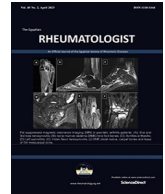




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## Case reports

## HLA B27-positive ankylosing spondylitis professional soccer player with a successful return to sports

Eduard Bezuglov<sup>a,b</sup>, Maria Shoshorina<sup>a,\*</sup>, Mikhail Butovskiy<sup>c</sup>, Yuri Kuklin<sup>d</sup>, Kamila Kubacheva<sup>e</sup>, Vladimir Khaitin<sup>f,g</sup>, Ryland Morgans<sup>a</sup><sup>a</sup> Department of Sports Medicine and Medical Rehabilitation, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia<sup>b</sup> High Performance Sport Laboratory, Moscow Vite University, Moscow, Russia<sup>c</sup> Football Club "Rubin", Kazan, Russia<sup>d</sup> Football Club "Ural", Ekaterinburg, Russia<sup>e</sup> Saint-Petersburg State Public Institution «City Hospital №40», Saint-Petersburg, Russia<sup>f</sup> Pavlov First Saint-Petersburg State Medical University, Saint-Petersburg, Russia<sup>g</sup> Football Club "Zenit", Saint-Petersburg, Russia

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## ABSTRACT

**Background:** Ankylosing spondylitis (AS) is a disease of young adulthood and without adequate treatment it dramatically reduces physical activity.**Aim of the work:** To present a case with AS that successfully returned to professionally playing sports after treatment.**Case presentation:** A 19-year-old Eastern European Russian professional male soccer player with AS complained of right ankle joint pain not related to any trauma or injury and gradually intensified. The player's regular medical tests during the preceding years and were unremarkable. He would occasionally complain of discomfort in the ankle joints, sacroiliac area and symphysis but did not limit his regular training activity. He received the standard treatment of sports injuries that included: 14 days of limited physical activity, ibuprofen 200 mg twice/day, cryotherapy and joint taping. Examination revealed mobile joints, regular in shape without any swelling. Erythrocyte sedimentation rate (ESR) was 60 mm/1st hr and C-reactive protein (CRP) 50 mg/dl. AS was diagnosed as he fulfilled the classification criteria. HLA-B27 was positive, left sacroiliitis was present on magnetic resonance imaging (MRI). The Bath AS disease activity index (BASDAI) was 5.9. Treatment also included golimumab 50 mg/month. He improved, returned to regular training and continued playing sports professionally amid supportive therapy. The last BASDAI was 1.5.**Conclusions:** AS patients with initially high levels of physical activity may restore professionally playing of sports when a proper management plan is provided. Further monitoring is warranted and the creation of a database for athletes with rheumatic diseases is recommended in order to standardize treatment protocols.© 2023 The Authors. Publishing services by ELSEVIER B.V. on behalf of The Egyptian Society of Rheumatic Diseases This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Ankylosing spondylitis (AS) is a synonym for radiographic axial spondyloarthritis (axSpA), and along with non-radiographic axSpA (less severe forms and early stages of AS) conform a broader disease of axSpA [1]. It is a relatively rare severe disease of the musculo-skeletal system and other organs and is characterized

by prolonged inflammation of the spine and various joints. The most commonly affected joints are the knees, sacroiliacs, ankles and spine. Extra-articular conditions are reported and involve the eyes and intestines [2,3]. Although, the exact cause of the disease is unknown, the association between AS and HLA-B27 has been confirmed [2,4–6,7]. AS is more prevalent in young adults, most commonly men aged 25–35 years [6,8] with a significant restriction of physical activity [9]. Diagnosis is based on the clinical picture and positive human leucocytic antigen B27 (HLA-B27) with an increase in systemic markers of inflammation such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). In early

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\* Corresponding author.

E-mail address: [kaisough@yandex.ru](mailto:kaisough@yandex.ru) (M. Shoshorina).<https://doi.org/10.1016/j.ejr.2023.06.001>

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stages, magnetic resonance imaging (MRI) allows the identification of inflammation in large joints [1,10].

The Bath AS disease activity index (BASDAI) allows a quick and safe assessment of therapy and a score > 4 is considered an indicator of an active process that requires a revision of the treatment strategy [11,12]. The treatment options include non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, disease-modifying antirheumatic drugs (DMARDs), tumor necrosis factor (TNF- $\alpha$ ) inhibitors and anti-interleukin-17 which may provide a prolonged remission [13]. Local steroids can also be administered for symptomatic relief.

