Medical Science and Discovery
ISSN: 2148-6832

Intra-articular Synovial Sarcoma of the Knee with Extension to the Distal Thigh: A case report

Teodora Delibašić[1], Dušan Rnjak[1-2], Dragana Grbić[3]

1 Primary Health Care Center Subotica, Subotica, Serbia
2 Gerontology Center Subotica, Subotica, Serbia
3 Primary Health Care Center Novi Sad, Novi Sad, Serbia

*** Corresponding Author:** Teodora Delibašić **E-mail:** romic.teodora@gmail.com

ABSTRACT

Objective: We present a case of intra-articular synovial sarcoma of the knee with expansion to the distal thigh with developed metastatic lung disease. The case was complicated by the detection of primary pulmonary adenocarcinoma.

Case: A 70 year age woman reported pain in the right knee during a routine check–up. Ultrasound (US) finding was inconclusive since the detected intra–articular tumor, appeared to be a partially organised haematoma. Magnetic resonance imaging (MRI) indicated the tumor corresponds to SS, and radical tumor resection was performed. Due to developed distant lung metastases, the patient received two different chemotherapy protocols. Good response to the second chemotherapy enabled video–assisted thoracoscopic surgery and removal of the remaining deposits in the left lung. Unexpected detection of primary adenocarcinoma of the lung and its metastases required a new chemotherapy protocol, which the patient is currently undergoing.

Conclusion: SS's insidious onset and infrequency often delay the diagnosis. Common occurrences of lung metastases require the selection of adequate chemotherapy, and continuous follow – up. Laboratory and radiographic monitoring remain mandatory to ensure the absence of both primary diseases and to detect recurrent metastatic activity.

Keywords: Synovial Sarcoma, chemotherapy, adenocarcinoma

INTRODUCTION

Synovial sarcoma (SS) is a rare, malignant, mesenchymal tumor, accounting for 5 – 10% of soft tissue sarcomas (STS) (1). SS is a misnomer as it does not arise from synovium (2). It can, unlike the majority of STS, occur at any age and everywhere in the body. The peak incidence is in the 30s (3) with the extremity being the most common site of primary disease (4). Patients often develop distant metastases, particularly to the lungs resulting in 5–year overall survival (OS) of around 60% in adults (3).

CASE

A 70 – year –old woman reported to the family physician with a pain in the right knee while walking. The symptom was occasional, sharp, and it passed spontaneously. With BMI 28.37 kg/m² she was overweight and had a history of hypertension.

After initial treatment with painkillers, swelling of the knee and slight restriction of the movement appeared. The patient was referred to an orthopedist for further assessment and diagnostics. X–ray showed moderate gonarthrosis. Therefore, collagen and calcium–lactate–based supplements were prescribed. Second physical examination revealed suprapatellar soft tissue formation. Additionally, the right knee ultrasound (US) showed an intra – articular tumor, which originally appeared to be a partially organised haematoma. Magnetic resonance imaging (MRI) of the knee and distal thigh indicated that the tumor sized 6,8 x 8,3 x 12,6 cm corresponds to synovial sarcoma, which expanded to the medial side of the femur along the distal diaphysis (Figures 1, 2).

Radical tumor resection was performed at a specialized tertiary center. Control MRI of the knee showed postoperatively impaired morphology of medial patellofemoral ligament (MPFL). Pathohistologically, the tumor was verified as high–grade biphasic synovial sarcoma.

Case Report Article

Received 09-03-2023

Accepted 18-03-2023

Available Online: 25-03-2023

Published 30-03-2023

http://dx.doi.org/10.36472/msd.v10i3.913

Chest computed tomography (CT) showed multiple metastases, 2 in the right lung and 3 in the left, all up to 20 mm in size. The patient received chemotherapy according to Adriamycin/Ifosfamide (ADM/IFO) protocol with Mesna (Uromitexan®) in IV cycles.

Control chest CT showed, unfortunately, progression of the metastatic disease. In the left lung, there were 5 secondary deposits; major ones sized 25 mm, in the basal segment of the lung, and 17 mm in size, located in S2. The patient underwent VIII cycles of the new Cisplatin/Ifosfamide (CDDP/IFO) protocol with a good response.

After completion of the chemotherapy, the patient became a candidate for a video–assisted thoracoscopic surgery (VATS) and removal of the remaining deposits. In the S10 of the left lung, one suspicious metastasis, 10 mm in size, was resected with a wide protective margin. The resection of 3 more subpleural changes and 1 in lingula were all sent to pathohistological verification.

