Metastatis of Soft Tissue Sarcomas

Fethi Derbel et al.[*]

Department of Surgery, University Hospital Sahloul, Sousse
Tunisia

1. Introduction

Although soft-tissue sarcomas account for <1% of all malignancies, they represent a high percentage of cancer-related deaths worldwide [1]. These tumors may arise in virtually any anatomic site, but most originate in an extremity (59%), the trunk (19%), the retroperitoneum (15%), or the head and neck (9%) [2]. Currently, more than 50 histologic types of soft tissue sarcoma have been identified, but the most common are malignant fibrous histiocytoma (28%), leiomyosarcoma (12%), liposarcoma (15%), synovial sarcoma (10%), and malignant peripheral nerve sheath tumors (6%) [3]. Rhabdomyosarcoma is the most common soft tissue sarcoma of childhood.

2. The role of the pathology

As part of the evaluation by a specialist multidisciplinary team, accurate histological characterisation is essential before initiating treatment. The mainstay of diagnosis is histological interpretation±immunohistochemistry, although cytogenetic and molecular genetics investigations and, occasionally, electron microscopy are useful ancillary tools. Cytological analysis of fine-needle aspirates has a limited role in primary diagnosis, but can be used to confirm recurrent disease, or nodal metastases.

The histopathology report is an interpretation based on tumour morphology and immunoprofile in the available sampled tissue, and clinicopathological correlation is mandatory.

Diagnosis is most frequently made on needle core biopsy material, and tumour subtype and grade can be determined in about 80% of core biopsies [4], although pathologists experienced in examining soft tissue tumours have a diagnostic accuracy of 95-99% [4,5]. The amount of tissue can be a limitation, as the biopsy may not represent the entire, frequently heterogeneous tumour, or may miss the tumour. For this reason, correlation

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[*] Sonia Ziadi[1], Medi Ben Hadj Hamida[2], Jaafar Mazhoud[2], Mohamed Ben Mabrouk[2], Abdallah Mtimet[2], Sabri Youssef[2], Ajmi Chaouch[3], Ali Ben Ali[2], Ibtissam Hasni[4], Mrad Dali Kaouthar[4], Jemni Hela[4], Moncef Mokni[1] and Ridha Ben Hadj Hamida[2]

[1]*Department of Pathology, University Hospital Farhat Hached, Sousse, Tunisia*
[2]*Department of Surgery, University Hospital Sahloul, Sousse, Tunisia*
[3]*Department of Anesthesiology and Intensive Care, University Hospital Sahloul, Sousse, Tunisia*
[4]*Department of Medical Imaging, University Hospital Sahloul Sousse, Tunisia*

between the clinicoradiological features and the histopathology report is essential, and rebiopsy considered if there is any discrepancy.

The mitotic count, amount of necrosis and degree of cellular atypia can be underrepresented in biopsies, and a significant proportion of tumours are upgraded after subsequent resection.

The limitations of histology should be appreciated. There is notable morphological overlap between different groups of malignant tumours, with different clinical behaviours and therapeutic responses.

Some tumours are resected after neoadjuvant chemotherapy, or post-adjuvant chemotherapy or radiation. Post-treatment changes include stromal fibrosis and tumoral infarct, the latter difficult to distinguish from necrosis, making grading difficult. Radiation can cause reactive atypia of stromal fibroblasts, obscuring distinction between tumour and stromal tissue.

The clinical behavior of most soft tissue sarcomas is similar and, as defined by the

staging system, is determined by the anatomic location (depth), grade, and size of the tumor. The histologic grade of a soft tissue sarcoma remains the most important prognostic factor.

The features that define the grade are the degree of cellularity, differentiation, pleomorphism, and necrosis as well as the number of mitoses. Certain tumors have an assigned grade based on the histologic diagnosis (eg, Grade 1 for well-differentiated liposarcomas; Grade 3 for rhabdomyosarcoma).

