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Delayed Intramuscular Metastasis From Clear Cell Renal Cell Carcinoma in the Biceps Brachii Mimicking a Soft-Tissue Sarcoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Yordan Stefanov Ivanov
CDE 2 Zdravka Dimitrova Petrova
BCDE 3 Rossen Alexandrov Spasov
F 1 Stefan Stefanov Tserovski
DF 1 Alexander Ivanov Gerchev

1 Department of Orthopedics and Traumatology, Medical Faculty, Medical University Sofia, Sofia, Bulgaria
2 Department of Pathology, Institute of Experimental Morphology, Pathology and Anthropology with Museum, Bulgarian Academy of Sciences, Sofia, Bulgaria
3 Department of Pathology, Lozenetz University Hospital, Sofia, Bulgaria

Corresponding Author: Yordan Stefanov Ivanov, "Academician Ivan Evstratiev Geshov" Boulevard, Sofia 1431, Bulgaria
Phone: +359888088219, e-mail: y.ivanov@medfac.mu-sofia.bg

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Patient: Female, 75-year-old
Final Diagnosis: Metastasis of renal clear cell carcinoma
Symptoms: Painful mass
Clinical Procedure: —
Specialty: Oncology • Orthopedics and Traumatology

Objective: Unusual clinical course

Background: Clear cell renal cell carcinoma metastases in extremity musculature are very rare and often present a diagnostic challenge because of their resemblance to soft-tissue sarcoma. We present a rare case of delayed biceps brachii metastasis from clear cell renal cell carcinoma, which occurred 15 years after the initial diagnosis.

Case Report: A 75-year-old Eastern European woman presented with a painful mass in her left arm. She had been diagnosed with and treated for clear cell renal cell carcinoma 15 years earlier. Physical examination demonstrated an oval-shaped soft-tissue mass in the proximal left arm. Ultrasound revealed a hypoechoic, well-vascularized soft-tissue tumor located in the biceps brachii muscle. Magnetic resonance imaging of the affected extremity showed a heterogeneous intramuscular tumor. Following multidisciplinary discussion, the patient underwent single-stage surgical treatment. The decision to proceed without a preoperative biopsy was specific to this case. Histological examination revealed metastasis from clear cell renal cell carcinoma. The patient had an uneventful postoperative course without functional deficit. After multidisciplinary restaging and evaluation, adjuvant immunotherapy was initiated. At the last follow-up, the patient had no complaints, signs of local recurrence, or functional deficits.

Conclusions: Skeletal muscle metastases from clear cell renal cell carcinoma have clinical and imaging characteristics that closely mimic those of soft-tissue sarcoma. Regardless of the disease-free interval, metastatic disease should be considered in the differential diagnosis when evaluating any new soft-tissue mass in affected patients. Our treatment strategy was individually selected for the present patient. Given the single-case nature of this report, our findings should not be considered a general management recommendation.

Keywords: Carcinoma, Renal Cell • Soft Tissue Neoplasms • Upper Extremity • Neoplasm Metastasis

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Introduction

Renal cell carcinoma is among the most common cancers worldwide, representing about 3% of all malignant tumors [1]. Clear cell renal cell carcinoma (ccRCC) is the most prevalent histological subtype, comprising approximately 70% to 80% of renal cell carcinoma cases [2,3]. The disease may remain clinically unrecognized during its early stages because initial symptoms are nonspecific or absent. Nevertheless, around 70% of patients have localized disease at diagnosis, whereas 10% present with distant metastases [3]. Typical sites of disease dissemination include the lungs, bones, liver, and brain [4]. Management of ccRCC depends on the disease stage. Common treatment strategies include targeted therapy, immunotherapy, cytoreductive nephrectomy, and, in some cases, radiotherapy [2,3]. For patients with localized disease, the 5-year survival rate is 70%; it decreases to 13% for those with distant metastases [1-3,5].