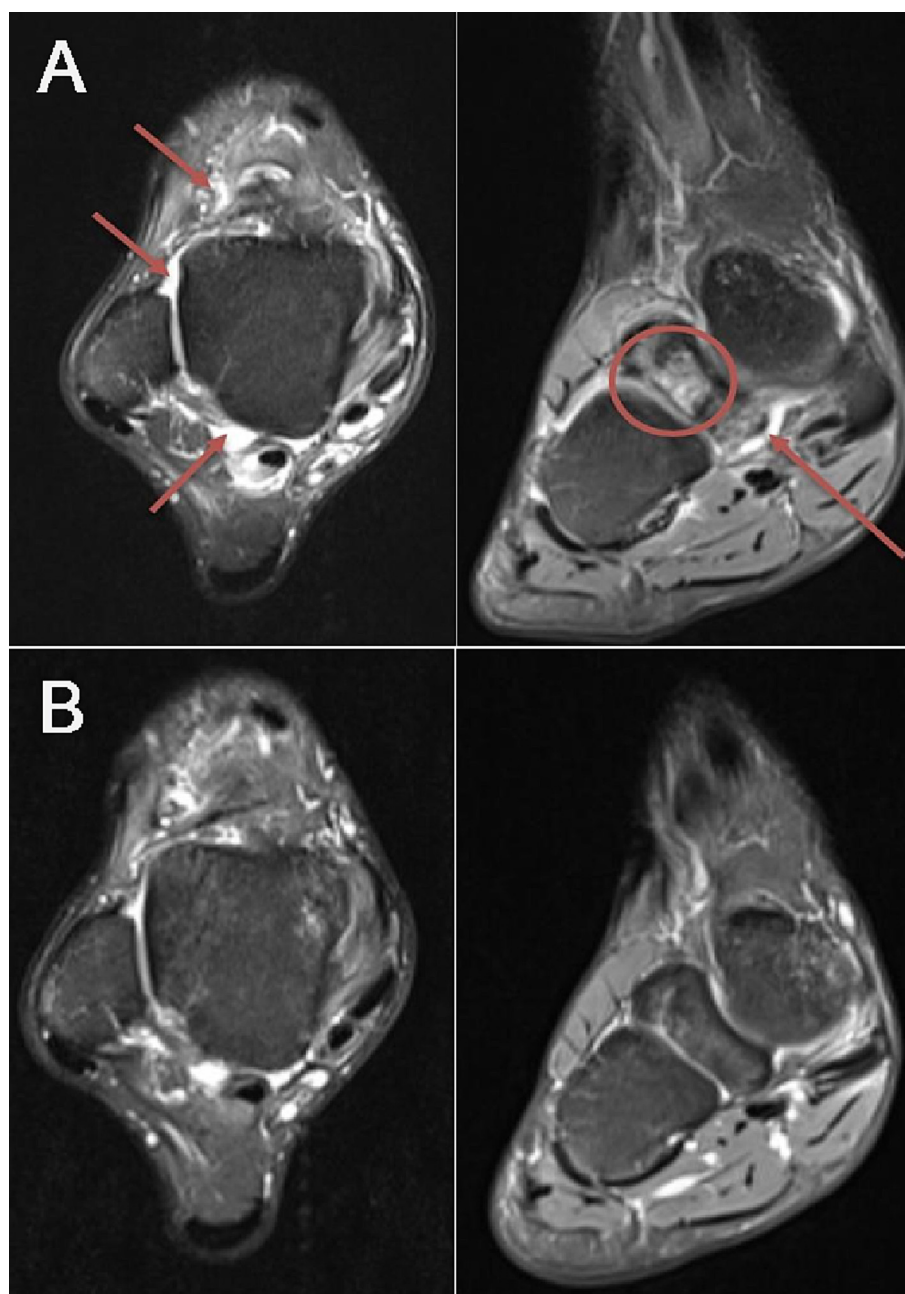
Professional sports place specific demands on the musculoskeletal system and involve frequent post-exercise inflammation of the muscles, tendons, bones and joints. In the vast majority of

cases, it is considered practically impossible to engage in professional sports with such a diagnosis.