3. Metastasis of sarcomas

The current American Joint Committee on Cancer (AJCC) staging criteria for soft tissue sarcomas rely on the histologic grade, the tumor size and depth, and the presence of distant or nodal metastases [6]. In the 2002 AJCC staging system, four tumor grades are designated: well differentiated (G1), moderately differentiated (G2), poorly differentiated (G3), and undifferentiated (G4). In this four-tiered system, Grades 1 and 2 are considered low grade and Grades 3 and 4 are considered high grade [6]. Some recommend using other grading systems based on necrosis [7]or mitoses and necrosis [8].

The metastatic potentials for soft tissue sarcomas by grade are as follows: 5% to 10% for low-grade lesions, 25% to 30% for intermediate grade lesions, and 50% to 60% for high-grade tumors [9].

 Superficial sarcomas are generally less aggressive than their deeper counterparts; for example, atypical fatty tumours in the subcutis do not metastasise or dedifferentiate and rarely recur, unlike similar intramuscular or retroperitoneal tumours [10].

The dominant pattern of metastasis is hematogenous. Lymph node metastasis of soft tissue sarcomas is rare; less than 5% show nodal spread. A few histologic subtypes, including rhabdomyosarcoma, epithelioid sarcoma, synovial sarcoma, angiosarcoma, clear cell sarcoma, and malignant fibrous histiocytoma, show a higher incidence of nodal involvement (10% to 20%) [11]. Alveolar rhabdomyosarcoma can present with widespread nodal as well as bone marrow metastases. Myxoid liposarcoma is known for metastasizing to other soft tissue sites [10].

Distant metastases occur most often to the lung. Of patients with extremity sarcoma, approximately 20% will have isolated pulmonary metastatic disease at some point in the course of their disease [12]. Although pulmonary metastases most commonly arise from
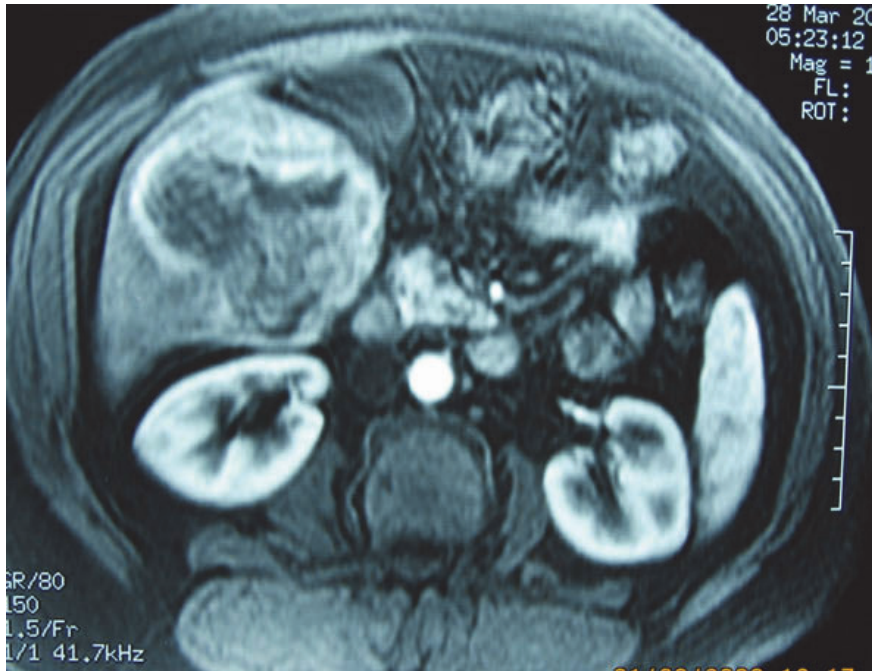
Fig. 1. Abdominal magnetic resonance imaging showing a 5-cm hepatic mass of segment V [26].
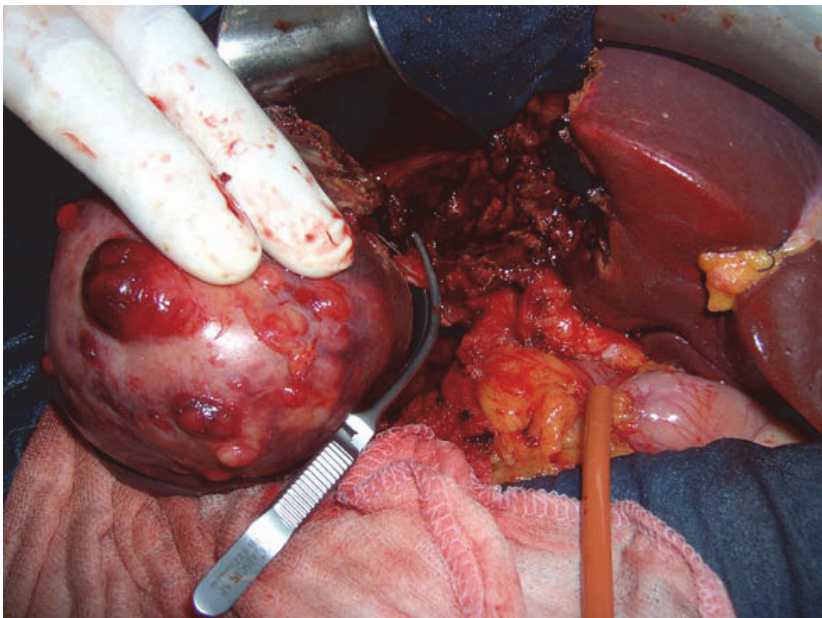

