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Case Report

# Unusual manifestation of synovial sarcoma: A rare case report with elevated beta HCG level ☆,☆☆

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ABSTRACT

Synovial sarcoma is a rare type of soft tissue sarcoma that typically arises in the lower extremities and rarely in the upper extremities. Here, we present an unusual case of a middle-aged man who complained of dyspnea, dry cough, and chest pain and was found to have a mass-like lesion on the ulnar side of his left wrist during physical examination. The patient also exhibited gynecomastia and had elevated $\beta$-human chorionic gonadotropin ($\beta$HCG) levels. Subsequent imaging and histopathological analysis of the wrist mass confirmed the diagnosis of synovial sarcoma with disseminated lung metastasis.

This article aims to provide a comprehensive overview of the clinical and pathological characteristics of synovial sarcoma, highlight the importance of considering synovial sarcoma as a differential diagnosis in patients with abnormal hormonal assays, and emphasize the need for clinicians to be vigilant about any pathologic lesions existing on the upper extremity to avoid late diagnosis and the development of advanced cancerous diseases.



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## Introduction

Synovial sarcoma is a rare type of soft tissue sarcoma that accounts for 5%-10% of all sarcoma cases. It predominantly affects young adults between the ages of 10 and 40 years old [1,2], with males being more commonly affected than females at a ratio of 1.2:1 [3]. Synovial sarcoma has a better prognosis in children compared to adults [4]. These tumors usually arise in close proximity to joints such as the ankle, knee, and wrist, with 62% located in the lower extremities and 21% in the upper extremities. They rarely involve the viscera of the abdomen and chest primarily [5].

Synovial sarcoma is closely associated with regional recurrence and remote metastasis, with the lungs being the most frequent site of metastasis, occurring in 74%-81% of cases. Lymph nodes and skeletons, especially long bones, are also common sites of metastasis [5,6]. Metastasis can occur simultaneously with the primary tumor (synchronous metastasis) or with a time gap from the original cancerous lesion (metachronous metastasis) [7]. While hormonal abnormalities are not typically associated with synovial sarcoma, there have been reports of tumor-producing hormones or hormone-like substances in certain cases [8,9].

This case report presents a rare instance of synovial sarcoma with elevated $\beta$-human chorionic gonadotropin ($\beta$HCG). It provides a detailed examination of the clinical and pathological features of synovial sarcoma, emphasizing the significance of hormonal abnormalities as a potential complication. By presenting this case, we aim to enhance the current understanding of the disease and raise awareness among healthcare professionals about its possible association with hormonal irregularities.

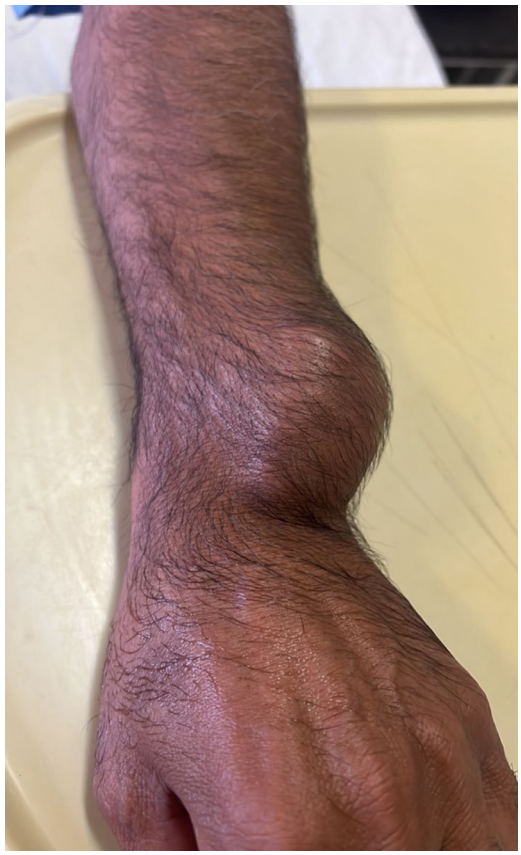

**Fig. 1 – The photograph shows an ulnar-sided lesion on the patient's left wrist. It appears well-defined with a smooth surface and has been growing gradually over the past few months.**

## Case presentation

A 42-year-old Iranian man presented to the Pulmonary Center of our hospital with a chief complaint of dyspnea, dry cough, and chest pain, which had been ongoing for 1 year. Over the past 4 months, his condition had progressively worsened, and he had developed additional symptoms, including hemoptysis, fever, unexplained weight loss, and loss of appetite. Furthermore, he stated that the chest pain worsened when taking deep breaths or coughing. The patient's past medical and family history was unremarkable.

