CASE REPORT

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

High-grade poorly differentiated retroperitoneal sarcoma. Report of a case and review of the literature

MANUELA BOSSI[1)], L. A. PAOLINO[1)], A. VALENTI[1)], LEA MARCIANO[2)], C. POLLIAND[1)], MARIANNE ZIOL[2)], C. BARRAT[1)]

[1)]*Service de Chirurgie Digestive et Métabolique*
[2)]*Service d'Anatomie et Cytologie Pathologique*
CHU Jean Verdier, A.P.H.P., Bondy, Cedex, France
Université Paris XIII, UFR SMBH "Léonard de Vinci"

Abstract

Retroperitoneal sarcomas (RPS) are uncommon tumors associated with a poor prognosis. This is particularly true in case of high-grade sarcomas of specific histological subtypes, as demonstrated by the largest surveys of the last decade. Up to the present day, unfortunately there are no powerful tools available except for surgery. On the other hand, the resection rate of RPS is significantly increased over the last decades allowing to deliver the best treatment available. This paper reports on the case of a young patient who was incidentally diagnosed with a retroperitoneal mass. The patient underwent surgery in our department and the histological report showed a spindle cell sarcoma of high grade of malignancy with an incomplete muscular phenotype. The patient was discharged on the seventh postoperative day and he is still free of local and distant recurrence.

***Keywords*:** sarcoma, retroperitoneum, resection.

Introduction

Retroperitoneal sarcomas are rare tumors with a poor prognosis dependent on biological factors, related to the tumors, but also on the ability of delivering the most appropriate treatment. Once again, a radical surgical resection seems to be the only possibility to improve the survival rate. We present here the case of a young man who was unexpectedly diagnosed of a retroperitoneal spindle cell sarcoma of high grade. The appropriate surgical treatment gave the best prognosis to the patient who is still free of recurrence. From the pathology point of view, the histological report was not straightforward to drawn up due to the high grade of dedifferentiation these tumors often have. In our case, the collaboration with a more specialized centre gave the possibility to obtain a more specific diagnosis. This case underlines how in front of a rare pathology that may be often misdiagnosed, it is vital to obtain without shame the collaboration of specialized centers to offer to the patient the best possibilities of cure.

Patient, Methods and Results

In January 2011, a 31-year-old man presented to the A&E Department of our hospital with right lower quadrant abdominal pain associated with asthenia and loss of weight. He referred neither vomit nor diarrhea, nor fever. The blood test showed only an elevated CRP (150 mg/L). AXR was unremarkable as well as the urine test. On palpation, the abdomen was tender in the right lower quadrant and there were no palpable masses and no rebound tenderness. The past medical history was unremarkable.

Due to the suspicion of an unusual case of acute appendicitis or acute pyelonephritis, an US scan was performed by the radiologist on call. Instead of finding an inflamed appendix or a problem on the urinary tract, the radiologist detected a huge necrotic-like and apparently well-demarcated mass next to the right kidney. The patient was immediately transferred to undergo a CT scan that confirmed the presence of a giant (15 cm in diameter), capsulated and partially necrotic retroperitoneal mass next to the right kidney but not arising from there (Figure 1).

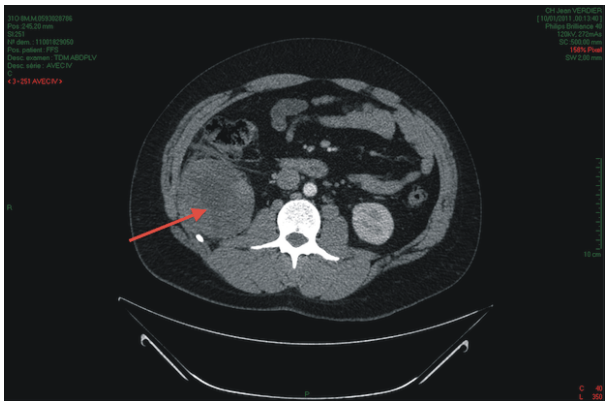

Figure 1 – ***Abdominal CT scan. Large mass in the retroperitoneal space looking partially necrotic.***

The patient was admitted to the Department of General Surgery and an operation to remove the tumor

was scheduled within a week. All tumor markers tested were negative. After a few days, the patient underwent the operation and the retroperitoneal tumor was removed successfully (Figure 2).