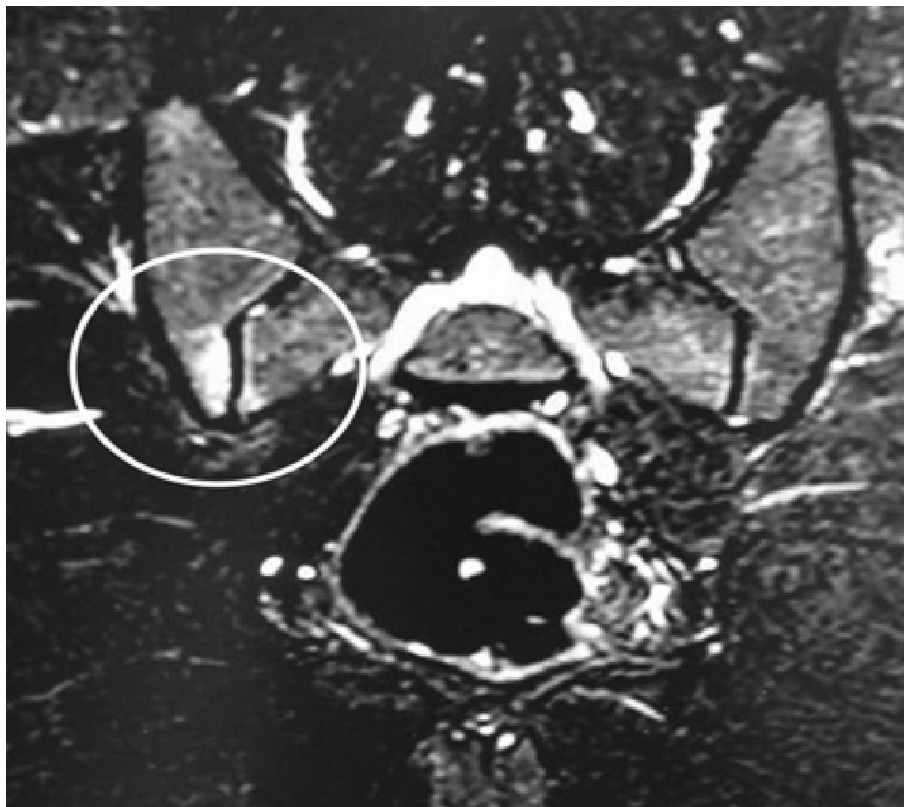
This is a leading article that presents the clinical changes of a young national team soccer player who returned to regular training after 16 months of treatment and medical rehabilitation.

## 2. Case presentation

In April 2018, a 19-year-old Russian (Eastern European) professional soccer player (height: 170 cm; weight: 65 kg; BMI: 22.5) with a 13 year playing history at a leading Russian Premier League soccer club and without any family history of inflammatory joint diseases, subjectively reported to the club doctor. The main complaints were pain in the right ankle joint, without prior connection



**Fig. 1.** Magnetic resonance imaging (MRI) of the right ankle. (A) Grade 1 on 2018 showing reactive bone marrow edema (BME) and (B) Grade 2 on 2020 showing reactive BME and sclerosis with reduced signs of synovitis.



**Fig. 2.** Magnetic resonance imaging (MRI) of the sacroiliac joints on 2019. Signs of sacroiliitis on the left side (taken in a circle). No sign of sacroiliitis on the right side.

with injury that gradually intensified over the previous days. Upon examination, the joint was considered normal with good mobility. The study was approved by the local ethical committee (N 11–19) and the written consent to participate was obtained from the patient.

During the previous five years prior to treatment, the player regularly completed medical tests twice a year with no remarkable signs of inflammation or changes in blood tests. Previously during the year, the player occasionally complained of discomfort in the ankle joints, sacroiliac area and symphysis, although did not limit his regular training activity and did not require therapy.

In April 2018, the reported negative symptoms were followed by the standard treatment of sports injuries that included: 14 days of limited physical activity, NSAIDs (ibuprofen 200 mg twice/day), cryotherapy and joint taping. Examination revealed mobile joints, regular in shape without any swelling. Regional lymph nodes were of normal size and body temperature was normal.

