An unusual sarcomatous retroperitoneal metastasis. A rare case report with a brief literature review

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Abstract

Retroperitoneal sarcomas are rare tumors associated with a high rate of recurrence and very bad prognosis. Their only efficient treatment is a negative-margin surgical resection that is extremely difficult to achieve. Retroperitoneal metastases from extremity sarcomas are considered unusual. In literature, such a metastatic pattern is described extremely rarely. In this paper we report a case of a very aggressive extremity chondrosarcoma, associated with local recurrence, multiple distant metastases, that finally led to a retroperitoneal metastasis. The recurrence and progression of the sarcoma in this localization were impressive, with a fast overcome of therapeutic options. Chemo- and radiotherapy have not proved to be efficacious in this context and they could have had a role in the deterioration of patient state of health. New tumor markers for the detection and follow-up of these tumors should be considered.

Key words: retroperitoneal metastasis, retroperitoneal sarcoma, chondrosarcoma, extremity chondrosarcoma, alkaline phosphatase

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Introduction

Sarcomas represent a heterogeneous group of rare malignant tumors derived from embryonic mesoderm, developed from muscle, adipose tissue, cartilage, bone, and cartilaginous or nervous tissues, with various localizations: extremities, trunk, retroperitoneum, head and neck (1,2,3) and over 100 different diagnostic subtypes (4). The very low incidence of these cancers (5) has limited our knowledge on their biological behavior, but also has impeded the agreement on a standard optimal reporting, diagnostic and therapeutic protocol (1,6,7,8,9).

Retroperitoneal localization of sarcomas is rare—only 0.1% of all cancers (4,10,11,12) and 10-20% of soft tissues sarcomas (13,14,15,16), but it is graced by a very bad prognosis (16), especially due to repeated local recurrences (37-60% five-year relapse rate) (3,9) even after a radical resection, with a five-year overall survival less than 50% (3). Retroperitoneal sarcomas frequently develop in a silent manner, until they reach gigantic dimensions (18,19) and affect by compression or by invasion vital structures (20,21) in the retroperitoneum (large vessels, nervous structures, kidneys, ureters), but also in the peritoneal cavity. Proximity to these structures or their direct involvement, as well as the limitation brought by the narrow anatomic space, hard to approach surgically, frequently make difficult a radical, aggressive excision, that is considered to be the only therapeutic solution (6,10,12,13,17,20,22,23).

Many information regarding retroperitoneal sarcomas have come by extrapolation from extremity sarcomas that, however, are characterized by a different biological behavior (1,6,15). Once a large surgical excision/amputation has been performed, possibly associated with radiotherapy, the prognostic is good, local recurrence is low and metastasizing, if occurs, involves especially the lungs (in 70% of cases) (24,25,26). Particularly small lesions, less than 5 cm at the time of diagnosis, are considered to have a relatively good prognosis. Between extremity sarcomas, cartilage sarcomas or chondrosarcomas, especially if well-differentiated, have a good prognostic (27), a high five-year survival rate, small recurrence rate and a low metastatic potential (10-15%), in the majority of cases to the lungs. Chondrosarcomas represent malignant tumors composed of cells that produce hyaline cartilage determining an abnormal bone and/or cartilage growth, of variable dimensions, especially in long bones, in their proximal extremity (28). They represent approximately a quarter of bone cancers and their optimal treatment is represented by radical surgery, currently “limb-sparing surgery” being preferred, a conservative surgery that associates comparable results to amputations, regarded as a last option (29,30).

Extremity-retroperitoneal sarcoma association is, however, rare. In literature, retroperitoneal metastases arising from extremity sarcoma are very seldom described (24) and there are even less data concerning optimal therapeutic solutions in such cases or regarding the results of surgery. Because this kind of association is quite uncommon and because starting from extremity sarcomas—more visible—we can extrapolate numerous elements to optimize our knowledge on retroperitoneal ones, in this paper we will present a case of dramatic evolution of a retroperitoneal metastasis arising from an extremity sarcoma.