Unexpected results revealed that the 10 mm deposit in the lower lobe of the lung was not malignant, while the deposit in the lingula corresponded to the tumorlet. Moreover, the largest of 3 subpleural changes, 9 mm in size, was recognized as primary acinar adenocarcinoma of the lung (stage IV, Eastern cooperative oncology group – ECOG, Performance Status 1 – PS1), and 2 others, sized 6 and 5 mm, were its metastases. Molecular testing followed, which determined that the adenocarcinoma was epidermal growth factor receptor-negative (EGFR wild type), anaplastic lymphoma kinase-negative (ALK), and programmed death-ligand 1-negative (PD-L1).

Owing to the developed metastatic lung disease from both the SS and pulmonary adenocarcinoma, the outcome of the treatment still remains uncertain. The patient is currently preparing for the next cycle of chemotherapy. Initial treatment with CDDP/ Gemcitabine (Gemzar ®) protocol) was changed due to renal function deterioration to Carboplatin/ Gemcitabine protocol.

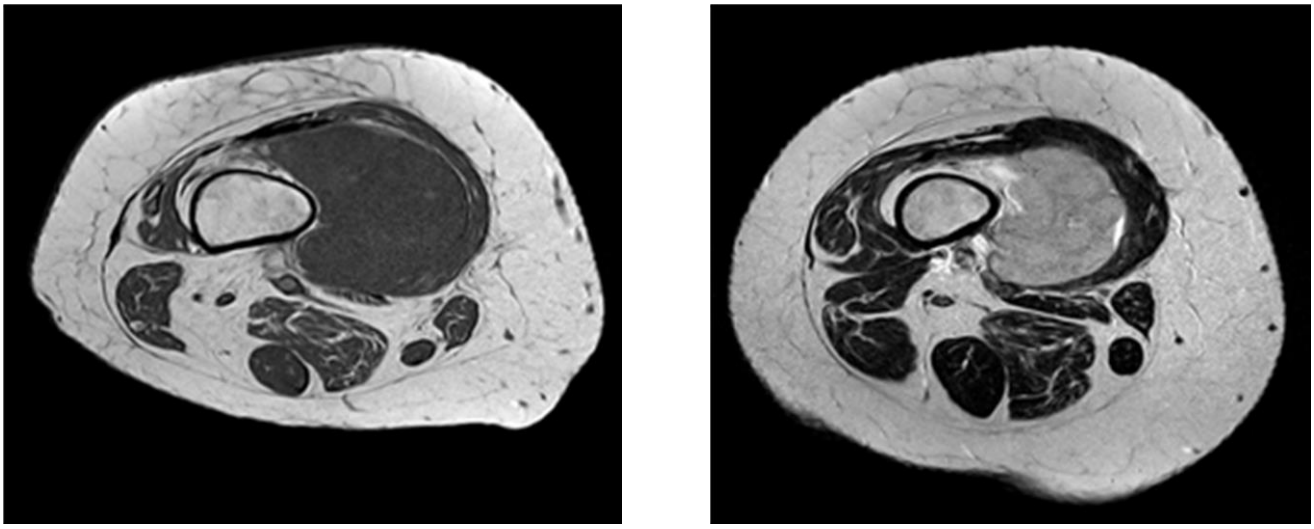

Figure 1: Axial T1- and T2-weighted MR images show an inhomogeneous mass representing synovial sarcoma.

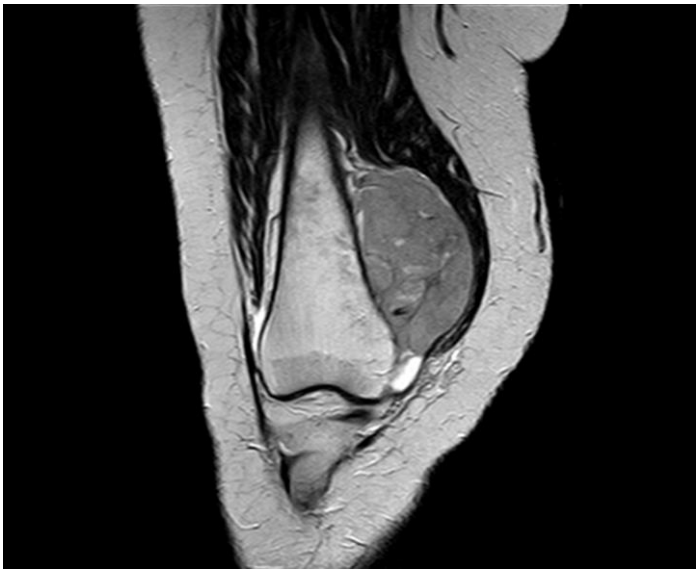

Figure 2: Coronal MR image shows SS expanding to the medial side of the femur along the distal diaphysis

