diagnosis of retroperitoneal masses during follow-up of germ cell tumours. Suspicious isolated recurrences of these neoplasms in unusual locations can require surgical excision to confirm diagnosis and avoid inappropriate treatment.

Introduction

PEComas (Perivascular Epithelioid Cell tumors) are rare mesenchymal neoplasms characterized by a myomelanocytic phenotype and frequently unpredictable clinical behaviour.[1] They can involve many anatomical sites and very few cases are reported worldwide.[2] When PEComas are diagnosed in soft tissues, they can mimic enlarged lymph nodes and represent a possible confounder during follow-up of other solid tumours.

Case report

We present the case of a 42-year-old man with a history of left testicular pure seminoma. The patient was diagnosed with a palpable left testicular mass in October 2005. Scrotal ultrasound revealed a left hypoechoic testicular lesion, with normal controlateral testis. The serum markers were negative. No retroperitoneal lymphadenopathy or distant metastases were detected at chest x-ray (CXR) and abdominal contrast-enhanced computed tomography (CT). An uneventful left radical orchidectomy was performed. The pathology showed a classical seminoma with necrotic areas and invasion of the rete testis (pT1,N0,M0,S0; stage IA according to the 2009 TNM classification). After we consulted with the interdisciplinary team, the patient underwent adjuvant radiotherapy (25.2 Gy) on the left lombo-aortic lymph nodes.

Follow-up included physical examination, serum markers every 4 months and CXR and abdominal CT scan every 6 months for the first 3 years, with negative results.

At the abdominal CT scan performed September 2008, we found a single, enlarged 2.5-cm mass lateral to the right common iliac artery consistent with lymphadenopathy (Fig. 1, part A, part B). The scrotal examination, the serum markers and the CXR were negative and the patient had no complaints. A positron emission tomography (PET) with fluorodeoxyglucose showed a hot spot (maximum standardized uptake value 3.76) in the area of the right common iliac lesion, which led us to a likely diagnosis of a late relapse of the testicular germ cell neoplasm. (Fig. 2) To confirm this diagnosis, a CT-guided fine needle aspiration biopsy was performed. (Fig. 1, part C). Cytology revealed epitheliomorphic cells with clear nuclei and large nucleoli, histiocytes and little lymphocytes. Based on the uncertain pathology, with the suspicion of a recurrent seminoma despite the unusual location and timing of relapse, a decision was made to perform a laparoscopic right-sided pelvic lymphadenectomy. Gross examination revealed a reddish, soft mass with a maximal diameter of 2.5 cm. The pathology showed mono and plurinuclear epitheliomorphic elements with large nucleoli and granular cytoplasm (Fig. 3, part A). The immunohistochemistry was negative for PLAP (placental alkaline phosphatase), β-HCG (human chorionic

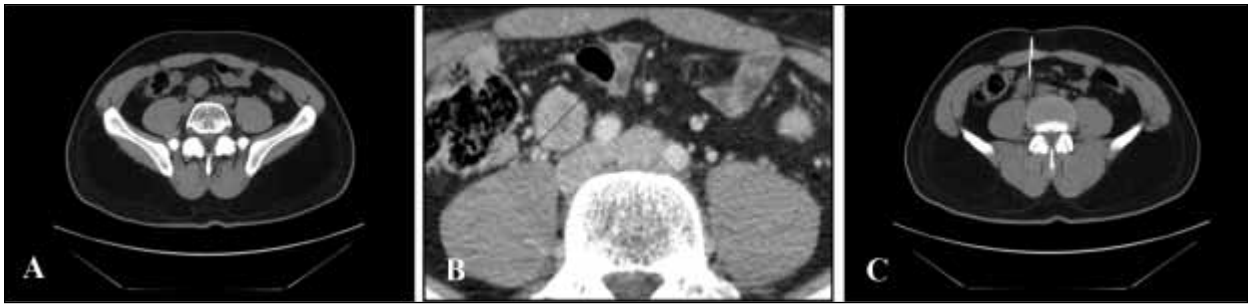

Fig. 1. The abdominal computed tomography (CT) shows a single, enlarged 2.5-cm mass lateral to the right common iliac artery consistent with lymphadenopathy (A, B). A CT-guided fine needle aspiration biopsy was performed to confirm diagnosis (C).