During the physical examination, the patient was found to have gynecomastia and a mass-like lesion on the dorsal ulnar side of his left wrist. The lesion was painless and nonmobile (Fig. 1). He mentioned that it had been present for 4 years, and since it did not cause any pain or issues, he had not sought medical attention for it. However, it has dramatically grown over the past several months. A subsequent chest X-ray revealed bilateral multifocal lung nodules throughout the lungs, and computed tomography (CT) imaging confirmed multiple bilateral nodules of varying sizes within the pulmonary parenchyma, suggesting disseminated lung metastasis (Fig. 2). Subsequent blood tests were conducted to evaluate tumor markers, given the suspicion of malignancy. The results showed elevated levels of beta-human chorionic gonadotropin ($\beta$-hCG) at 102 mIU/mL. Other laboratory findings are presented in Table 1.

The core needle biopsy of the wrist mass revealed a hypercellular neoplasm composed of sheets and fascicles of spindle and ovoid cells with hyperchromatic nuclei, inconspicuous nucleoli, and sparse cytoplasm, intermixed with staghorn branching vessels (hemangiopericytic vessels). These neoplastic cells exhibited positive immunoreactivity for Transducin-like enhancers of Split-1 (TLE1), CD99, and epithelial membrane antigen (EMA), while h-caldesmon, smooth muscle actin (SMA), S100, SOX10, and signal transducer and activator of transcription 6 (STAT6) were negative (Fig. 3). Further analysis via Fluorescence in Situ Hybridization (FISH) identified a rearrangement on chromosome 18q11.2, confirming a diagnosis of $\beta$-hCG-secreting synovial sarcoma for the patient's wrist mass, as shown in Figure 4.

Given the presence of metastases at the time of diagnosis, surgical intervention was not an option. Therefore, the patient was referred to an oncologist for further management. The patient is currently undergoing a chemotherapy regimen consisting of 6 cycles of Adriamycin, Ifosfamide, and Mesna.

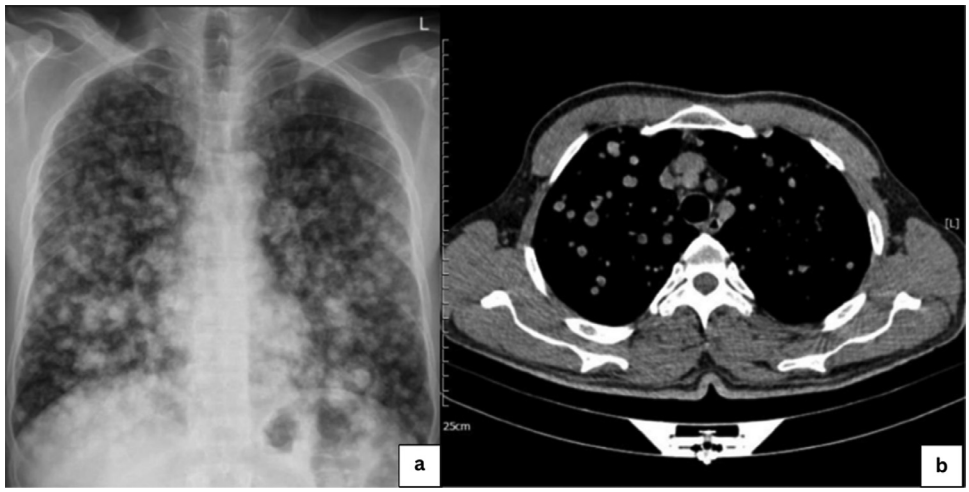


**Fig. 2 – (A) Chest X-ray revealing bilateral multifocal lung nodules distributed throughout the lungs. (B) A chest CT scan showed multiple bilateral nodules of varying sizes in the pulmonary parenchyma, which was suggestive of disseminated lung metastasis.**

