Ankylosing spondylitis (AS) is a chronic inflammatory disease that is the most frequent and severe subtype of seronegative spondyloarthropathies. It typically affects the axial joints, most notably the sacroiliac joints; however, other sites of involvement, including peripheral joints and extra-articular manifestations, are also observed. Pharmacological management of AS includes disease-modifying anti-rheumatic drugs (DMARDs) such as anti-tumor necrosis factor (TNF) agents to control the disease progression. However, patients with AS may still present impairments accompanied by pain and decreased function and quality of life (QoL). In some cases, the systematic effect of AS disease and adverse effects of DMARDs and anti-TNF agents may be catastrophic for the patient. In the current meta-analyses, anti-TNF drugs have been shown to increase the risk of melanoma and skin cancers.

In this report, we present a unique case of both drug-related malignant melanoma (MM), and wrist arthritis, a very rare peripheral joint involvement in an AS patient, which provides a contribution to the literature.

CASE REPORT

A 49-year-old Caucasian male patient was admitted to the outpatient clinic complaining of right wrist pain and movement limitation. His wrist pain existed for three months, and he had morning stiffness of about 30-min to 1-h on his right wrist. He had no history of hand trauma or congenital...
disorders in the past. His medical history revealed that the patient was diagnosed with AS 25 years ago, and his brothers were also diagnosed with AS. The patient was diagnosed with AS by meeting all the modified New York criteria with radiologically defined sacroiliitis, as well as symptoms and signs of decreased chest expansion, low back pain lasting longer than three months and not relieved by rest, and multi-planar limitation of lumbar spine movements. The patient had a right total hip replacement (THR) 23 years ago, and the right hip prosthesis was revised one year ago. The left THR applied 14 years ago and the right total knee replacement (TKR) 23 years ago. Besides, 23 years ago, bilateral pantalar and tarsometatarsal arthrodeses were performed with an interval of three months.

The DMARD treatment started, when the patient was 35 years old. Besides, treatment with 25 mg of etanercept was applied for 10 years, and adalimumab treatment (fully human recombinant immunoglobulin G1) was started in the following year and continued for one year. Following this treatment, a brown skin lesion appeared on the plantar side of his foot, and local excision was performed in this area. The pathology report confirmed a diagnosis of melanoma in situ (MIS). Anti-TNF-alpha (TNF-α) treatment was discontinued due to the thought that the lesion may be related to treatment. Later, extensive resection and skin grafting were performed on the same area (Figure 1). After this treatment, recurrence did not occur, and the patient and did not receive any medical treatment.

On admission, vital signs and lung sounds were normal. The vertebral examination revealed thoracic kyphosis, limited cervical, and lumbar mobility, and decreased chest expansion. The tragus-wall distance was 23 cm in size. The Schober’s test was positive (4 cm) and chest expansion was 2.4 cm. In the upper extremity examination, right wrist movements were painful and scored 5 points on the Visual Analog Scale. Right wrist extension and flexion were 20°. The Duruöz Hand Index score was 18 out of 90, with higher scores being indicating poorer function. The range of motion in the other joints of the upper extremity.

Figure 1. Local excision site in the plantar side of his foot.

Figure 2. Radiography findings showing arthritis in midcarpal and radiocarpal joints. (a) Lateral radiography of wrists. (b) Anteroposterior radiography of wrists.
Wrist arthritis and malignant melanoma in AS

was normal. Old incision scars were observed in the lateral of both hips, anterior to the right knee, both ankles, and dorsal feet. There was a 3-cm apparent length discrepancy in the lower extremity. The Bath Ankylosing Spondylitis Functional Index score was 6.4 out of 10, with higher scores being indicating poorer function. The Bath Ankylosing Spondylitis Mobility Index score was 4 out of 5, with higher scores being indicating lower mobility. The Bath Ankylosing Spondylitis Disease Activity Index score was 3.4 out of 5, with higher scores being indicating disability. Functional impairment due to AS adversely affected health-related QoL. The mental component score of Short Form-12 was 31.15, and the physical component score of Short Form-12 was 51.53.