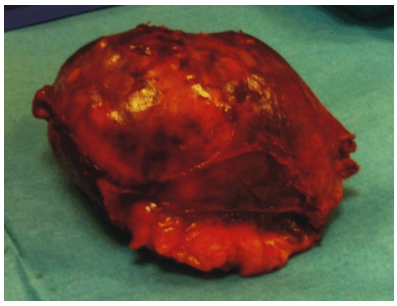

Figure 2 – ***Surgical resection. A well-encapsulated mass with a mix of cystic, hemorrhagic and necrotic areas.***

The postoperative period was free of complications and the patient was discharged on the seventh post-operative day.

The macroscopic histological report showed a well-encapsulated mass of 15×10×6 cm and 478 g of weight, with a mix of cystic, hemorrhagic and necrotic areas. Focally, the tumor reached the surgical margins (minimal distance = 0 mm).

The microscopic report showed a tumor with a clearly fasciculated architecture, constituted by spindle cells with an eosinophilic cytoplasm and elongated nuclei. The morphological aspect gives evidence of a smooth cell differentiation with an important aniso-nucleosis (Figure 3a). The nuclei are irregular and hyperchromatic (Figure 3b). More than 20 mitoses in 10 fields may be observed and the necrotic areas are present in about 50% of the fields (Figure 3c). The immunohistochemical examination showed that the tumoral cells are actin negative, but strongly desmin positive, which may be suggestive for a leiomyosarcoma (Figure 3d).