gonadotropin), CD117, CD30, S100, pancytokeratin, and intensely positive for HMB45 (Fig. 3, part B, part C). Some stromal elements were non-specifically positive for vimentin and CD68. Eight lymph nodes were also assessed with diagnosis of reactive changes. Based on these findings, the final histological diagnosis was PEComa of soft tissue. We classified the neoplasm according to Folpe's classification of PEComas.[3] Based on the size <5 cm, the non-infiltrative behaviour and the absence of mitosis, necrosis and vascular invasion, the PEComa was classified as "benign." Therefore, no adjuvant treatment was recommended. After 38 months from lymphadenectomy, the patient is alive with negative clinical and radiological follow-up.

Discussion

PEComas are defined by The World Health Organization as "mesenchimal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells."[4]

The PEComa family includes angiomyolipomas, clear cell "sugar" tumour of the lung, lymphangioleiomyomatosis, clear-cell myomelanocytic tumours of the falciform ligament/ligamentum teres and rare clear-cell tumours of other anatomical sites, the so called "PEComa-NOS" (not otherwise specified).[5] In a recent literature review, Bleeker and colleagues described 234 cases of PEComa-NOS.[2] The origin of this neoplasm is still unknown; it could derive from the undifferentiated cells of the neural crest or have a myoblastic or pericytic origin. The neoplastic cells appear as epithelioid cells with a clear to eosinophilic cytoplasm and they are usually immunoreactive to HMB45 (melanocytic marker), sometimes to smooth muscle actine and negative to epithelial markers.[1] Folpe and colleagues reported 26 cases of PEComas of soft tissue, mainly of gynecological origin, with only one involving the retroperitoneum.[6]

Retroperitoneal PEComa of soft tissue is rare and can arise near large vessels, thereby potentially mimicking enlarged lymph nodes. This can represent a clinical issue in patients affected by neoplasms that typically spread to retroperitoneal nodes, since in such cases the presence of a new-onset PEComa may lead to the erroneous diagnosis of tumoural relapse or progression. In the present case, the patient was diagnosed and treated for a testicular classical seminoma and had an uneventful follow-up for 3 years before being diagnosed with a right peri-iliac mass, which was eventually found to be a soft tissue PEComa. This mass was initially perceived to represent a late lymph node relapse of the germ cell tumour (GCT). Late relapse of GCTs are rare and defined as recurrences diagnosed after a disease-free interval of at least 2 years following the completion of primary therapy in the absence of metachronous tumours. Their incidence is about 2% to 4% and retroperitoneum represents the preferential site.[7] Recently, Fedyanin and colleagues identified seminoma and older age as predictive factors for a late relapse in chemotherapy-naïve patients with stage I testicular GCT.[8]

In our case, the diagnosis of late relapse represented an unexpected finding due to the stage of disease at diagno-

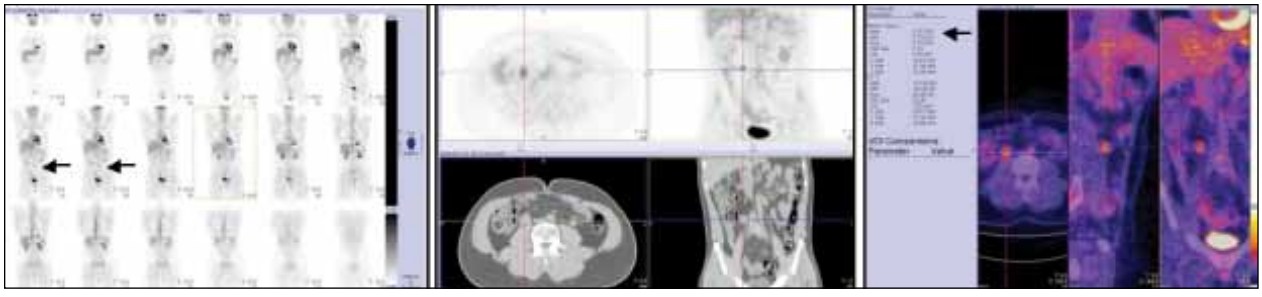

Fig. 2. A positron emission tomography and computed tomography showed a hot spot (maximum standardized uptake value 3.76) laterally to the right common iliac artery.