Skeletal muscle metastases from ccRCC are rare, occurring in only 1% to 2% of cases [4]. Involvement of the biceps brachii muscle is even rarer, and only a small number of cases have been reported in the literature [6,7]. This report presents the clinical, imaging, and histopathological characteristics of an unusual and rare metastatic pattern in an older adult with ccRCC. Recognition of this unusual presentation may help clinicians consider delayed metastatic ccRCC when evaluating a new intramuscular mass in patients with a history of ccRCC.

Case Report

A 75-year-old Eastern European woman presented to our department with complaints of a painful mass in her left arm. She had an Eastern Cooperative Oncology Group performance status of 0 and was a nonsmoker. Her body mass index was not recorded at the time of presentation and therefore was not reported. The patient had a history of ccRCC diagnosed 15 years earlier. Her disease had been classified as stage II (T2N0M0) according to the Tumor-Node-Metastasis classification, and she had undergone surgical treatment consisting of a left nephrectomy with a reported R0 resection. The histological grade of the original ccRCC could not be retrieved from the patient's medical records and thus was unavailable for reporting. Regular follow-up was performed for 10 years, without signs of disease dissemination or progression. The patient also had a history of type 2 diabetes and arterial hypertension. There was no notable family history or history of other clinically significant interventions. No additional health hazards were noted.

Physical examination revealed an oval-shaped soft-tissue mass located in the proximal region of the left arm. The lesion was firm, mobile, and painful on palpation. The overlying skin showed no notable alteration. There were no changes in the neurovascular status of the affected extremity. No limitations in the range of motion of the left shoulder or elbow joints were observed.

Radiography of the affected area did not detect any notable changes. Ultrasound revealed a hypoechoic, well-vascularized soft-tissue tumor located in the biceps brachii muscle. Magnetic resonance imaging of the affected extremity showed an elliptical, heterogeneous intramuscular tumor in the biceps brachii muscle. On T2-weighted sequences, the lesion had an isointense peripheral signal with a hyperintense center. On T1-weighted sequences, the tumor was predominantly isointense (**Figure 1**). The tumor dimensions were 9 × 5 × 4 cm, with a volume of 94 cm^3. Contrast administration revealed well-vascularized areas within the lesion and some neovascularization in the surrounding region. Pretreatment positron emission tomography/computed tomography (PET/CT) was also scheduled, but the patient declined the examination. Laboratory tests did not reveal any clinically significant abnormalities.

Findings from the physical examination and imaging studies were discussed by our institutional multidisciplinary oncology team. Considering the patient's medical history of ccRCC, soft-tissue metastasis was regarded as the most likely diagnosis. The differential diagnosis also included liposarcoma, myxoid liposarcoma, and undifferentiated pleomorphic sarcoma. A preoperative biopsy was not performed. This decision was based on patient-specific factors, such as the apparent resectability of the tumor with wide surgical margins and its marked vascularity, which raised concerns about serious hemorrhage and additional compartment contamination. An individualized approach was therefore adopted, and definitive surgical excision was performed.

Surgical treatment was conducted under interscalene brachial plexus block anesthesia. A direct anterior approach over the tumor was used. The biceps brachii muscle was released by resecting the tendons of both the short and long heads proximally. Distally, resection was performed at the musculotendinous junction. Great care was taken to preserve the musculocutaneous nerve. This nerve passes through the coracobrachialis muscle and beneath the biceps brachii muscle; it innervates a large portion of the brachialis muscle. Preservation of this nerve was important to maintain elbow flexion and limb function. Frozen-section analysis of the specimen was not conducted during surgery. No serious hemorrhage occurred, and estimated blood loss was 200 mL. The total operative time was 115 minutes. Samples for histological examination and resection margin assessment were obtained from the tumor specimen.