DISCUSSION

Synovial sarcoma accounts for 5–10% of all tissue sarcomas (1) and affects men and women equally (5). Although the peak incidence is in the 30s (3), in our case, it was presented in a 70– year–old. As for location, extremity presents the most common site of the primary disease (4), but some rare cases originate in the head, neck, chest or abdomen (5). Our patient's intra–articular form is extremely rare, and there have been few reports of well–documented cases (1,6).

Classified among sarcomas of uncertain differentiation, synovial sarcoma (SS) may be divided into three histological variants: biphasic, monophasic, and poorly differentiated types. It should always be considered a high-grade sarcoma, characterised by local invasiveness and a propensity to metastasise (7).

Due to the insidious onset, there is often a delay in diagnosis. Patients present with palpable, slowly growing masses, with or without pain (8). Delayed diagnosis in our case significantly contributed to the spreading of the tumor to the distal thigh.

MRI is a modality of choice for the diagnosis and initial staging of synovial sarcoma (9), and it was used in our case as well. After the radical resection of the tumor, pathohistological verification confirmed the diagnosis.

In our, as in most other cases, distant metastases are located in the lung (80%), although they can appear in lymph nodes (up to 20%), bone (9.9%) and liver (4.5%) (10) which results in 5 – year overall survival (OS) of around 60% in adults (3). According to other studies (10), once metastasised, curative treatment is hardly achievable, with the exception of late and resectable oligometastatic disease when patients are treated with palliative chemotherapy.s Compared to STS as a group, SS is highly chemosensitive to specific agents.

For SS, in fit patients, the first–line combination treatment of Ifosfamide and Doxorubicin is recommended over monotherapy with Doxorubicin (11). The second-line palliative chemotherapy of the first choice is ifosfamide or its combination with other drugs (3, 4). Alternative drugs are Pazopanib or Trabetacin in case the patients received Ifosfamide – Doxorubicin in the first – line. Pazopanib is presently the only approved targeted therapy for synovial sarcoma as a tyrosine kinase inhibitor (3). In our case, the second protocol, Ifosfamide/Cisplatin, was used with a good response.

The question about the benefit of the metastasectomy remains inconclusive. According to Pan et al. (12), half of the observed patients who relapsed with predominantly lung metastases received metastasectomy and had an OS of 7.8 years compared with patients with an OS of 2.3 years who did not receive metastasectomy.

The importance of more sarcoma subtype–specific trials, which are to be undertaken, can not be emphasised enough. Recognising and understanding the large diversity in clinical behaviour, biology and genetic make – up of the different STS will lead to developing more tumor –specific therapy (3). It is still early days for epigenetic modulators and immunotherapy.

Malignant lung tumors, on the other hand, are the most common malignant disease in the republic of Serbia. According to the data of the Repubic Institute for statistics, about 5.200 newly diagnosed cases are registered in Serbia every year. In women, it is a malignant neoplasm in the third place by the frequency, following malignant neoplasms of the breast and colorectum (13).

The main risk factor for any lung cancer, including adenocarcinoma, is smoking tobacco due to the numerous carcinogens present. Other risk factors include a family history of lung cancer or occupational exposures to other agents (14). Our patient reported smoking 20 cigarettes a day for over 30 years. Moreover, her family history was positive to lung cancer. Lung cancer patients have a 5-year survival rate of less than 12% to 15%.The mean age when adenocarcinoma is diagnosed is 71 years, and it has replaced squamous cell cancer as the most prevalent non–small cell carcinoma (14).

Distant metastases include mostly lungs, brain and bones. In the presence of the EGFR or ALK gene mutation, antitumor treatment is possible with EGFR tyrosine kinase and ALK inhibitors (15). PD-L1- positive patients can also be treated with therapeutic antibodies (16).

CONCLUSION

Finally, our last chemotherapeutic protocol was changed due to the nephrotoxicity caused by the cumulative use of cisplatin, which has been reported in other studies (17). The results of the Swedish study (18) are encouraging for the use of carboplatin/gemcitabine protocol. Clinical follow-up, laboratory, and radiographic monitoring remain mandatory to ensure the absence of both primary disease as well as to detect recurrent metastatic activity.

