

CASE REPORT

The role of immunohistochemistry in the diagnosis and management of synovial sarcoma

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Abstract

Synovial sarcoma (SS) is a malignant soft tissue tumor representing 5–10% of all soft tissue sarcomas. Most synovial sarcomas are found at the extremities, especially in the lower limbs. A 28-year-old female presented at the Department of Plastic and Reconstructive Surgery, "Dr. Pius Brînzeu" Clinical Hospital, Timișoara, Romania, for evaluation of a mass located in the anterior region of the elbow. Imagistic, histological and immunohistochemically evaluations established the diagnosis of monophasic spindle cell SS G2. Block excision of the tumor with oncological safety margins was performed followed by total elbow arthroplasty. The patient then received radio- and chemotherapy. The case was followed-up at regular intervals for local recurrence and metastases and was free of symptoms at two years. Early diagnosis of SS, multimodal therapies and performing an arthroplasty of the elbow allowed the patient to resume daily activities. The unpredictable evolution requires regular follow-up for a long period of time.

Keywords: synovial sarcoma, upper limb malignancy, elbow arthroplasty.

Introduction

Synovial sarcoma (SS) is a malignant soft tissue tumor representing 5–10% of all soft tissue sarcomas [1–3].

The tumor was named synovial sarcoma after its common periarticular location and histological similarities with the developing synovium [1]. According to current research, primitive mesenchymal cells or myoblasts are the probable origins of SS [4, 5]. Although it can affect all age groups, it is predominately diagnosed in young adults. SS was reported to be slightly more frequent in male individuals [2].

SS can be found nearly any anatomical location but most are at found at the extremities [1]. It is one of the most common soft tissue sarcomas of the upper extremity alongside epithelioid sarcoma and pleomorphic sarcoma [6].

SS is associated with the chromosomal translocations t(X, 18; p11, q11) concerning the *SS18* gene on chromosome 18 and one of the *SSX* genes on chromosome X [1, 2].

SS has three histological subtypes: monophasic (the most common variant of SS), biphasic, and poorly differentiated [1, 3]. The monophasic variant is more commonly encountered in adults, while in pediatrics the monophasic and biphasic variants have a similar distribution [1, 2].

Aim

We present a case of elbow SS. Although this pathology requires a multidisciplinary view, the role of morphopathology is fundamental in guiding the medical team

towards a correct approach and a successful treatment both oncologically and functionally.

Case presentation

A 28-year-old Caucasian female presented initially in the Department of Plastic and Reconstructive Surgery, "Dr. Pius Brînzeu" Clinical Hospital, Timișoara, Romania, in 2014, for evaluation of a mass located in the anterior region of the right elbow. These complaints started some months ago without recalling any trauma history or significant personal medical conditions. The mass evolved, increasing in size and causing pain and discomfort. The patient noted difficulty with activity and bending her elbow secondary to increased pain.

The clinical examination and medical history do not bring significant information to narrow down the list of possible diagnosis.

A punch biopsy examination is performed. Histological and immunohistochemically evaluations of the collected tissue fragments established the diagnosis of monophasic spindle cell SS G2. Based on the immunohistochemically results and on the macroscopic and microscopic aspects of the tumor, the differential diagnosis with the following tumors was made: malignant peripheral nerve sheath tumor, fibrosarcomatous dermatofibrosarcoma protuberans (DFSP), solitary fibrous tumor and Ewing's sarcoma.

Imaging investigations are being carried out: contrast-enhanced magnetic resonance imaging (MRI) scan and basic MRI scan of the upper right limb revealed a tumor with lobular contour, septate appearance, located in the anterior part of the elbow dislodging nearby structures. The tumor has heterogeneous signal in T1, T2 and short *tau* inversion recovery (STIR) weighted images, with structures under a cm in size expressing a hemorrhagic-based hyperintense signal in T1 and T2.

The mass expresses an intense and heterogeneous aspect in gadolinium-based contrast enhancement.

The contrast-enhanced computed tomography (CT) scan of the upper right limb reveals the tumor's feeding artery emerging from the lower part of the brachial artery.

The contrast-enhanced upper limb angiography reveals a mass with a heterogeneous aspect, 6/4.5 cm in size and not causing lysis of the bone structures while displacing without encapsulating the nearby vascular structures.