Gross examination of the tumor revealed an intramuscular soft-tissue mass measuring 9 × 5 × 4 cm, yellowish in color

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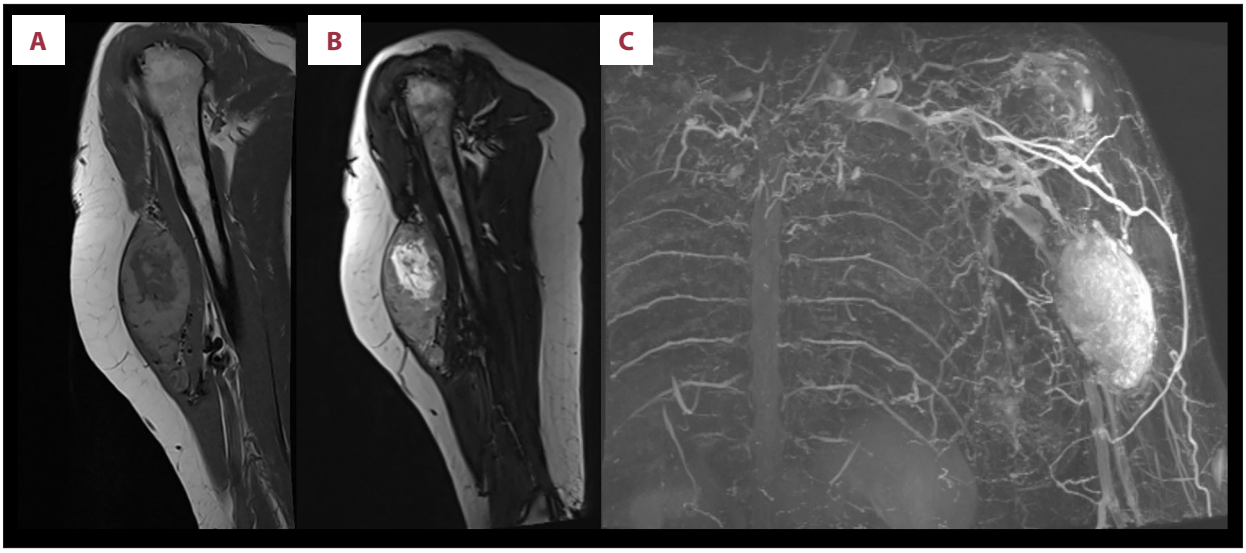


Figure 1. Magnetic resonance imaging of the biceps brachii mass. (**A**) Sagittal T1-weighted image demonstrating an intramuscular soft-tissue mass within the biceps brachii. (**B**) Sagittal T2-weighted image revealing a heterogeneous appearance of the lesion. (**C**) Contrast-enhanced vascular sequence demonstrating prominent vascularity of the tumor and surrounding tissue.



Figure 2. Gross examination of the excised specimen. An intramuscular soft-tissue mass measuring 9 × 5 × 4 cm, yellowish in color and of moderate density.

and of moderate density (**Figure 2**). Microscopic examination showed that the tumor had a nested structure with thin fibrous septa and consisted of cells with homogeneous, pale cytoplasm. The cells had round, centrally located hyperchromatic nuclei with prominent nucleoli. The tumor cells formed glandular structures with microhemorrhages in their lumina. No areas of necrosis were observed. The mass was covered by a pseudocapsule and demonstrated an acinar growth pattern that extended between muscle fibers. Immunohistochemical analysis was performed using the following markers: cytokeratin AE1/AE3, cytokeratin 20, vimentin, CD10, renal cell carcinoma marker, and CD34 (**Figure 3**). Strong positive expression of renal cell carcinoma and CD10 in the tumor cells, as well as CD34 in the vessel walls, was observed, highlighting the extensive vascularization of the metastatic lesion. The morphological characteristics and immunohistochemical phenotype confirmed that the metastatic lesion originated from ccRCC. The final pathology report confirmed negative resection margins.