Within a three-week period following the initial onset of pain in the ankle joint, pain was reported in the knee joint, lumbar and thoracic spine. Calf muscle hypotrophy also occurred and markers of inflammation significantly increased (ESR 60 mm/1st hr, CRP 50 mg/dl). After a thorough examination, AS was diagnosed based on the clinical picture, lesion location, blood tests (ESR, CRP) and positive HLA-B27 as well as the MRI findings (Fig. 1). Proton density weighted-MRI (fat saturation) in adjacent sections of the calcaneus and scaphoid bone with surrounding edema including the region of the subtalar sinus and also showing synovitis in the ankle joint. MRI showed changes of the left sacroiliac joint while there were no signs on the right side (Fig. 2). X-ray of the thoracic and lumbar spine, the hip and ankle joints were without any significant features. He fulfilled the classification criteria for axSpA [1]. There were no diagnostic challenges.

The BASDAI [11] was assessed and initial score was 5.9 denoting activity. The rehabilitation program was implemented for 16 months during which he returned to the general group training in August 2019 and was followed-up till May 2022.

Initially, for the first 6 months of therapy, the clinical picture was stable, however during the 10th month, a regression in symptoms occurred. This prompted a change in therapeutic methods that resulted in a positive progression. The patient has been stable for more than two years (up to May 2022), continued to play professional soccer and has completed 20 competitive matches of 70–90 min each. The only treatment has been 50 mg golimumab once/month. Outlines of therapeutic interventions are presented in Table 1. Therapy included complete rest (no training), celecoxib 400 mg/day consumption, intra-articular injections of betamethasone into the inflamed joints of the foot (0.5 ml of betamethasone + 0.5 ml of lidocaine once/week for two weeks), ankle immobilization (orthotic splint-Bauerfeind®), cryotherapy (20 min. twice/day), magnetotherapy (permanent magnetic field up to 300 min./ day).

After six months of therapy, the severity of clinical symptoms began to decrease and the patient's condition stabilized. However, by the 10th month of therapy, the condition worsened, which led to a change in therapy and thus an improvement in the clinical picture. Secukinumab was initiated for its known effective and safe use in axSpA [14,15].

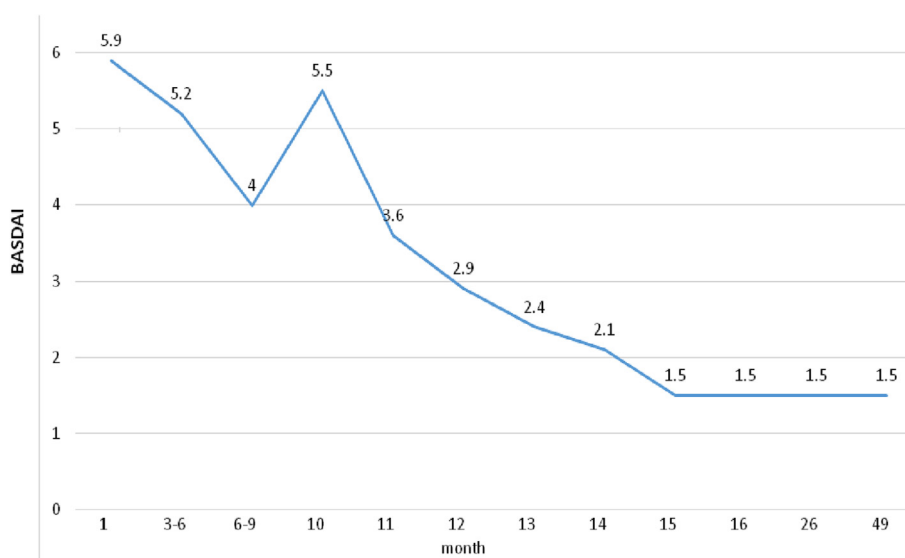
Therapy in January 2019 included methotrexate (MTX) 20 mg/ week followed next day by folic acid 10 mg/week, and secukinumab 150 mg subcutaneously (SC) once/month. Additionally, the athlete received calcium (500 mg/day), vitamin D (5000 IU/day) and alendronate (10 mg/week). Additionally, muscle strengthening, massage, and physiotherapy (magnetotherapy, electrical stimulation, cryotherapy) were integrated. Consequently, the BASDAI decreased. Blood parameters and acute phase reactant started to

**Table 1**

The characteristics and progress of the patient over the entire period of treatment.

