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An Asymptomatic Bone Tumor Case Presenting with Elevated Acute Phase Reactant and Weight Loss Complaints

Akut Faz Reaktanı Yüksekliği ve Kilo Kaybı Şikayetleriyle Başvuran Asemptomatik Bir Kemik Tümörü Vakası

Büşra Öztoprak ŞAHİN[1]

Zekeriya KESKİN[1]

[1] Sivas Cumhuriyet University, Faculty of Medicine, Department of Internal Medicine, Sivas, Türkiye

Corresponding author:
Büşra Öztoprak Şahin, Sivas Cumhuriyet University, Faculty of Medicine, Department of Internal Medicine, Sivas, Türkiye

E-mail:
busraoztoprak@cumhuriyet.edu.tr

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ÖZET

Atipik kartilajenöz tümör (ACT) yavaş büyüyen bir tümördür. Hastalar çoğunlukla ağrı şikayetiyle başvururlar, ancak bazen lezyonlar tesadüfen tespit edilebilir. Yüksek akut faz reaktanı (AFR) kronik inflamasyonla seyreden birçok hastalığın seyrinde görülen bir laboratuvar bulgusudur. Olgumuzda AFR yüksekliği ve kilo kaybı ile başvuran hastanın tanı aşaması anlatılmaktadır. Hasta enfeksiyon, romatizmal hastalıklar ve maligniteler açısından detaylı olarak araştırıldı. Pozitron emisyon tomografisi (PET-CT) ve manyetik rezonans görüntüleme (MRG) sonrasında herhangi bir şikayeti olmayan hastaya humerus bölgesinden alınan biyopsi sonucu ACT tanısı konuldu. Bu olgu sunumunda AFR yüksekliğinin ne kadar detaylı ve titizlikle incelenmesi gerektiği, AFR yüksekliğinin altında beklenmeyen patolojilerin ortaya çıkabileceği vurgulanmakta ve tanı aşamaları detaylı olarak anlatılmaktadır..

Anahtar kelimeler: Atipik kartilajenöz tümör, Akut faz reaktanı, Kilo kaybı, Kemik tümörleri.

ABSTRACT

Atypical cartilaginous tumor (ACT) is a slow-growing tumor. Patients mostly present with complaints of pain, but lesions can sometimes be detected incidentally. High acute phase reactant (APRs) is a laboratory finding seen in the course of many diseases with chronic inflammation. In our case, the diagnosis process of a patient who presented with high APRs and weight loss is described. The patient was investigated in detail for infection, rheumatic diseases, and malignancies. After positron emission tomography (PET-CT) and magnetic resonance imaging (MRI), ACT was diagnosed with a biopsy from the humerus region, which had no complaints. This case report emphasizes the importance of thoroughly investigating elevated APRs, as they may conceal unexpected pathologies. The diagnostic steps leading to the final diagnosis are explained in detail.

Keywords: Atypical cartilaginous tumor, Acute phase reactant, Weight loss, Bone tumors.

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INTRODUCTION

ACT is a slow-growing tumor with low-grade malignant potential. Although it shares histopathological features with grade 1 chondrosarcoma (CS1), ACT is associated with a more favorable prognosis, particularly when located in the long bones. In such cases, the lesion is referred to as an "atypical cartilaginous tumor".[1] ACT is frequently seen in adults and is most commonly located in the medullary regions of long bones such as the femur, humerus and tibia.[2] Patients mostly present with complaints of pain, but lesions can sometimes be detected incidentally.[3]

APRs are biomarkers that increase or decrease in serum due to any inflammation. Cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), and interferon-gamma (IFN-gamma) initiate the production of APR. The most commonly used in clinical practice is c-reactive protein (CRP). In addition, the erythrocyte sedimentation rate (ESR), an indirect indicator of systemic inflammation, is also frequently used. Symptoms and findings reflected in the patient's clinic are fever, chronic disease anemia, anorexia, somnolence, weakness, and cachexia.[4]

In this case report, a patient diagnosed with ACT located in the proximal humerus, who presented with weight loss and fever, anemia and high APR, without any complaints about the musculoskeletal system, will be discussed.