Case report

An 18-years old patient, without significant antecedents, hired in the field of agriculture, was admitted to Oncology Institute “Al. Trestioreanu”, Bucharest with a relatively though, unpainful, approximately 3/3 cm tumor located at the distal third of the left femur, appeared after local minor trauma. At admission, the patient had a good general state of health. Tests revealed an unspecific inflammatory syndrome and a rise in alkaline phosphatases. Radiography: patella alterations and CT with contrast medium: a 27/23 mm osteolysis region in the left femur, above the level of the medial condyle region and partially at the level of the left medial femoral epicondyle with important periosteaal reaction and extension to the surrounding soft tissues, presenting calcifications, a well-delimited, iodophilic capsule, compressing and infiltrating left vastus medialis muscle. Tumor-biopsy: relatively well-differentiated chondrosarcoma and immunohistochemistry: moderately aggressive biological potential (S100 positive diffusely, VIM positive, Ki67 positive in tumor cells, desmin-negative). Tumor volume was evaluated at 233 cm³ and neoadjuvant chemotherapy was started. After 2 months, control IRM evidenced the tumor having a 6.6/6.8 cm diameter axially, 11.3/7.7 cm in a sagittal plane, involvement of the joint capsule, of the zone of crossed ligaments insertion and also of popliteal vascular and nervous bundle. After 5 series of chemotherapy, a surgical resection (in a specialized clinic) of distal left femur on a length of 17 cm was performed, along with the insertion of a left knee arthrodesis (Fig. 1). Postoperative evolution of the patient was favourable and chemotherapy was continued after the intervention too. At 1 month after the surgery the oncologic control found out the normalization of alkaline phosphatase values. Two months from the intervention, although no signs of recurrence were obvious, high alkaline phosphatase levels were registered. Ten months after the operation, the patient came unexpectedly with a 2 cm, firm, fixed, local recurrence in the medial third of the left femur. The radiography evidenced a 1.5 cm somatic lesion attached to the left femur, above the level of the medial condyle region and partially at the level of the left medial femoral epicondyle with important periosteaal reaction and extension to the surrounding soft tissues, presenting calcifications, a well-delimited, iodophilic capsule, compressing and infiltrating left vastus medialis muscle.
cm diameter area of inhomogeneous diffuse osteocondensation. An amputation in the medial third of the left femur was done and chemotherapy was reinitiated.

At two months after the amputation the patient came again complaining of shortness of breath, cough, right posterolateral thoracic pain. Radiography and CT-examination (Fig. 2 A,B,C) revealed multiple lung tumors with microcalcifications, with characteristics of chondrosarcoma metastasis and accompanying pleural reaction.

The patient was directed towards a thoracic surgery clinic where multiple atypical resections were performed, however with the persistence of other two right basal pulmonary metastases. After other three chemotherapy series, the remaining metastases had also been excised. After the intervention, the patient continued chemotherapy, but also started radiotherapy. After other 8 months, abdominopelvic echography (Fig. 3) and control CT examination identified a retroperitoneal mass, under the left kidney, of approximately 7.2/6.57 cm, spontaneously dense, homogeneous, developed outside the kidney, appearing to be in continuity with left psoas muscle, pleading for a left kidney abscess.