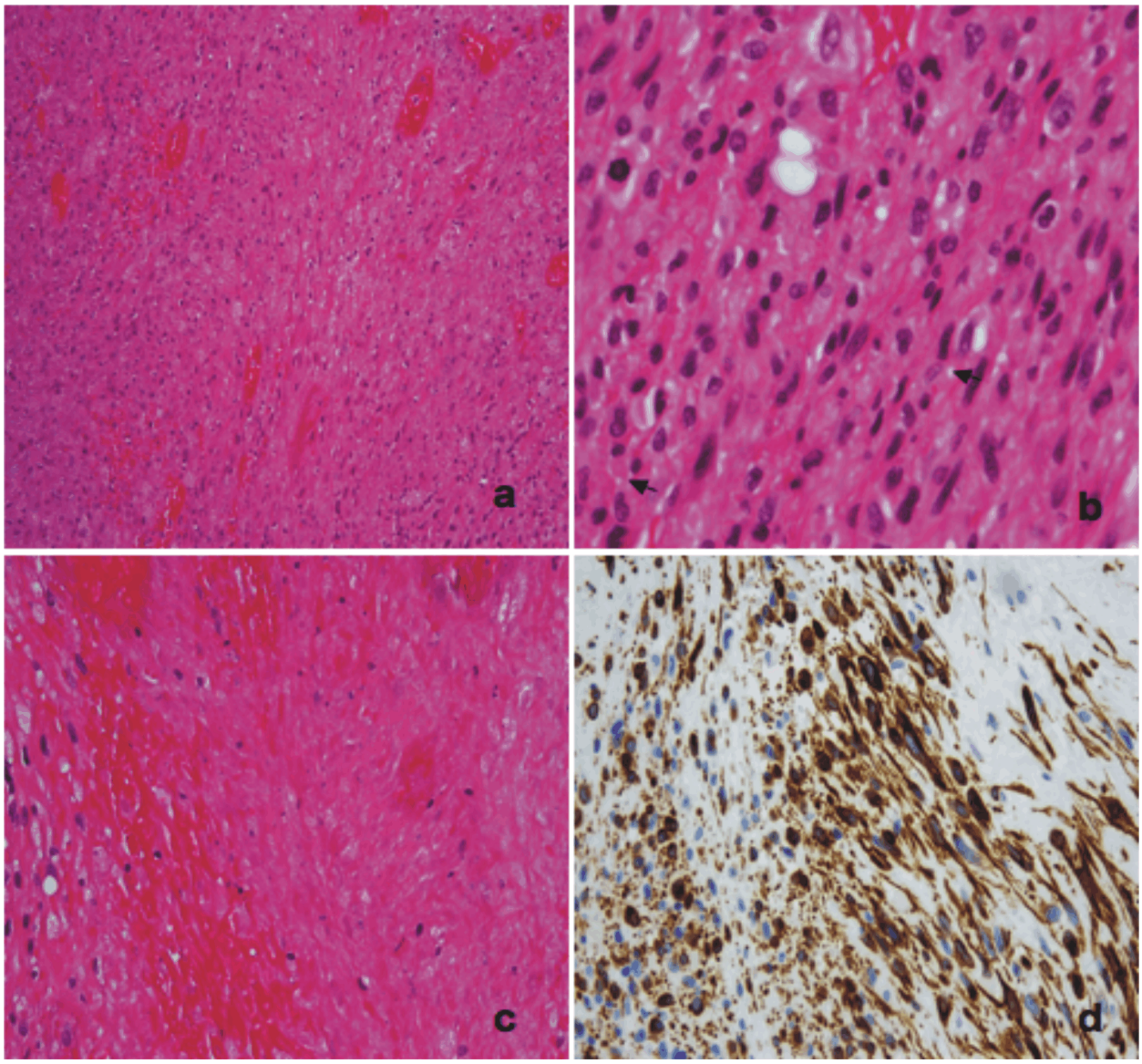

Figure 3 – ***Histological images: The tumor proliferation has a fascicular architecture. It is composed of fusiform cells with eosinophilic cytoplasm and elongated nucleus. (a) This morphological aspect is suggestive of a muscular differentiation (score 2 of differentiation). (b) At a high magnification, an important anisonucleosis with irregular and hyperchromatic nuclei and more than 19 mitoses/high power field are evident (score 3 for number of mitoses). (c) Less than 50% of the tumor was necrotized (score 1 for tumoral necrosis). (d) The tumor cells have a strong positivity for the desmin, which was suggestive of leiomyosarcoma.***

The cells are completely negative for cytokeratins AE1/AE3, PS100, CD117 and CD34. The tumoral cells have also a poor positivity for the CD31. The Ki67 proliferation index was 20%. The lesion was thought to correspond to III grade leiomyosarcoma (differentiation 2, necrosis 1, mitosis 3 = total score 6) according to the FNCLCC system (*Fédération Nationale des Centres de Lutte Contre le Cancer*).

Due to the peculiarity of the case, we decided to refer the patient to the "Institut de Cancérologie Gustave Roussy" in Villejuif. Another histological examination was performed there, confirming a spindle cell sarcoma of high-grade of malignancy with an incomplete muscular phenotype. The suspect of a retroperitoneal liposarcoma was rejected due to the unsuccessful research of the MDM2 gene with the FISH technique.

Discussion

Sarcomas are rare tumors that arise from mesenchymal origin tissue. Soft tissue sarcomas (STS) may arise virtually in any part of the human body while retroperitoneal sarcomas (RPS) take origin from the retroperitoneum and they account for 15% of all STS [1, 2]. Among all the RPS, liposarcomas are the most representative and the ones associated to the best prognosis [1, 3], while leiomyosarcomas and sarcomas NOS (not otherwise specified), the histological type found in our patient, are associated with a worse prognosis than liposarcomas [1]. RPS are usually detected when they are huge masses that cause abdominal pain or discomfort, and frequently the clinical picture gets misunderstood. In our case, it seemed normal to rule out an acute appendicitis and a urinary tract problem in a young man with right-sided abdominal pain.