Acknowledgments: None

Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. This research did not receive and a specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions: TD: Research of the literature, **DR, DG:** Patient examinations and therapy, patient follow-ups, **TD:** Manuscript preparation, writing and revisions.

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study. Written consent was obtained from each patient to use their hospital data.

REFERENCES

1. Bergovec M, Smerdelj M, Bacan F, Seiwerth S, Herceg D, Prutki M. Intraarticual synovial sarcma of the knee rising from the lateral meniscus – a case report. Orthopaedics & Traumatology: Surgery & Research. 2018; 227 – 230.

2. Khan Y, Carey-Smith R, Taylor M, et al. Treatment and outcomes for synovial sarcoma patients in Western Australia: the role of neoadjuvant chemoradiotherapy. Cancer Reports. 2020; 3:e1268. https://doi.org/10.1002/cnr2.1268

3. Desar IM, Fleuren ED, van der Graaf WT. Systemic treatment for adults with synovial sarcoma. Curr. Treat. Options in Oncol. 2018; 19: 13.
4. Eilber FC, Brennan MF, Eilber FR, Echardt JJ, Grobmyer SR, et al. Chemotherapy is associated with improved survival in adult patinets with primary extremity synovial sarcoma. Ann Surg 2007; 246: 105–113.
5. Kraunsdorf MJ. Malignant soft – tissue tumors in a large referral population: distribution ofdiagnoses by age, sex and location. AJR 1995; 164: 129 – 134.
6. Ishida T, Iijima T, Moriyama S, Nakamura C, Kitagawa T, Machinami R. Intra – articular synovial sarcoma mimicking chondromatosis. Skeletal Radiol. 1996; 25: 766 – 769.
7. Fletcher KU, Mertens F, eds. WHO Classification of tumors. Pathology and Genetics. Tumors of soft tissue and bone. Lyon- IARC Press; 2002.
8. Brennan MF, Singer S, Maki RG, et al. Sarcomas of the soft tissues and bone. Cancer: principles and practice of oncology, vol.35 Philadelphia. PA: Lippincot Williams &Willkins. 2005; 1584.
9. Kransdorf MJ, Murphey MD. Radiologic evaluation of soft – tissue masses: a current perspective. AJR. 2011; 175: 575 – 587.
10. Vlenterie M, Litiere S, Rizzo E, Marreaud S, Judson J, et al. Outcome of chemotherapy in advanced synovial sarcoma patients: review of 15 clinical trials from the European Organisation for research and treatment of cancer – Soft tissue and bone sarcoma group. Setting a new landmark for studies in this entity. Eur J Cancer. 2016; 58: 62 – 72.
11. Judson I, Verweij J, Gelderblom H, Hartman JT, Schoffski P, Blay JY et al. Doxorubicin alone vs. intensified doxorubicin plus ifosfamide for first – line treatment of advanced or metastatis soft tissue sarcoma: a randomized controlled phase 3trial. Lancet Oncol 2014; 15(4): 415 – 23.
12. Pan M, Merchant M. Risk factors including age, stage and anatomic location that impact the outcomes of patients with synovial sarcoma. Medical Sciences. 2018; 6(1):21. https://doi.org/10.3390/medsci6010021
13. Mihajlovic J, Pechiuangolou P, Miladinov – Mikov M, Zivkovic S, Postma MJ. Cancer incidence and mortality in Serbia 1999 – 2009. BMC Cancer 2013; 13:18.
14. Myers DJ, Wallen JM. Lung Adenocarcinoma. In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing. 2021; Available from: https://www.ncbi.nlm.nih.gov/books/NBK519578/
15. Cao L, Lv L. Breast metastasis from EGFR/ALK negative lung adenocarcinoma: A case report. Medicine. Baltimore. 2020; 99: 49.
16. Inamura K, Yakouchi Y, Sakakibara R, Kobayashi M et al. Relationship of tumor PD – L1 expression with EGFR wild – type status and poor prognosis in lung adenocarcinoma. Jpn J Clin Oncol. 2016; 46(10): 935 – 941.
17. Miller RP, Tadagavadi RK, Ramesh G, William BR. Mechanisms of cisplatin nephrotoxicity. Toxins 2010; 2: 2490 – 2518.
18. Sederholm C, Hillerdal G, Lamberg K, Kölbeck K, Dufmats M, Westberg R, Gawande SR. Phase III trial of gemcitabine plus carboplatin versus single-agent gemcitabine in the treatment of locally advanced or metastatic non-small-cell lung cancer: the Swedish Lung Cancer Study Group. J Clin Oncol. 2005; 23(33): 8380-8.