Clinical appearance of the patient with no signs of infection, with elevated levels of ESR and LDH and patient precedents pleaded for a retroperitoneal sarcomatous metastasis. A surgical intervention in our Clinic of Oncologic Surgery was done and a firm, 10 cm-diameter, posteriorly-fixed tumor, at the left inferior pole of the kidney was found. A resection of the retroperitoneal mass was carried out. The result of the histopathologic exam was sarcomatous metastasis. After another month, control echography evidenced the presence of an approximately 53/46 mm nodular tumor remnant along with the apparition of a new 6.6/6.8 cm tumor in the left flank, associating retroperitoneal adenopathies. A surgical re-intervention was carried out and a voluminous left lumbar tumor attached posteriorly, extended from pelvic superior aperture to the superior aspect of left kidney, invading the kidney, left psoas muscle and peritoneum was found, along with voluminous latero-aortic adenopathies muffling the large vessels. The intervention was limited to exploratory laparotomy and tumour biopsy: sarcomatous metastasis. A chemotherapy series was instituted again. Echographic control revealed the growth of the mass to 10.58/8.37 cm (Fig. 4) and a distorted architecture of left kidney completely included in tumor mass.

A new echography control (after 3 chemotherapy series) showed tumor extension to 13.77/10.03 cm (Fig. 5) and additionally, a 95/57 mm voluminous retroperitoneal adenopathic block.

With the failure of previous chemotherapy regimen, a palliative treatment with Topotecan and Carboplatin was recommended. After that, the patient was again admitted to the hospital complaining of superior abdominal pain and echographic examination demonstrated the progression of the retroperitoneal tumor to 16.47/10.11 cm (Fig. 6) and the apparition of numerous nodular structures adjacent to it, extending from epigastrium to left iliac fossa (Fig. 7); also, at the level of epigastrium - a hypoecholic tumor, with irregular contour, of 12.88/8.64 cm (Fig. 8); multiple big retroperitoneal adenopathies.

Figure 2. A, B, C. Lung chondrosarcoma metastases and accompanying pleural reaction

Figure 3. Retroperitoneal metastasis
The evolution of the patient was severe: severe anaemia, important leukopenia, very elevated levels of LDH and alkaline phosphatases. After other two months, the patient came back with diffuse abdominal pain, extremely enlarged abdomen; shortness of breath, polypnea; tachycardia; generalized oedema because of the severe hypoproteinaemia and venous compression by the tumor; inflammatory syndrome; very high levels of LDH and alkaline phosphatases; severe electrolytic disequilibrium; severe renal failure. A hydro-electrolytic re-equilibrating and symptomatic treatment was instituted. The last CT control, effectuated after other two months, evidenced the progression of tumor dimensions, extending from the right hypochondrium to the left flank, with a diameter of 28/20 cm, that was solid, calcified, with air bubbles, seeming to include the descending colon, developed inferiorly towards urinary bladder pole and anteriorly coming in contact with the abdominal wall, the case being beyond surgical, but also medical treatment. The patient did not come again for scheduled controls and, in the context of tumor galloping growth and of his precarious state, we can only consider as explanatory cause the exitus of the patient.

Discussions

This case impresses through the high recurrence rate of the primary tumour and particularly of the sarcomatous metastases. The aggressive growth in dimensions in a very short interval is unusual if we take into consideration that the primary tumour was a well-differentiated chondrosarcoma, with a moderately aggressive biological behaviour and of relatively small dimensions at the time of its discovery. Low and intermediate-grade chondrosarcoma are statistically associated with a 90%, respectively 81% five-year survival rate, a 0% and 10-15% metastatic potential and a low, respectively moderate local recurrence rate. Also, chondrosarcoma usually involve the proximal zone of long bones and rarer distal extremities (28). It is also surprising the young age, of 18 years, for the apparition of this chondrosarcoma, less than the 20-60 years age interval considered to be preferentially affected by these tumor forms (31).

Studies have shown that conservative interventions - "limb-sparing surgery" - offer results that are comparable to amputation per primam (29,32). In this case, according to current recommendations, a surgery to conserve the lower limb as much as possible was preferred, but with surgical limits as large as possible to target radicalism. No initial radiotherapy was applied; instead, the patient started a neo-adjuvant and
Adjuvant chemotherapy regimen, that it is currently known to be efficient in osteosarcomas, but inefficient, just as radiotherapy in the case of chondrosarcomas (33). During initial chemotherapy, the tumour had shown an increase, according to MRI examination.