**Table 1 – The laboratory test findings of the patient.**

| | Results | Units | Range |
|---|---|---|---|
| Bun | 50 | mg/dL | 7–18.6 |
| Cr | 1.1 | mg/dL | 0.5–1.4 |
| AST | 59 | IU/ L | Up to 40 |
| ALT | 128 | IU/ L | Up to 40 |
| ALP | 349 | IU/ L | 64–306 |
| ESR | 42 | mm/h | Up to 20 |
| CRP | 36 | mg/L | Up to 6 |
| Hb | 15.2 | g/dL | 12–15 |
| Platelets | 322000 | $10^3$ /μL | 150–450 |
| Neutrophils | 71 | % | - |
| Lymphocytes | 21 | % | - |
| Mixed | 8 | % | - |
| LDH | 758 | Units | 140-280 |
| Ca | 9.8 | mg/dL | 8.5-10.2 |
| AFP | 3.7 | mg/mL | Up to 10 |
| CA-15-3 | 45.8 | U/mL | Up to 30 |
| CA-19-9 | <2 | U/mL | Up to 37 |
| ACE | 47 | U/L | 8-52 |
| PSA | 0.4 | ng/ mL | Up to 4 |
| BhCG | 102 | mIU/mL | <5 nonpregnant females<br><2 males |

ACE, Angiotensin-Converting Enzyme; AFP, Alpha-Fetoprotein; ALP, Alkaline Phosphatase; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; BhCG, Beta Human Chorionic Gonadotropin; BUN, Blood Urea Nitrogen; Ca, Calcium; CA-15-3, Cancer Antigen 15-3; CA-19-9, Cancer Antigen 19-9; Cr, Creatinine; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; Hb, Hemoglobin; LDH, Lactate Dehydrogenase; PSA, Prostate-Specific Antigen.

## Discussion

Soft tissue sarcomas are a heterogeneous group of mesenchymal neoplasms that can arise from different types of soft tissues, such as fat, muscle, and connective tissues [10]. While the exact cause of soft tissue sarcomas is largely unknown, genetic predisposition is reported in over 90% of cases [11]. Synovial sarcoma is a rare type of soft tissue sarcoma that primarily affects the extremities. Involvement of the upper extremities is uncommon, with a reported incidence of 4%-8.5% among all synovial sarcoma cases [12]. Furthermore, this tumor predominantly occurs in young adults and is known for its aggressive behavior, frequently leading to high rates of metastasis [1,10].

Synovial sarcoma is classified histologically into 3 types: monophasic, biphasic, and poorly differentiated. The monophasic type comprises spindle cells, while the

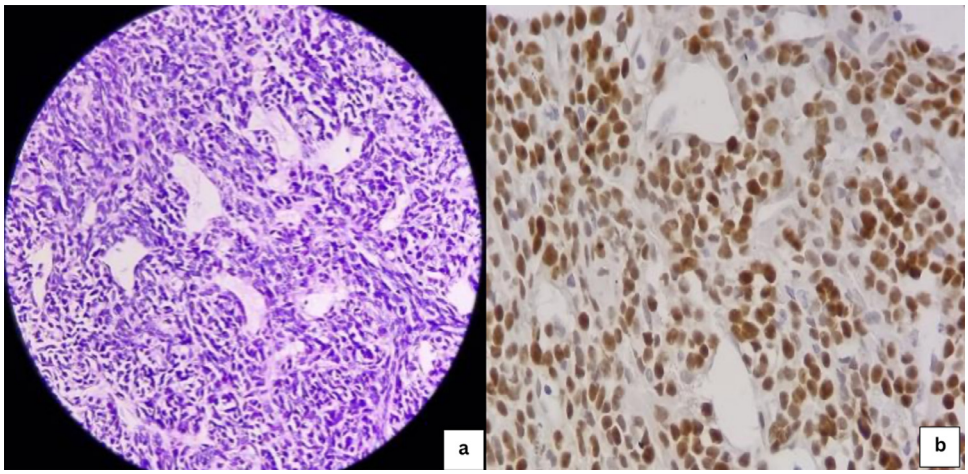


**Fig. 3 – Histological and immunohistochemical analysis of wrist mass. (A) Hematoxylin and eosin (H&E) staining reveals a hypercellular neoplasm consisting of sheets and fascicles of spindle and ovoid cells with hyperchromatic nuclei. (B) Positive immunohistochemical staining for TLE1 further confirms the diagnosis of synovial sarcoma.**