CASE

A 52-year-old female patient was referred to our outpatient clinic from another clinic with anemia, elevated CRP and ESR. The patient's history included long-standing back pain, loss of appetite, and 15 kg weight loss in 3 months. The back pain was not accompanied by morning stiffness and was aggravated by movement. He came to us with spondyloarthropathies previously excluded by sacroiliac MRI. Weight loss was not accompanied by fever or night sweats. She had previously been diagnosed with diabetes mellitus (DM), hypertension and asthma, and was using insulin glargine 1x20 units, metformin 2x1000 mg, empagliflozin 1x10 mg, montelukast 1x10 mg, acetylsalicylic acid 1x100 mg, bisoprolol 1x5 mg. The examination results at application are given in Table 1.

Table 1. Examination results at application.

Parameter	Results
ESR	**48 mm/h**
CRP	**109 mg/L**
MCV	**64 fl**
RBC	5,01 10^{12}/L
Ferritin	36 µg/L
Iron	**18 µg/L**
Iron binding	371 **µg/L**
Transferrin saturation	**% 5**
Vitamin B12	**1528 ng/L**
Folic acid	4,7 µg/L
TSH	1,28 mIU/L
Free t4	1,37 ng/dl
HbA1c	**8,62 mmol/mol**
Anti HIV	Negative
Anti HCV	Negative
Anti HBs	Negative
HBsAg	Negative
CA-15-3	14,5 U/ml
CA-19-9	9,31 U/ml
CA-125	7,46 U/ml
CEA	1,44 µg/L
Creatinine	0,50 mg/dl

Afterwards, further examinations were performed to investigate the etiology of APR elevation and anemia. No pathology was detected in the gynecological examination, upper endoscopy and colonoscopy performed on the patient due to iron deficiency anemia (IDA). No pathology was detected in the labeled

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leukocyte scintigraphy performed with the preliminary diagnosis of spondylodiscitis due to low back pain. The patient underwent mammography and thorax-abdominal computed tomography (CT) imaging to exclude possible malignant conditions. No malignancy was detected in mammography. There were no abnormal findings in CT except for stomach wall thickness.

No pathogens were grown in urine, blood and sputum cultures taken for possible infective pathologies. Tests for brucella, tuberculosis and syphilis were negative. Additionally, autoantibody tests for connective tissue diseases were negative. Detailed results of the examinations are given in Table 2.

Table 2. Results of etiological tests for AFR elevation

Parameter	Results
ANA	Negative
C3	161 mg/dL
C4	38 mg/dL
Anti-CCP	Negative
PCT	0,04 ng/mL
Anti ds DNA	Negative
Brucella Rose Bengal	Negative
Brucella Wright Agglutination	1/20
T.pallidum VDRL	1/20
Sputum ARB	Negative

After these examinations, the patient underwent PET-CT in which no underlying pathology could be detected. PET-CT showed 18F-FDG uptake with a slightly increased SUVmax of 1.9 in the intramedullary area starting from the proximal 1/3 of the left humerus. Thereupon, a lesion was observed in the humerus MRI that caused intramedullary cortical scalloping at the level of the humerus shaft, was hyperintense in T2A series, hypointense in T1A series, did not show soft tissue extension, was approximately 10 cm long, and showed ring and arc-shaped contrast enhancement in the postcontrast series, and ACT was considered in the foreground. The relevant MRI and PET-CT images are shown in figure 1 and 2. Based on these findings, the patient underwent a bone biopsy and the result came back as an atypical cartilaginous tumor. Afterwards, the patient was operated by orthopedics and referred to radiation oncology and medical oncology for necessary oncological treatments. In the postoperative follow-up, the patient's APRs returned to normal (ESR 14 mm / h, CRP 2.61 mg / L) and she gained 12 kg.

Figure 1. ACT's appearance on MRI (associated lesions are indicated by white arrows.)

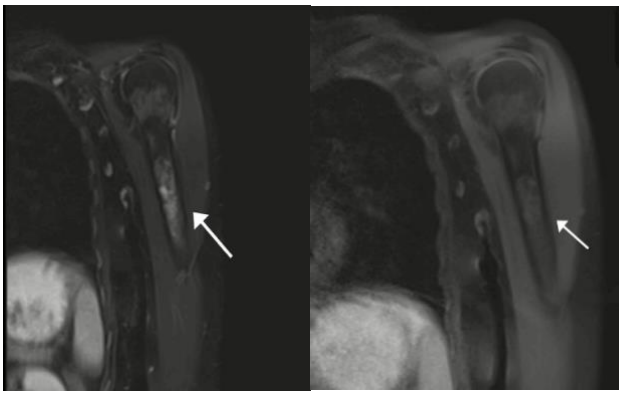
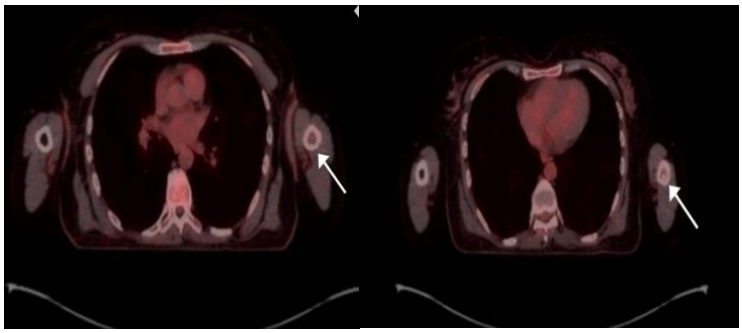