The period of time until the first recurrence and the overall free-disease survival was of 10 months that is superposable on existing findings, in the majority of cases local recurrences appearing in the first two years. The management of the first recurrence implied amputation that eliminated the problem of local relapse.

Lung metastasizing is not surprising, knowing that 60%-80% of extremity sarcoma metastases have lung localization (24-26). Pulmonary metastases from sarcomas appear by hematogenic dissemination of tumor cells (34). In this case, lung metastases were multiple and they appeared 2 months from the amputation and 12 months from the initial intervention. Their treatment was represented by surgical excision that was followed by good results and the absence of pulmonary relapse. However, it is remarkable the finding that even before their medical imaging evidence, alkaline phosphatase serum levels had shown an important rise after a long period of normality in the free-disease periods; also, the discovery by imaging coincided with patient admission to the hospital for thoracic pain and it had no anticipative power.

Retroperitoneal metastases arising from extremity sarcomas are, however, quite uncommon. In literature, few descriptions of extremity sarcoma having as evolving expression a retroperitoneal metastasis are found (24). The time interval from the primary tumour surgery to retroperitoneal metastasis was of 20 months and the period between lung and retroperitoneal metastases was of 8 months. In the intermetastatic period alkaline phosphatases and LDH values had been normal. Their significant rise a little before perceiving the retroperitoneal metastasis could indicate a parallelism between tumour activity and the values of these enzymes. The majority of retroperitoneal sarcomas have remarkable big dimensions, of over 10 cm at the time of their diagnosis and their growth is fast and insidious (5,12,19). In the intermetastatic period the overall state of health of the patient was good, without any sign of disease, the retroperitoneal metastasis being discovered incidentally by control CT examination at a dimension of approximately 10 cm (intraoperative finding). Initially, the metastasis involved strictly the retroperitoneal space, but affected afterwards secondary retroperitoneal and peritoneal organs. The discovery of a tumor remnant at only 1 month after the surgery, but also the apparition of a new structure proves how difficult a radical excision can be (1) and how deceitful the impression that a radical surgery had been performed can be, as noticed in literature (with description of frequent positive resection margins and high local failures) (1, 6,16,35). That is why, in literature, the recommendation for an aggressive surgery is frequent (7,36), with excisions at big distance away from tumour bed, even with the sacrifice of nearby organs or blood vessels with or without their reconstruction (37) or even the approach of a compartmental resection involving all neighbouring organs, even if they were not invaded by the tumor. In 75-77% of retroperitoneal sarcoma, mortality is caused by the impossibility of surgical treatment of recurrences that are more and more aggressive (12,16,37,38,39). In the illustrated case, surgical resection of the relapses was impossible because of the tumor invasion of the entire retroperitoneum, muffing of the large vessels by big adenopathic blocks and possible by invasion, but also because of the intraperitoneal invasion. Currently, it is considered that non-radical excision, biopsy-laparotomy, debulking surgery are associated with a survival rate similar to that of simple observation (1,3,36,38, Lazar AM - unpublished observation), but, instead, they can draw postoperative complications, supplementary material and moral costs, being therefore unadvisable.

In these circumstances, an intervention is still carried out, even when the certitude of a radical surgery is missing, for several reasons: absence of an international standard for the management of these cases, with different perspectives between surgical teams and medical centres (8) with different experiences (some authors considering that non-radical resection still increase survival rate) (20,40) and some considering that en-bloc resection does not add tumor control (14), with studies/trials only on small series (4,6,22), because of the insufficient knowledge of imaging accuracy in reflecting intraoperative truth, the recommendation of some surgeons to surgically intervene for the first recurrence (36,38), and for palliative reasons (22,40).