Because RPS are rare tumors, only some specialized centers have really large case records. Among these centers, the *Memorial Sloan-Kettering Cancer Centre* (MSKCC) in New York showed in 1998 a record of 500 RPS treated between 1982 and 1997 and more in general in 2002 a record of 2084 localized primary STS treated between 1982 and 2000 [3, 4]. More recently, in 2009, a large survey of 1365 patients with RPS was published by the *Johns Hopkins University School of Medicine in Baltimore* and in 2008 another survey of 1091 STS was published by the *Anderson Cancer Centre* in Houston [1, 5]. All these studies demonstrate that the key point in the cure of STS in general and RPS in particular lies between the biology of the tumor itself and the ability of delivering the most appropriate treatment, basically consisting in a primary en bloc surgical resection. The recognized biological factors that influence the RPS prognosis are the histological type of the tumor and the disease grade [1, 4]. As above mentioned, the liposarcoma is the most frequent histological subtype and is associated with the best prognosis; leiomyosarcoma and sarcoma NOS have a worse prognosis while rhabdomyosarcoma and hemangiosarcoma are associated with a much more dramatic one. The different histological grade (3–4 *vs.* 1 or high *vs.* low) [1, 4] is another statistically significant predictor of survival. The tumor size does not influence survival for RPS [1], while it does for STS in general as the primary site does (non-extremity *vs.* extremity) [5]. Our patient had a spindle cell sarcoma of high grade of malignancy with an incomplete muscular phenotype, an uncommon histological final report not easy to get and clearly associated with a bad prognosis.

Concerning the possible treatment delivered, the best one is a primary surgical resection with not only gross but also microscopic negative margins [1, 3–6]. As demonstrated in 2005, by the *Institute of Oncology* in Ljubljana, on a group of 155 patients treated for RPS, the 5-year and 10-year survival rates for patients with R0 resection were 75% and 64% while for R1 resection were 25% and 8% respectively [6]. Similar results were obtained in 2002 by the MSKCC group about STS in terms of local recurrence free survival, distant recurrence free survival and disease related death. According to a population-based analysis of the SEER (*Surveillance, Epidemiology and End Results*) cancer registry, the RPS resection rate has increased significantly over time passing from 54.8% in 1973 to 78.5% in 2001 [2]. This is probably due to the improvement in CT image quality and the increased use of extensive resection including adjacent organs.

Concerning prognosis, local recurrence is the major cause of mortality for RPS in contrast with extremity sarcomas where the principal cause of death is distant metastases. This depends on difference in anatomic location but also in tumor biology. Local control may be improved with adjuvant or neoadjuvant treatment, but, unfortunately, now there is no real evidence on their benefit. Concerning RT, only a small percentage of patients receive a form of RT (preoperative, postoperative or IORT). This is due to the RT induced toxicity in particular on the GI tract, and the complexity related to the timing and dose. It has been already showed that adding external RT to surgery improves local control but we need anyway more studies to better specify the value of RT in improving the cure of RPS and its optimal delivering method [7].

Chemotherapy has still a controversial role in the adjuvant and neoadjuvant treatment of RPS but, in particular, novel anticancer agents have an increasing role in advanced disease. Chemotherapy is in fact the main stay of treatment for patients with locally advanced inoperable or metastatic disease [8].

Due to the peculiarity of the case, once discharged the patient was referred to the specialized centre mentioned above to have an appropriate follow up and eventually a postoperative treatment. Until now, he is free of local and distant recurrence.

Conclusions

RPS are usually diagnosed as locally advanced masses that frequently require large en block resection to achieve a radical treatment that may give a survival benefit. In fact, current data again today suggest that radical surgery is the only chance for a potential curative treatment.

For all these reasons, it is mandatory to perform a primary R0 resection to deliver the best treatment and consequently the best prognosis. When this is not feasible for the surgical team involved, it is vital to refer the patient to a specialized centre.

Up to now, our patient, followed by an Oncological Institute in Paris with scheduled CT scan, is still free of local and distant recurrence despite the aggressiveness of his sarcoma.

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Corresponding author
Manuela Bossi, MD, Service de Chirurgie Digestive et Métabolique, CHU Jean Verdier, Université Paris XII-UFR SMBH "Léonard de Vinci", A.P.H.P., Avenue du 14 Juillet, 93143 Bondy, Cedex, France; Fax (33) 0148026161, e-mail: bossimanuela@yahoo.it

Received: May 10th, 2012

Accepted: August 3rd, 2012