Figure 2. ACT's appearance on PET-CT (associated lesions are indicated by white arrows.)



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DISCUSSION

We present an asymptomatic case of ACT without arm pain. The diagnostic process, which started with high APR and weight loss, was unexpectedly completed with the detection of a tumor in the left humerus, in which he had no complaints. ACT and CS1 have the same histological features. Lesions diagnosed as ACT in long and short bones are typically classified as CS1 when located in the axial skeleton. ACT are more common intermediate tumors, while CS1 are malignant. The incidence of ACTs has increased over time due to both the aging population and incidental findings resulting from increased diagnostic imaging. Early diagnosis is crucial for effective treatment and better outcomes in ACT.[5] However, our main purpose in discussing our case is to emphasize the necessity of careful and comprehensive investigation of high AFR.

APRs may increase or decrease as an indicator of inflammation for many reasons such as infections, rheumatic diseases, trauma and malignancy. However, they are not specific to a disease on their own. Acute phase reactants such as ESR and CRP, which are affected by physiological conditions such as age, gender and race, should be evaluated together with the clinical presentation of the patient.[6] In our case, the reason why the patient was referred to us was high APR, and there were complaints of fatigue and loss of appetite associated with systemic inflammation. In order to exclude infective conditions, cultures were taken from the necessary body fluids along with the physical examination as described above, and no infectious pathogen was detected. Chronic infections such as brucella, syphilis, hepatitis, Human Immunodeficiency Virus (HIV) infection, and tuberculosis were excluded. Since she complained of back pain, leukocyte labeling scintigraphy showed that there was no spondylodiscitis. In terms of rheumatological diseases, no findings were detected in the patient during the rheumatological examination. As mentioned in the case section, no autoantibody positivity was found. Considering the patient's values at the time of application, there was IDA, and considering the clinic, no pathology was detected in the gastrointestinal system and gynecological examination in terms of malignancies that could cause IDA. The point to note here is that although ferritin is an acute phase reactant, it is not as high as CRP and ESR. This has been linked to the underlying iron deficiency. It has been emphasized that the inflammatory state affects iron parameters, and in these cases, when evaluating IDA, a more comprehensive evaluation is required, not just ferritin.[7] In addition, it has been determined in some studies that ferritin may not increase sufficiently in cases of inflammation, even in the presence of IDA.[8] In our case, no findings were detected to explain the current clinical picture in the mammography, tumor markers, and thorax and abdomen CT scans of the patient who was screened for underlying malignant conditions. In this case, PET-CT has become necessary. Advanced imaging technologies, especially PET-CT, are frequently used in cancer diagnosis and treatment. PET-CT is a well-established imaging method that provides high sensitivity for the detection of conditions such as cancer, vasculitis, and chronic infection.[9] In our case, PET-CT was performed and mild involvement was seen in the patient's humerus, and ACT was suspected with the subsequent MRI. The point to be emphasized here is that the patient had no symptoms that would lead to

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a diagnosis related to the humerus. Afterwards, the diagnosis of ACT was confirmed with a biopsy taken from the patient and the patient was operated on by the relevant department. After the treatment, the patient showed regression of APRs and gained weight.

In conclusion, high APRs is a laboratory finding seen in the course of many diseases with chronic inflammation. It is a condition that needs to be investigated in detail, especially in patients without any obvious symptoms, and if necessary, it needs to be examined multidisciplinary. Many patients are referred or apply to our clinic with high APRs. In our case here, we present a case that presented with only fatigue and weight loss and high APRs. The patient's detailed diagnosis stages are described above, and he was diagnosed with ACT from the humerus, where he had no complaints. This case emphasizes how detailed and meticulously APR elevation should be examined and how unexpected pathologies may arise under APR elevation.

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