It is remarkable the very fast progression of the retroperitoneal metastasis, even during chemotherapy, but also the development of other metastases in the same space. The progression of the retroperitoneal remnant was of 30 mm per month during the first 2 months after the exploratory laparotomy; afterwards the growth was even more accelerated, the tumor almost doubling its volume and invading the entire abdomen, including peritoneal organs in only eight months from the initial discovery of the retroperitoneal metastasis. Growth rate per month has already been taken into account by some as an outcome predictor in certain histological types (41). We cannot observe an obvious factor stimulating tumor growth except for, maybe, the introduction, in lack of other therapeutic options, of palliative treatment with Topotecan and Carboplatin. Chemo- and radiotherapy have not been efficacious in this case, but could associate significant toxicity that is similar to the opinion of other authors that find their utility questionable (1,10,20,29,37,38).

The retroperitoneal metastasis became symptomatic by abdominal pain relatively late, as already described in literature (10), long after its discovery by medical imaging (at approximately four months). Significant alteration in patient state of health took place at 8 months after primary retroperitoneal tumour discovery. This might explain why retroperitoneal sarcomas are usually discovered with a significant delay (16), that still surprises some authors (11). Echographic descriptions were similar to CT information and were also confirmed by intraoperative discovery. Therefore, echographic examination, preferably CT or MRI (1,10), should be periodically used, even for a long time after the surgery, in the follow-up of these patients, being extremely useful for a faster discovery of...
recurrences and metastases and possibly in increasing survival time. During the periods of tumour silenctum, the values of enzymes such as alkaline phosphatases and LDH were normal, their levels increasing significantly at tumor reactivation. For a histopathologic tumor type such as chondrosarcoma, after the amputation of the affected limb, the dynamics of these enzymes, known as markers for osteogenic activity (42) could precociously signal, even before medical imaging methods, primary tumour, its recurrence or metastasizing, as reported by others for extraskeletal osteosarcomas (43).

We lack precise knowledge on the finality of this young man, but in the given context, we cannot take into equation a long survival after the registered last control at Bucharest Oncology Institute “AI. Trestioreanu”. The overall survival of this patient can be estimated at 28 months.

We cannot specify risk factors associated with the development of this extremely aggressive tumour type. Elements to suggest hereditary defects (Ollier disease, Marfucci syndrome, multiple hereditary exostosis, Wilms tumour) were absent (28). The patient, working in agriculture, could have been exposed to certain chemical substances, which have been incriminated in the etiology of sarcomas (44), but the young age of this patient makes such an association unlikely. The geographic localization of the patient near Slatina, an area with several industrial units that release several toxic chemicals, even though they do not exceed admissible levels for each type (45), could have, maybe, additive effects. Minor local trauma that led to tumour discovery most likely represented only a signal-factor and not a triggering one (30).

Conclusions
Retroperitoneal metastasizing from extremity sarcoma is rare, but possible, and should be taken into account in patient long-term follow-up.

Surgical resection seems to be efficient only for extremity sarcoma (where local progress can be controlled, even if sometimes with the price of patient invalidity) and for lung metastases. However, surgical and combined therapies appear to fail regarding retroperitoneal involvement. Frequently, retroperitoneal involvement is associated with repeated surgical interventions that many times do not prolong survival, but traumatize, alter patient quality of life and may bring complications. In overcome cases, patient manifest symptomatology cannot be adequately controlled because of the limits of palliative treatment.

As the incidence of retroperitoneal sarcomas is very low and existing studies have been carried out on small groups of patients with limiting statistic power, we cannot establish with certainty if a compartmental surgery is always opportune vs. a locally aggressive radical surgery to enhance the survival of such patients. A regular control of operated patients, even at long distance from the intervention, should be done; echography, CT and MRI examinations are useful and accurate instruments in orientating the surgeon on tumour localization and extension. Markers, such as alkaline phosphatases and LDH for chondrosarcoma, should be considered for the detection and follow-up of each subtype of sarcoma. It is advisable that, in cases where imaging data suggest the impossibility of radical resection, a surgical intervention be excluded, because it would subject the patient to an additional unjustified trauma.

References