The CT scan, done with and without contrast enhancement of the thorax, revealed no visual evidence abnormality.

The surgical intervention was performed by practicing the block excision of the tumor, with oncological safety margins together with the distal 1/3 of the humerus, elbow joint, radial head with adjacent tissue, radial nerve embedded in the tumor block, and the insertions of tendon extensors.

After that, total elbow arthroplasty with modular Implant Cast MUTARS prosthesis (Figure 1), defect coverage with local flaps. Biopsy referral of excised parts: postoperatively, restoration of flexion/extension of the forearm was achieved. Extension movements are abolished at the distal radio-carpal joint and all five fingers. Radial nerve sensitivity is absent. The post-operative course was uneventful.

Macroscopic and microscopic features of the tumoral mass

Macroscopic features: on the cut surface of the tumor, a lobulated, slightly nodular contour, yellow-gray colored, with 5/4/3 cm size and inhomogeneous solid appearance of firm consistency with fawn brown and whitish areas.

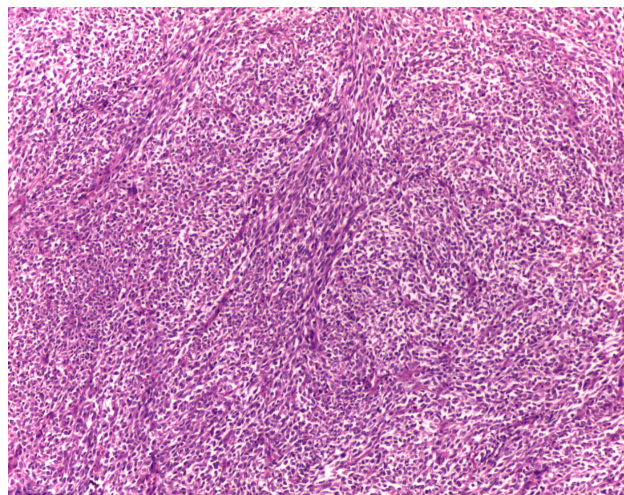


Figure 2 – Spindle cell synovial sarcoma: malignant mesenchymal proliferation with vague fascicular architecture made out of spindle cells and round shaped cells with ill-defined cellular limits, hyperchromatic nuclei, and increased nuclear/cytoplasmic ratio [Hematoxylin–Eosin (HE) staining, ×100].

Microscopic features: malignant mesenchymal proliferation with spindle cells and vague fascicular architecture. Poorly defined areas with round shaped cells and ill-defined cellular limits. Oval and round nuclei with nucleoli (Figure 2). A variable mitotic rate is described, from areas with 2–3 mitoses/high-power field (HPF) to areas with 10 mitoses/10 consecutive HPFs (Figure 3) and other HPF without notable mitotic activity.

The stroma is slightly fibrillary and displays small areas of hyalinization. Hypocellular areas with myxoid stroma areas are described.

Variable degree of vascularization, hemangiopericytoma-like vessels, sites of vascular hyalinization, areas of extravasated erythrocytes, frequently spread mast cells.

Away from the main tumor are described tumoral nests infiltrating the perimysium of the striated muscle tissue and the subcutaneous cellular tissue (Figure 4).

Immunohistochemical (IHC) assessment: positive IHC staining for anti-epithelial membrane antigen (EMA) antibody, with variable intensity for approximately 75% of tumoral cells; CD31 positive for vascular endothelium; CD99 positive for tumoral cells (Figure 5). Anti-pan-cytokeratin (CK) AE1/AE3 antibody staining reveals rare, highly positive cells.

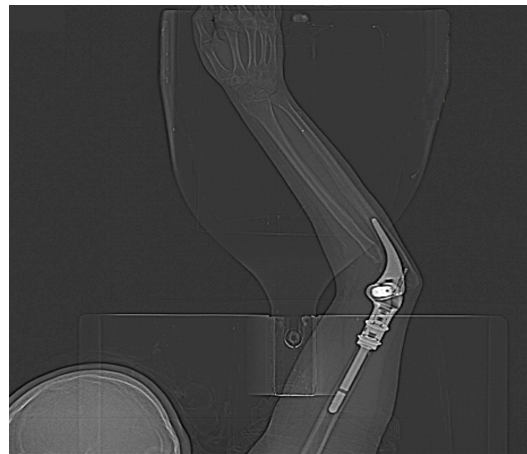


Figure 1 – Total elbow arthroplasty with modular Implant Cast MUTARS prosthesis.