The laboratory findings were normal at the time of admission to the clinic. Besides, X-ray examinations at the time of admission to the clinic, the patient revealed ankylosis, squaring, and kyphoscoliosis in the vertebrae. There was Stage 3 arthrosis in the sacroiliac joint and arthritic changes in the right wrist (Figure 2). The THR was observed in both hips. Signs of loosening were observed in the right knee prosthesis. According to the Kellgren and Lawrence, Grade 4 arthritis was observed in the left knee, and there was pantalar and tarsometatarsal arthrodesis in the bilateral ankle (Figure 3).

The patient was informed that data from the case would be submitted for publication and gave his consent.

DISCUSSION

Patients with AS can present impairments accompanied by pain and a decrease in both function and QoL, such as axial involvement, tyoical skin manifestations, altered gait kinematics, higher risk of uveitis, and dactylitis, pulmonary function impairments, and decrease in exercise capacity.[1-5] It has been shown that peripheral arthritis observes in about a third of cases, with asymmetrical involvement of one large joint like the hip, knee, or shoulder.[2] Recent studies have demonstrated that symptomatic enthesisopathy of the shoulder is common in patients with AS, and coxitis is the only

![Figure 3. Multiple joint replacements and arthrodesis. (a) Right operated total knee replacement and left gonarthritis, anteroposterior radiography. (b) Bilateral operated total hip replacement, anteroposterior radiography. (c) Bilateral operated ankle, pantalar, and tarsometatarsal arthrodesis, anteroposterior radiography. (d) Bilateral operated ankle, pantalar, and tarsometatarsal arthrodesis, lateral radiography.](image-url)
predictive factor for shoulder enthesitis.\textsuperscript{[1,2]} A study reported a 60-year-old AS patient with swan-neck deformity on both hands.\textsuperscript{[6]} The radiograph of the hands showed no bone erosions, but magnetic resonance imaging of the hands showed enthesitis. Our case is an unusual presentation due to having the right and left THR, right TKR, and pantalar and tarsometatarsal arthrodesis on both sides. Our case was admitted to the outpatient clinic with a complaint of right wrist pain, and the range of motion of the right wrist significantly decreased without another involvement in the right upper extremity. There was few case reports on AS with wrist involvement in the literature.\textsuperscript{[9]} Therefore, our case is a rare representation of the possible catastrophic effect of AS disease on peripheral joints.

The DMARDs such as anti-TNF agents may slow the progression of the disease of AS. However, they have a limited role in treating advanced established arthritis of the joints.\textsuperscript{[3]} Due to the immunosuppressive properties of TNF-α antagonists, it is plausible that these biologics may increase the risk of the occurrence of malignancies or the reactivation of latent malignancies.\textsuperscript{[8]} A recent study examining the potential association between TNF inhibitors treatment and MM in rheumatoid arthritis (RA) patients has shown that RA patients have an increased risk of melanoma compared to RA patients not treated with biological drugs.\textsuperscript{[9]}

The safety profile of anti-TNF-α therapy is conflicting about major organ systems, serious infections, and malignancies. A systematic review and meta-analysis provided reassurance to physicians and patients that the treatment of RA patients with TNF inhibitor did not increase the risk of malignancy, particularly lymphoma.\textsuperscript{[10]} However, it appeared to increase the risk of skin cancer, including melanoma. Our case is important, due to the documented diagnosis of MIS with the pathology report of a brown skin lesion on the planter side of the foot after TNF inhibitor therapy. A large-scale meta-analysis and systematic review reported that anti-TNF therapy increased the risk of skin cancer, including melanoma, although it did not affect the overall risk of developing cancer in patients with inflammatory arthritis, including AS.\textsuperscript{[8]} These findings may support the thought that the possible predisposing effect of TNF inhibitor treatment on increasing the risk of malignancies or the reactivation of latent malignancies in patients with AS. Therefore, the advantages of treatment with anti-TNF-α agents should be weighed against possible systematic disadvantages. It should be considered that the consequences of stopping anti-TNF treatment may be severe, particularly in cases where no other treatment is available.

In conclusion, it is possible to increase the health-related QoL with medical and surgical treatments in AS. Although there are major surgical interventions, orthopedic solutions are offered for peripheral joint involvement in eligible patients. Close monitoring of patients receiving anti-TNF therapy in terms of side effects is important. Studies with large case series are needed to investigate the short and long-term side effects of anti-TNF drugs in AS patients.

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