Date	Clinical picture	Physical loading	Blood	Treatment	Dose
Initially (1–2 mo) Apr–May 2018	Pronounced; BASDAI (5.9)	Rest	ESR: 20 CRP: 20 Iron: 5 Hb: 11 Ferritin: 35	Celecoxib Sulfasalazine Betamethasone Immobilization Cryotherapy Magnetotherapy	400 mg/d 0.5–3 g/d/w/2 wks IA (ankle/foot joints) Orthosis (Bauerfeind®) 20 min. twice/d Up to 300 min/d
(3–6 mo) June–Sept 2018	Pronounced; BASDAI (5.2)	Light ex. <i>No football specific ex.</i>	ESR: 60 CRP: 50 Iron: 3 Hb: 10.5 Ferritin: 30	Sulfasalazine Celecoxib Doxycycline Cryotherapy Magnetotherapy	2 g/d 400 mg/d 200 mg/d 20 min twice /d Up to 300 min/d
(7–9 mo) Oct–Dec 2018	Stable; BASDAI (4)	Training in the gym and on the field	ESR: 15 CRP: 11 Iron: 15 Hb: 11.8 Ferritin: 38	Sulfasalazine Ibuprofen Secukinumab Cryotherapy Magnetotherapy	500 mg/d 400 mg 150 mg SC 1–4/mo 20-min. twice/d Up to 300 min/d
(10 mo) Jan 2019	Pronounced; BASDAI (5.5) BME (foot/ pubic bones)	Exercise therapy	ESR: 60 CRP: 50 Iron: 3 Hb: 10 Ferritin: 30	Secukinumab Cryotherapy US therapy with hydrocortisone Magnetotherapy	150 mg SC 1/mo 20 min twice /d 20-min. once/d Up to 300 min/d
(11–16 mo) Feb–July 2019	Stable; BASDAI (3.6/2.9/ 2.4/2.1)	From 16 mo gp training ms exercise	ESR: 6 CRP: 0.5 Iron: 17 Hb: 13.8 Ferritin: 15	Methotrexate Golimumab Folicacid	Gradual ↑ till 20 mg/w 50 mg SC /mo 10 mg 12 h after MTX
(26 mo) June 2020	Stable; BASDAI (1.5)	Regular training activities	ESR: 6 CRP: 0.8 Iron: 17 Hb: 14.8 Ferritin: 40	Golimumab	50 mg SC /mo
(49 mo) May 2022	Stable; BASDAI (1.5)	Regular training activities	ESR: 5 CRP: 0.9 Iron: 18 Hb: 14.6 Ferritin: 39	Golimumab	50 mg SC /mo

Side effects and allergic reactions were not recorded. ESR: erythrocyte sedimentation rate (mm/1st hr), CRP: C-reactive protein (mg/dl), Hb: hemoglobin (g/dl), Iron in umol/l, Ferritin in ng/ml, BASDAI: Bath ankylosing spondylitis disease activity index, BME: bone marrow edema.

**Fig. 3.** The Bath ankylosing spondylitis disease activity index (BASDAI) during the treatment period. Activity is considered high when BASDAI is > 4.

be normalized. Since March 2019, secukinumab was replaced by golimumab for its availability and in view of the suggested evidence supporting its value in AS [16–18].

Over the following four months, therapy did not change, and physical activity progressed while the condition remained stable. No extra-articular lesions were observed during the entire dura-

**Table 2**

Athletes with rheumatic diseases successfully recovered and resumed sports.