The patient had an unremarkable postoperative course. No neurological or vascular deficits were noted. Active elbow flexion was preserved. Physical therapy was initiated the day after surgery. The patient was discharged from the hospital on postoperative day 5.

After the histological diagnosis of skeletal muscle metastasis from ccRCC had been established, the case was reviewed by the institutional oncology team. The patient agreed to postoperative PET/CT, which revealed no additional lesions in the lungs, bones, lymph nodes, or other soft tissues. According to the International Metastatic Renal Cell Carcinoma Database Consortium criteria, the patient was classified as intermediate risk (2 points), based on two adverse prognostic factors: hemoglobin level below the lower limit of normal and absolute neutrophil count above the upper limit of normal. [8]. After multidisciplinary evaluation, the treating oncologist recommended initiation of combination immunotherapy. This treatment strategy was strictly individualized and considered factors such as advanced age, limited compliance, and the patient's personal preferences. The selected treatment protocol consisted of standard-dose nivolumab and ipilimumab for 4

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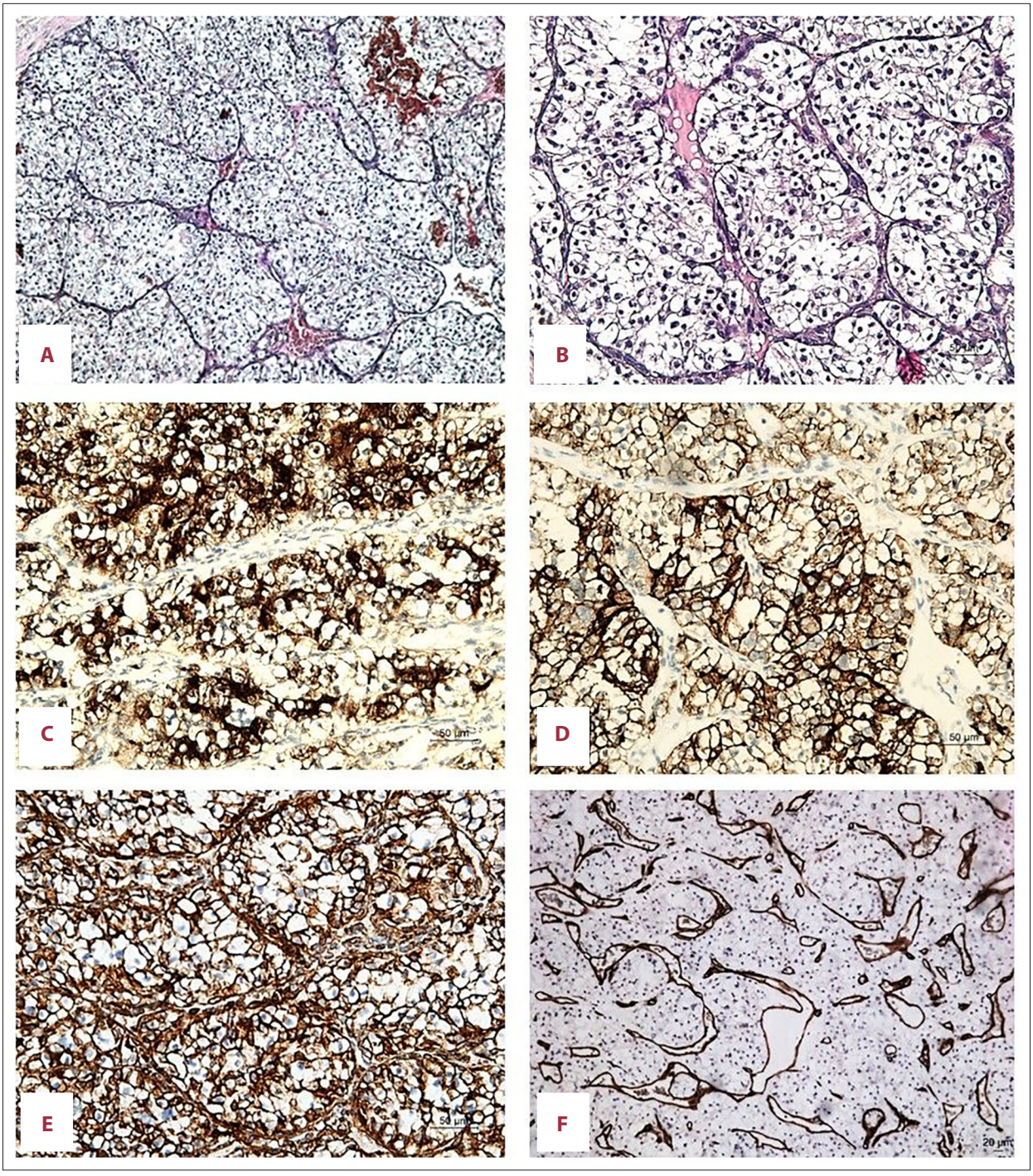