Fig. 2. Operative view showing a large firm mass in segments V and VI of the liver [26].
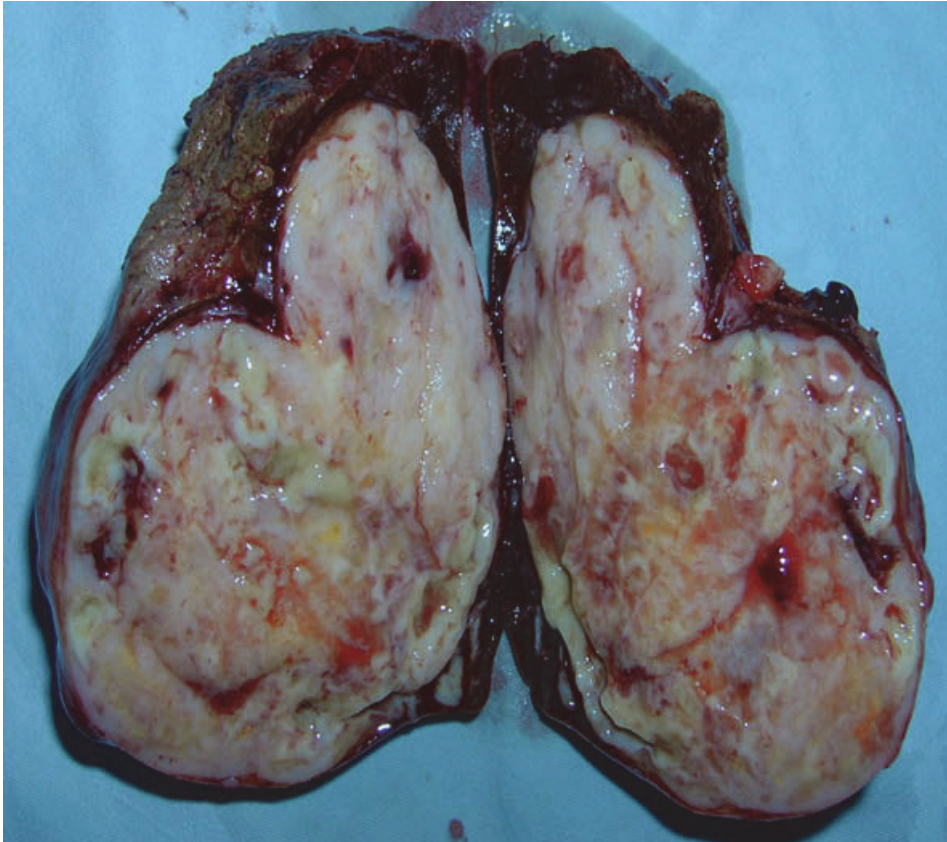
Fig. 3. Section in the mass in segments V and VI [26].

primary tumors in the extremities, they may arise from almost any histologic variant or primary site [13]. Extrapulmonary metastases usually appear after lung metastasis and represent disseminated disease [14]. Initial metastases to other sites such as the liver, brain, and soft tissue distant from the primary tumor are rare [15, 16]. In our study, we report one case of liver metastases of malignant fibrous histiocytoma[fig 1-4]. Pezzi et al. reported that most metastases of MFH occurred in the lungs (90%), followed by bone (8%). However, liver metastases of this tumour are very rare (1%) [24] [26].