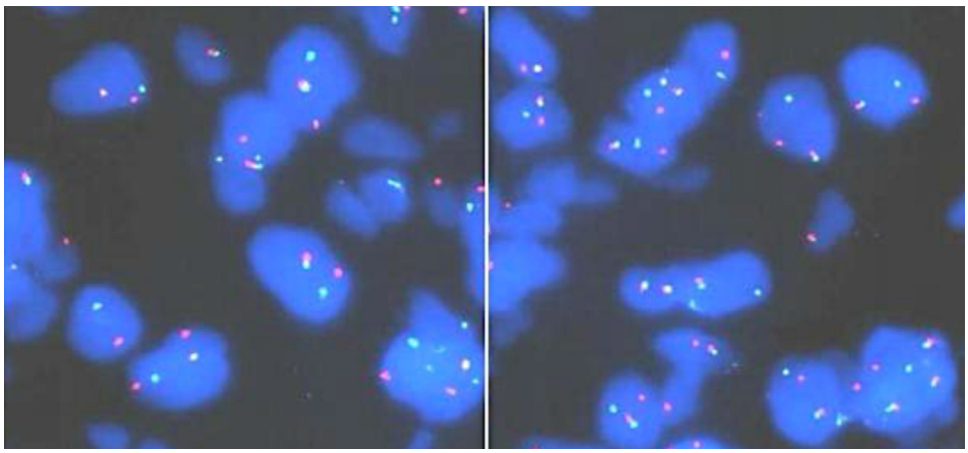

**Fig. 4 – Interphase FISH analysis for the SS18 (SYT) gene break-apart rearrangement. The slide was hybridized with Leica SS18 (18q11) dual-color break-apart probes (cat no: 10713), with the green probe targeting 18q11.2 proximal to the SS18 breakpoint and the red probe targeting 18q11.2 distal to the breakpoint. A total of 67 cells were independently scored by 2 individuals, revealing evidence of SS18 gene rearrangement via translocation in the proximal region. In 55 cells (82%), 1 or 2 fused yellow signals, along with 1 or 2 separate red and green signals, were observed. In 12 cells (17.9%), 2 fused yellow signals were present, confirming a positive result for the SS18 (18q11) rearrangement.**

biphasic type consists of epithelial-like cells, spindle cells, and glandular formation areas. The poorly differentiated type is characterized by polymorphism, hypercellularity, high mitotic rate, hyperchromatic nuclei, and small round cell proliferation [11]. Immunohistochemistry (IHC) is an important tool for diagnosing synovial sarcoma, with nuclear staining of the TLE1 being a key marker for neuronal and epithelial differentiation [13]. In addition, epithelial markers such as EMA, Cytokeratin 7, Cytokeratin 19, and mesenchymal marker Vimentin are co-expressed in synovial sarcoma, with EMA being more sensitive than cytokeratin [14]. Most synovial sarcoma cases show positivity for BCL2, CD99, and S100 [15]. Previous studies have revealed that sarcomas rarely secrete $\beta$HCG, which can be confirmed by IHC staining of resected sarcomatous masses. In female patients, it is important to consider the possibility of pregnancy when evaluating serum $\beta$HCG levels [8,9,16]. A previous systematic review suggested that the ability of sarcomas to secrete $\beta$HCG may be associated with poor prognosis, poorly differentiated tumors, and higher tumor grades [17].

Recent studies have suggested that hormonal abnormalities may also contribute to the development and progression of synovial sarcoma. For example, a study by Nakayama et al. [18] found that expression of the progesterone receptor (PR) was significantly higher in synovial sarcomas than in other types of soft tissue sarcomas. Furthermore, they demon-

strated that treatment with a PR antagonist reduced cell proliferation and induced apoptosis in synovial sarcoma cells in vitro. Another study by Naka et al. [19] reported that insulin-like growth factor 2 (IGF-2) was highly expressed in synovial sarcomas and that this expression was associated with poorer prognosis. They also observed that treatment with an IGF-1 receptor inhibitor inhibited the growth of synovial sarcoma cells in vitro and in vivo.

Moreover, the measurement of $\beta$-hCG beta hCG levels can provide valuable information for the diagnosis, treatment, and management of synovial sarcoma, although it should always be interpreted in conjunction with other clinical and pathological findings. Further research is needed to elucidate the precise mechanisms underlying these abnormalities and to develop targeted therapies for synovial sarcoma based on these findings.

## Conclusion

Synovial sarcoma is a rare and aggressive soft tissue malignancy with a diverse range of clinical manifestations. The presence of elevated $\beta$-hCG levels and gynecomastia are atypical features of synovial sarcoma and should be included in the differential diagnosis when these symptoms are observed. Early identification and treatment are essential to improve patient outcomes and quality of life. Further research is needed to better understand the underlying mechanisms of these unusual clinical presentations and to develop more effective therapeutic options for this challenging malignancy.

## Data availability

The data that support the findings of this study are available from the corresponding author upon request.

## Consent for publication

The authors have obtained written informed consent from the patient to publish his case (including the publication of images).

## Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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