Figure 3. Histopathological examination showing a metastatic lesion with morphological and immunophenotypic characteristics of clear cell renal cell carcinoma. Hematoxylin and eosin staining (**A**, original magnification × 100; **B**, × 200). Immunohistochemical staining for renal cell carcinoma marker (**C**, × 200), CD10 (**D**, × 200), vimentin (**E**, × 200), and CD34 (**F**, × 100). Scale bars = 50 µm.

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Table 1. Clinical timeline.

Day	Event
1-5	Initial visit: physical examination, imaging studies (radiography, ultrasound, and contrast-enhanced magnetic resonance imaging), and laboratory tests
6-11	Hospital admission, surgical treatment, postoperative rehabilitation, and hospital discharge
12-16	Histological evaluation and definitive histological diagnosis
17-28	Oncology consultation, positron emission tomography/computed tomography, and immunotherapy initiation
30	First postoperative follow-up

cycles, administered every 3 weeks; this combination is not an established adjuvant regimen after complete metastasectomy. Follow-up nearly 1 month after surgery included physical examination, ultrasound, and magnetic resonance imaging. The patient was satisfied with the treatment outcome and had no current complaints or functional limitations. The next follow-up was scheduled for 6 months after surgery; regular annual follow-up would continue thereafter. Regular PET/CT follow-up for the primary disease was also scheduled by the treating oncologist. A brief timeline of the case is presented in **Table 1**.

Discussion

The main contribution of our case lies in several relevant clinical observations. First, it highlights the potential for very late metastasis in patients with ccRCC after nephrectomy and the importance of extended follow-up. Second, muscle metastases from ccRCC often exhibit clinical and imaging features that mimic those of soft-tissue sarcoma. A high index of suspicion should be maintained in these cases, along with histological verification. Finally, our case demonstrates that excision of both the tumor and biceps brachii muscle may achieve complete excision with negative margins and preserve good limb function in selected cases. This treatment strategy—applicable only to the present case—is part of our individualized approach.

Skeletal muscle metastases from ccRCC present a unique diagnostic challenge, mainly because of their clinical similarity to soft-tissue sarcoma. Previous reports in the literature include isolated biceps brachii involvement as well as synchronous upper-extremity metastases, highlighting the variable presentation of this unusual pathology [1,4]. Distinguishing features of our case include the patient's advanced age, solitary biceps brachii involvement, and prolonged interval after treatment of the primary renal tumor. Biological mechanisms underlying the rarity of skeletal muscle metastases from ccRCC remain unclear. Several hypotheses have been proposed, including the inhibitory effects of lactic acid on angiogenesis, the presence of protease inhibitors within the extracellular matrix, and local immune activity [1]. These factors may create an unfavorable local microenvironment that interferes with metastatic implantation and growth. The occurrence of a solitary biceps brachii metastasis in our patient demonstrates that these protective mechanisms are not absolute, and the contribution of each factor remains hypothetical.