Diagnosis	Russia <i>this case</i>	USA [22]	Italy [23]	USA [24]	USA [25]
<b>RD</b>	AS	PsA	BD	AS	AS
<b>Age (y)</b>	19	39	29	32	young
<b>Gender</b>	Male	Male	Male	Male	Male
<b>Sport</b>	Soccer	Football	Athlete	Military team	Athlete
<b>Family hx</b>	–ve	+ve	–	–ve	–
<b>Features</b>	Arthralgia Rt ankle joint no inflammation.	Arthritis Rt knee joint (effusion).	ROU, skin rash, EN, DVT, fever, epididymitis, uveitis.	Radiating pain/LOM Rt shoulder Cx/hip pain	Sacroiliac joint instability and dysfunction
<b>Prior injury</b>	–ve	+ve	–	–ve	–
<b>Start therapy =&gt; Effect</b>	↓activity, NSAIDs, cryotherapy, joint taping => stable	NSAIDs => improved IA steroid => relief	AZA, Prednisone	Exercise, heat, PT, pain modalities => ↓Cx/hip pain	NSAIDs, gradual activity => no pain
<b>After initial therapy</b>	Knee/lumbo-dorsal pain, calf ms hypertrophy, ↑ESR/ CRP, +ve HLA-B27	Large effusion Synovitis, LOM chondromalacia patellae	ROU, skin rash, macular edema (ME), ↓visual acuity (VA) +ve HLA-B51	LOM shoulders /spine, ms weakness, ↑CRP, +ve HLA-B27	–
<b>Continued treatment =&gt; Effect</b>	Rest, celecoxib, IA steroid foot, cryo/magnetotherapy => Improvement	Synovitis resected cartilage debrided	Steroid, CsA, AZA => ↓ME, infliximab => ↓skin lesions, ↓ME, ↑VA	Cx stretches, ms ex, ROM shoulder/spine, NSAIDs, fluticasone => Improved	
<b>After continued therapy</b>	Regressing in 10th month	knee effusion, Ps, ↑ESR, +ve ANA, –ve RF/HLA-B27	Infliximab, AZA => remission		
<b>New therapy</b>	SKB, MTX, PT => improved, ↓ESR/CRP. then Golimumab.	Etanercept, MTX => remission After arthroscopy => re-injury			
<b>Return to play</b>	PT 16 mo Golimumab	without relapse	after 2 years	–	Symptom free gentle work

AS: ankylosing spondylitis, PsA: psoriatic arthritis, BD: Behçets disease, ROU: recurrent oral ulcers, EN: erythema nodosum, DVT: deep venous thrombosis, LOM: limited range of motion, NSAIDs: non steroidal anti-inflammatory drugs, IA: intra-articular, Ps: psoriasis, ESR: erythrocyte sedimentation rate, ANA: antinuclear antibody, RF: rheumatoid factor, ME: macular edema, VA: visual acuity, Cx: cervical, CsA: cyclosporine A, AZA: azathioprine, SKB: secukinumab, MTX: methotrexate, ms ex: muscle exercise, PT: physiotherapy.

tion. The patient returned to regular training activities in early August 2019 performing in the first professional match on 19th August 2019. Since June 2020, only golimumab 50 mg/month was received under supervision of hospital medical staff after preliminary blood tests.

During the entire treatment period, the patient did not experience any side effects and attended all training sessions. The patient did not incur any injuries or illnesses that prevented match-play, and no restrictions for participation in competitive matches were recommended. During the following two year period, ESR and CRP levels did not exceed 5 and 1.5, respectively, and the BASDAI index was 1.5 (Fig. 3).

### 3. Discussion

The most common outcome for athletes diagnosed with AS is a decrease in locomotor activity associated with inflammatory joint damage. The course of the disease can be different, but commonly joint mobility is irreversibly reduced and the diagnosis of AS makes returning to sports participation impossible due to chronic inflammation [19], a decrease in bone mineral density and an increased risk of fractures [9], and a reduction of core stability and balance [20]. Notably, only one publication describes the case of AS in an athlete which described the successful treatment with a monthly course of indomethacin. However, following the cessation of clinical symptoms, the athlete was no longer involved in sports [21].

This is one of the few successful cases reported in the literature of athletes returning to sport after rheumatic diseases [22–25] (Table 2). As in the current case, diagnosis was not immediate. This is important for professionals to detect the disease early and start treatment to avoid career losses. However, in the studied patient, inflammation did not occur even with a maximum training load,

arguably achieved by the administration of MTX and golimumab. On-going therapy allows the continuation of a professional football career. However, constant monitoring of inflammation markers is necessary for timely correction of therapy. Provided the expensive cost, it is essential that the medication is administered by an experienced medical practitioner.

This case study confirms the previously described efficacy of golimumab in the treatment of AS. It was shown that monotherapy with medium doses of this drug allows not only a return to the usual daily activities but also to continue participation in competitive games.

There are cases of athletes returning to sports with rheumatoid arthritis (tennis player Caroline Wozniacki, a professional hockey player from Finland) but they are not described in the existing literature.

In conclusion, the case presented herein describes the first clinical case of a young professional soccer player with AS returning to his professional activity. Further monitoring is warranted and the creation of an athlete database with similar diseases in order to standardize patient treatment protocols with initially very high levels of physical activity is essential.

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### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.



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