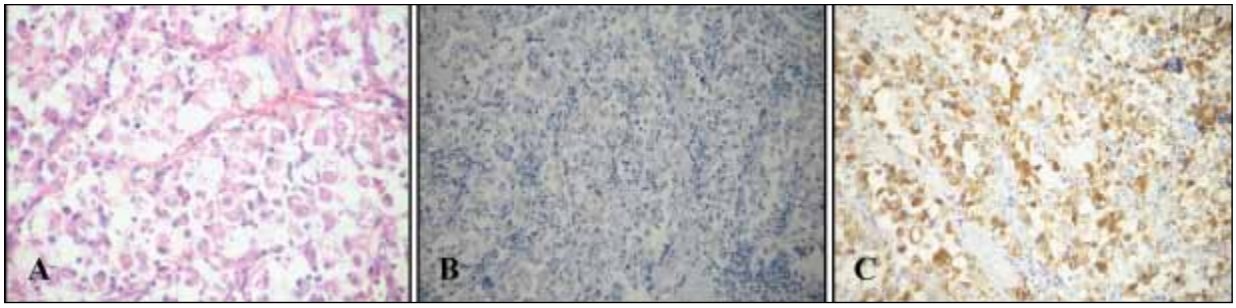

Fig. 3. Pathology on surgical specimen. Hematoxylin-eosin staining: epitheliomorphic cells with clear nuclei and large nucleoli, histiocytes and little lymphocytes (A). Immunohistochemistry: negative for b-HCG (B), but extensively positive for HMB45 (C).

sis and to the unusual location of the retroperitoneal mass, contralateral to the original side of the testicular tumour. These considerations, together with the fact that the first cytological assessment on percutaneous biopsy could not establish a definitive diagnosis and CT and PET imaging did not show any other sign of recurrent disease, led us to decide to surgically excise the peri-iliac mass to obtain a precise histological diagnosis on the entire specimen. Furthermore, in our view the procedure could also have a therapeutic and potentially curative intent. The final histological diagnosis of PEComa of soft tissue was mainly based on the epithelioid morphology and on the strong positivity for HMB45 of the tumoural cells.

According to the criteria proposed by Folpe and colleagues, PEComas are classified as benign (no worrisome features: tumor size inferior to 5 cm, non-high nuclear grade and cellularity, mitotic rate inferior to 1/50 HPF, absence of necrosis and vascular invasion), of uncertain malignant potential (nuclear pleomorphism or tumor size greater than 5 cm) and malignant (2 or more worrisome features).[3] Since the histological characteristics of our case are typical of benign PEComas, we decided to avoid any adjuvant treatment after surgical excision.

To date, surgical resection is the main curative treatment for this rare neoplasm, as chemotherapy and radiotherapy have not shown significant benefits. Genetic analysis demonstrated that the mTOR pathway is activated in PEComas[9] and therefore mTOR inhibitors (such as temsirolimus and rapamycin) have been administered in clinical trials to patients at higher risk with encouraging results.[10]

In our case, the diagnosis of PEComa avoided an improper indication to chemotherapy for recurrent GCT, which could be indicated based only on clinical findings. Surgical resection of the iliac mass seemed to be curative since the patient is disease-free after a follow-up of 38 months.

Conclusion

Our case demonstrates that the presence of rare soft-tissue neoplasms, such as PEComas, should be taken into account in the differential diagnosis of retroperitoneal or iliac masses during follow-up of patients with GCTs to avoid inappropriate treatment. Furthermore, the presence of isolated recurrences of GCTs in unusual locations may warrant surgical excision to confirm diagnosis.

Competing interests: None declared.

This paper has been peer-reviewed.

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