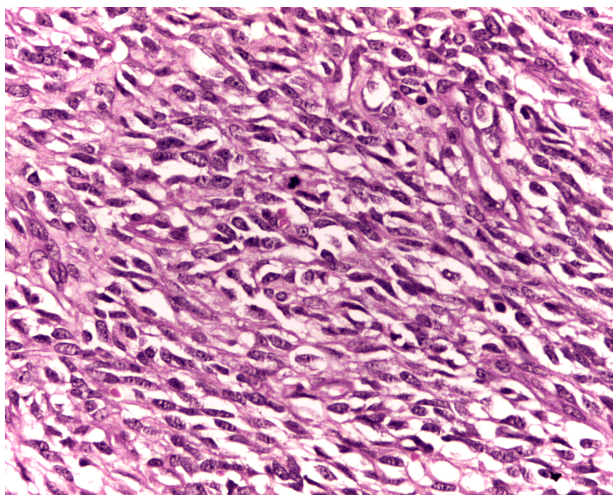


Figure 3 – Poorly defined malignant mesenchymal proliferation with spindle cells and oval shaped cells, solid pattern, slightly fascicular: nuclear atypia and mitotic activity is observed (HE staining, ×400).

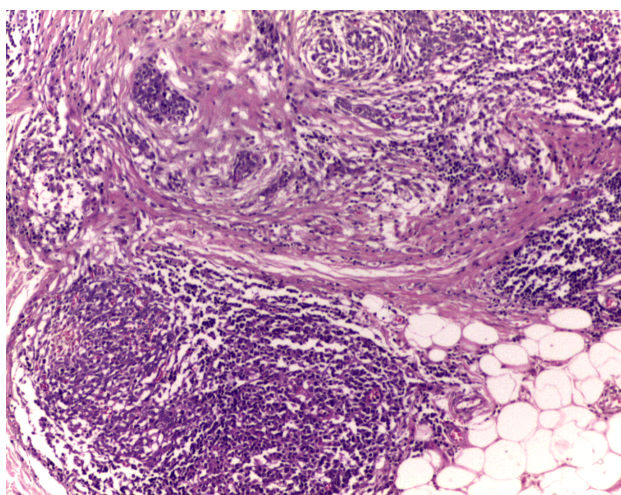


Figure 4 – *Peripheral tumor area with small compact tumoral cell nest, nodular architecture, infiltrating into the adipose tissue, followed by non-specific chronic inflammatory response (HE staining, ×100).*

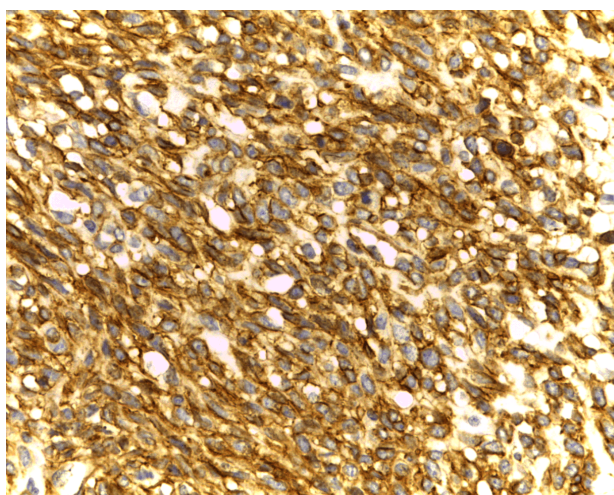


Figure 5 – *Relatively uniform tumoral cells, mostly round-oval shaped, some slightly elongated, with compact unorganized arrangement: positive staining for CD99 (Anti-CD99 antibody immunomarking, ×400).*

Negative IHC staining for anti-CK7, anti-S100 and anti-CD34 antibodies (not confirmed intravascular tumoral nests). The patient was referred to Oncology Center. She received adjuvant radiotherapy 50 Gy/20 Fr in 31 fractions (due to the presence of vascular invasion and a close resection margin). Then, the patient underwent six cycles of adjuvant chemotherapy (Epirubicin and Ifosfamide). Chemotherapy was well tolerated.