Liposarcoma has a documented tendency for spread to distant extrapulmonary sites other than regional lymph nodes [17, 18, 19]. Cheng et al [17] reported on 60 patients with extremity liposarcoma, of which 22 developed metastases. Of these 22 liposarcoma patients, 13 had exclusively extrapulmonary disease on recurrence.

Distant soft tissue was the most common location of unusual initial spread reported by Cheng et al, including the brain and abdomen [17]. Many investigators have noted an increased prevalence of myxoid liposarcoma to exhibit unusual metastases compared to other subtypes of liposarcoma [19].
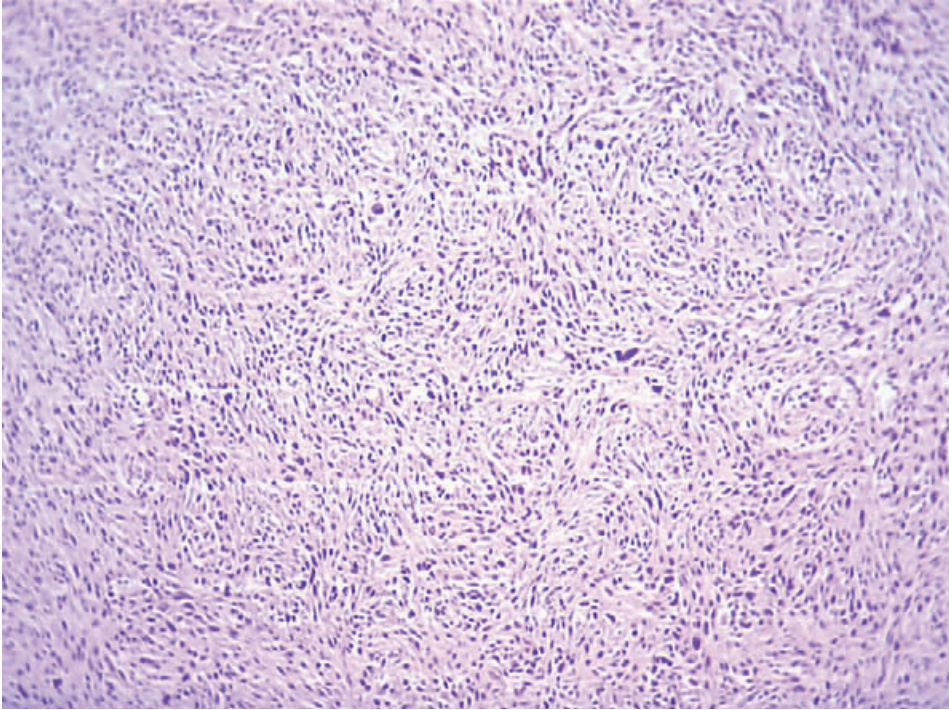
Fig. 4. Histological examination showing spindle-shaped and pleomorphic malignant cells intermingled with bizarre giant cells and inflammatory cells with a storiform pattern [26].

Other large series including all histologic types of high-grade sarcoma have reported unusual metastatic patterns. Potter et al found 15 distant extrapulmonary metastases in their series of 563 patients (2.7%) [20]. Vezeridis et al [21] also documented extrapulmonary distant metastases, but both of these studies were failing to demonstrate a consistent pattern in terms of anatomic location of the initial unusual metastatic site.

In our experience, over a period of 10 years (1998-2007), 13,737 cases of cancer are registered in the central region of Tunisia. 357 (2.6%) cases are soft tissue sarcomas, and 40 (11.2%) of them were diagnosed with metastatic disease.

Histological types who give most metastases are synovial sarcoma, stromal tumor and undifferentiated sarcoma (Table No. I). The lung was the most common site of metastatic sarcomas.