The use of multiple imaging modalities and histological evaluation is usually required for a definitive diagnosis. Conventional radiography often does not reveal any abnormalities but may be useful for assessing additional bone involvement. Ultrasound should be used when evaluating a new soft-tissue mass because it may help differentiate benign from potentially malignant tumors. In our case, ultrasound revealed an intramuscular, hypoechoic mass with pronounced vascularity, which was highly suspicious for sarcoma. Similar imaging findings have been described in several recent case reports of skeletal muscle metastases from ccRCC [9-11]. We consider the lack of a preoperative PET/CT examination a limitation of this case—it hindered our decision-making and individualized treatment planning. Thus, contrast-enhanced magnetic resonance imaging was used to supplement the imaging data needed to develop an adequate treatment strategy. The patient agreed to undergo PET/CT only after histological diagnosis, highlighting potential challenges in the follow-up process.

In the present case, the intramuscular location allowed complete excision of the tumor with negative margins and preservation of limb function. A similar approach was described by John et al in a case of ccRCC metastasis to the triceps brachii muscle [12]. The decision to proceed directly to surgical excision was made after multidisciplinary discussion. Current guidelines generally recommend image-guided core-needle biopsy prior to definitive treatment of a suspicious soft-tissue mass [4]. We proceeded with direct surgical treatment because the lesion was highly vascular, posing a potential risk of serious hemorrhage and additional compartment contamination. Accordingly, this was an individualized, case-specific management decision and should not be interpreted as a general recommendation. We acknowledge the absence of a preoperative histological diagnosis as a limitation of this case. Had the lesion been identified preoperatively as a primary soft-tissue sarcoma, histological verification and multidisciplinary treatment planning would have been required before definitive treatment. Marra et al reported a case in which both surgical excision and subsequent biopsy were unsuccessful because of severe hemorrhage from a soft-tissue metastasis of

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ccRCC [13]. Data from the literature suggest that surgical excision of solitary metastases from ccRCC may be associated with improved 5-year survival; reported rates range from 35% to 50% [14]. The role of additional treatment, including immunotherapy, targeted therapy, or radiotherapy, depends on individual patient characteristics and clinical details [1,4,9,15]. Optimal management of solitary metastatic ccRCC remains uncertain, and limited evidence is available to guide patient selection. An individualized, multidisciplinary approach may help identify suitable candidates for local treatment by considering disease extent, resectability, patient characteristics, and potential treatment-related risks [16]. The adjuvant treatment strategy in our case was selected after available treatment options had been discussed with the patient and was specifically tailored to her clinical circumstances.

This report provides detailed clinical, imaging, and histopathological characteristics of skeletal muscle metastasis from ccRCC, potentially aiding the recognition of this unusual metastatic pattern. Although we achieved success with single-stage surgical treatment, our experience is based on a single case and should not be considered universally applicable. Surgical excision may be a treatment option for selected patients with a history of ccRCC; an isolated, resectable skeletal muscle metastasis; and adequate postoperative functional status. However, decisions regarding treatment strategy should be made only after multidisciplinary restaging. This treatment strategy should not be generalized to patients with multiple metastases or unresectable lesions. The single-case nature of this report represents its main limitation, along with the short-term follow-up period and lack of preoperative PET/CT.

Conclusions

Skeletal muscle metastases from ccRCC have clinical and imaging characteristics that closely mimic those of soft-tissue sarcoma. Regardless of the disease-free interval, metastatic disease should be considered in the differential diagnosis when investigating any new soft-tissue mass in affected patients. Our treatment strategy was individually selected for the patient described in this report. Given the single-case nature of this report, our findings should not be considered a general management recommendation.

Department and Institution Where Work Was Done

Department of Orthopedics and Traumatology, Medical University of Sofia, University Specialized Orthopedic Hospital Boycho Boychev, Bulgaria.

Patient Consent

The patient provided written informed consent for publication of this report.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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