In May 20, 2014, a second surgical procedure takes place for obtaining a functional position of radiocarpal and metacarpophalangeal joints.

The transposition of the musculotendinous complex of *flexor carpi radialis longus* is performed, followed by its anchorage at the level of insertion of the *carpus extensor* tendons. An end-to-side anastomosis is performed between *extensor common digitorum* and the tendons of *extensor carpi radialis longus*, thus obtaining a functional position of radiocarpal and metacarpophalangeal joints.

The case was followed-up at regular intervals for local recurrence and metastases and is free of any symptoms.

Discussions

Prognosis

Unfavorable factors for the SS are larger tumor size (>5 cm), metastases at the moment of diagnosis, highly histological grade (Table 1), trunk-related disease, inadequate resection as primary surgical treatment [7]. One study with a follow-up of 10 years concluded that the five-year survival was 74.2%, 10-year survival was 61.2%, and 15-year survival was 46.5%. Metastases can be observed in 50% to 70% of patients [7]. The most common areas of metastasizing are pleura and lung, less common bone or lymph nodes. Metastases can appear over a long period of time (a mean of 5.7 years old), so a long-term follow-up is required while recurrences at the primary site appear after a mean of 3.6 years [1, 7].

The poorly differentiated SS has a worse prognosis [1]. Considering the findings of current research, it has not been established whether monophasic SS has a similar or worse overall survival (OS) rate compared to biphasic SS [1, 7–9].

Treatment

SS requires a multimodality therapy, consisting of surgery, radiotherapy and chemotherapy [1, 6]. Synovial sarcomas have increased chemosensitivity compared with other soft tissue sarcomas (STS). Alkylating agents, such as Ifosfamide seems to be particularly effective options [10].

One retrospective analysis had concluded that patients who received Ifosfamide and Epirubicin had a greater overall survival, recurrent free survival and disease-specific survival rates [11–13].

A wide resection of the tumor involving joints implies choosing a surgical method that will allow the patient to resume its daily as much as possible. For the elbow joint, the following options are taken into consideration: amputation or reconstructive surgeries, such as arthrodesis, osteoarticular allograft, allograft-prosthesis composite (APC), and prosthetic reconstruction. Our Center relies more and more on reconstruction *versus* amputation [14, 15]. Isolated metastases can also be addressed with surgery and adjuvant therapy [16].

Elbow total arthroplasty seems to have a positive regarding emotional acceptance and daily-based activities.

The most common post-operative complication is nerve palsy; the chronic mild pain was less common, while failure and infection are rare findings.

There was a higher incidence of nerve section, neurological complications and infection in patients treated with preoperative radiotherapy [12]. The elbow joint is complex and very sensitive to injury and invasive surgery. Since this case underwent a wide resection, there was limited postoperative stiffness due to extrinsic causes. Future perspectives may improve outcomes with early diagnosis and screening as well as increase awareness with potential for malignancy of upper limb masses [17–19].

Staging

In tumor differentiation scores of sarcomas, according to the *French Federation of Cancer Centers* system, SS has a score of 3. This implies that SS grading starts at grade 2 (Table 1) [13].

Table 1 – Tumor differentiation scores of sarcomas according to the French Federation of Cancer Centers system [13]

Parameter	Criterion
Tumor differentiation	
Score	1 Sarcoma histologically very similar to normal adult mesenchymal tissue.
	2 Sarcoma for defined histological subtype (e.g., myxoid MFH).
	3 Sarcoma of uncertain type, embryonal and undifferentiated sarcomas.
Mitosis count	
Score	1 0–9 mitoses/10 HPFs
	2 10–19 mitoses/10 HPFs
	3 ≥20 mitoses/10 HPFs
Microscopic tumor necrosis	
Score	0 No necrosis
	1 ≤50% tumor necrosis
	2 >50% tumor necrosis
Histological grade	
Grade	1 Total score: 2 or 3
	2 Total score: 4 or 5
	3 Total score: 6, 7 or 8

MFH: Malignant fibrous histiocytoma; HPF: High-power fields.

Conclusions

Despite early diagnosis of SS, multimodal therapies, and performing an arthroplasty of the elbow that allows the patient to resume daily activities, the SS remains unpredictable and requires regular follow-up for a long period of time.

Conflict of interest

The authors declare that they have no conflicts of interest.

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