Postulating that soft-tissue sarcomas metastasize via the venous system may account for the predominance of distant recurrence in the lungs. The mechanism of extrapulmonary metastasis is less clear. In 1946, Tedeschi [22] proposed the concept of pluricentric anlage, referring to systemically altered lipid metabolism causing stimulation of undifferentiated mesenchymal cells to explain patients he observed with fatty tumors in multiple soft-tissue locations. While this concept has been used to explain the development of multiple subcutaneous nodules in patients with neurofibromatosis, it seems to be a less robust explanation for the usual clinical course of sarcoma [23]. The mechanism of unusual distant metastasis remains obscure.
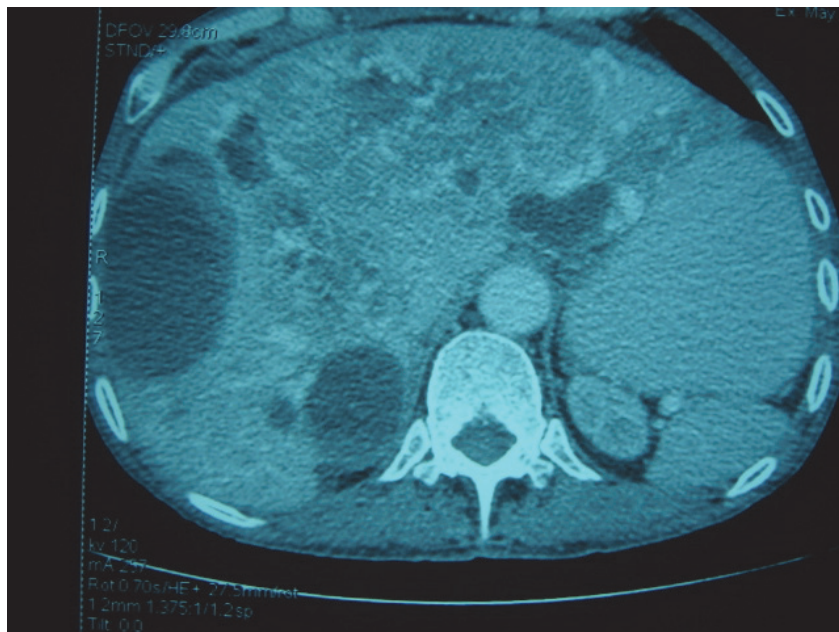
Fig. 5. Abdominal CT scan showing multiple cystic metastasis of a GIST with intracystic enhancing nodules

Histologic type	All of cases	Sarcomas Stage IV	Metastatic site
Undifferentiated sarcoma	82	11 (13,41%)	Lung (6), liver (5), bone (1), lymph node (1)
stromal tumor (GIST)	33	7 (21.21%)	liver (6), peritonium (1)
Synovialosarcoma	21	6 (28.57%)	Lung (6), bone (2)
Leiomyosarcoma	26	5 (19.23%)	Lung (6), bone (2), lymph node (1)
Ewing sarcoma	7	3 (42.85%)	Lung (3), brain (1)
Rhabdomyosarcoma	23	3 (13%)	Lung (1), peritonium (2)
Malignant fibrous histiocytoma	25	2 (8%)	peritonium (1), lymph node (1)
Desmoplastic Intrabdominal round cell tumor	8	2 (25%)	Rectum (1), bladder (1)
Fibrosarcoma	14	1 (7.14%)	Liver (1)
Other sarcomas	118	0	
Total	357	40 (11.2%)	

Table 1. Histological type of sarcoma stage IV and metastatic sites
(1998-2007: The Central region of Tunisia)

Liver metastasis of GIST are frequent. It mainly occurs after incomplete resection of the primitive lesion. Surgical resection is the preferred treatment, but there is a high rate of recurrence. Imatinib is the treatment of choice for these cases. With effective treatment, GIST becomes entirely cystic. Upon reactivation, the cysts develop intracystic enhancing nodules [25]

We report a case of liver metastasis of GIST that occurred three years after the incomplete resection of the intestinal tumor treated with Imatinib. The CT scan showed the development of intracystic enhancing nodules within Six months of Imatinib.

4. References

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