CASE REPORT

Bilateral sacroiliitis and uveitis comorbidity: brucellosis? Ankylosing spondylitis?

Lütfi Akyol,¹ Kerim Aslan,² Metin Özgen,¹ Mehmet Sayarlioglu¹

¹Department of Internal Medicine Division of Rheumatology, Ondokuz Mayıs University Hospital, Samsun, Turkey

²Department of Radiology, 19 Mayıs University Hospital, Samsun, Turkey

Correspondence to

Dr Lütfi Akyol,
drakyol19@gmail.com

Accepted 8 September 2015

SUMMARY

We present a rare case of a comorbidity of sacroiliitis and brucellosis infection. A 28-year-old woman received irregular medication due to ongoing backache and hip pain for 5 years. The patient presented to our hospital for evaluation of visual loss and was diagnosed with uveitis. Sacroiliac MRI was performed to investigate the inflammatory backache and hip pain, and the aetiology of the uveitis, revealing the presence of sacroiliitis. The patient's blood test results were as follows: positive brucellosis Rose Bengal test and positive tube agglutination test with a titre of 1/640. The patient was treated with doxycycline and rifampicin for 8 weeks for the brucellosis infection, and with acetaminophen for the ankylosing spondylitis. The patient's back and hip pain decreased significantly 8 weeks later; however, the uveitis was not controlled by the treatment. Therefore, anti-tumour necrosis factor (infliximab) treatment was started.

BACKGROUND**Uveitis**

Uveitis is one of the most common inflammatory eye diseases and constitutes 10% of the causes of blindness worldwide. Four types of uveitis have been identified based on the anatomic location of the inflammatory process: anterior uveitis, intermediate uveitis, posterior uveitis and panuveitis. The aetiology of the occurrence of uveitis depends on environmental, cultural and genetic factors. Uveitis is the most common extra-articular manifestation in patients with seronegative spondyloarthritis and can also occur in up to 25% of patients with ankylosing spondylitis (AS). Tumour necrosis factor (TNF) inhibitors have been shown to improve symptoms in rheumatological diseases as well as in uveitis.^{1–3}

Spondyloarthropathy

AS is the prototype of spondyloarthritis, which affects the axial skeleton. The Modified New York Criteria, European Spondyloarthropathy Study Group Criteria and Amor Criteria are currently used in the diagnosis of spondyloarthropathy. According to the Modified New York criteria, diagnosis of AS is frequently achieved late without the detection of symptoms during assessment. This is because a period of 6–10 years must pass between the onset of early symptoms and the start of axial inflammation for radiographic sacroiliitis to be defined (grade 2 bilateral or grade 3 or 4 unilateral). To resolve this problem, the Assessment of Spondyloarthritis International Society

Classification Criteria was developed and the term 'axial spondyloarthritis' was adopted.⁴

Brucellosis

Brucellosis is a zoonotic disease caused by *Brucella* spp. Infection occurs through consumption of meat, raw milk, or other dairy products. Although the incidence of the disease has decreased, it is still an important problem in endemic areas such as Turkey. Brucellosis may be acute or chronic. It may involve the lungs, kidneys, central nervous system, heart, skeletal system and eyes in 10–15% of patients. Uveitis frequently occurs when the disease involves the eye. The clinical diagnosis of brucellosis requires isolation of the bacteria with a blood or tissue culture or the presence of specific antibodies via an agglutination test, complement fixation test, radioimmunoassay, or ELISA.⁵ Although uveitis is idiopathic with a prevalence of 30–40%, it may be comorbid with some rheumatological and infectious diseases. In this study, while researching the diseases that can cause uveitis, we aimed to raise awareness of infectious diseases, such as brucellosis, that can be present along with uveitis as well as to outline the factors related to AS.

CASE PRESENTATION

A 28-year-old woman experienced backache and hip pain over a period of approximately 5 years. The pain was worse while waking (though it was occasionally bad enough to wake the patient during the night); she reported of an ache and limited movement in the back and hip area, which normally lasted for longer than an hour, with symptoms decreasing on movement. Her symptoms decreased significantly after taking painkillers. No swelling, rashes, or increased heat in the joints was noted. The patient recently reported of malaise, fatigue and loss of appetite, all of which had increased significantly. Five years earlier, the patient was informed that she had inflammatory rheumatism and was prescribed a large number of painkillers, the names of which she did not know, as well as sulfasalazine. The patient used these medications regularly for approximately 1 year and then stopped taking them on her own accord. She then reported of visual turbidity, and the intensity of the turbidity increased over the last few months until the start of complete visual loss. At this point, the patient presented to the department of ophthalmology of our institution and was found to have intense panuveitis (figure 1). The patient's rheumatological examination revealed backache that had been ongoing for 5 years. There was no history of

CrossMark

To cite: Akyol L, Aslan K, Özgen M, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211461

Figure 1 Adhesion of the iris to the lens at 360° (posterior synechia), iris pigments on the lens (blue arrows) (secondary to uveitis attacks) and cataract development (red arrow) (chronic uveitis).

chronic disease, and physical examination did not show peripheral arthritis. The patient's FABERE/FADIR tests and sacroiliac joint compression test were positive, and the laboratory test results were as follows: haemoglobin, 10.6 g/dL (12–17); erythrocyte sedimentation rate (ESR), 66 mm/min (0–20); and C reactive protein (CRP), 62 mg/L (0.0–3.5). A sacroiliac joint graph showed bilateral grade 2 sacroiliitis. Sacroiliac MRI showed that the sacroiliac joint distance appeared to be equal bilaterally. However, irregularities were present on both sides of the bilateral joint, along with cortical erosion and an obvious increase in subchondral sclerosis on the iliac wings (figure 2). Based on the patient's backache, elevation of acute-phase reactants, and sacroiliac radiography and MRI findings, the patient was diagnosed with AS. A systemic examination of the patient

Figure 2 Sacroiliitis in a 28-year-old woman. Coronal oblique fat-suppressed T2-weighted (A and B) and contrast-enhanced fat-suppressed T1-weighted axial (C) MRIs of the sacroiliac joints, show bilateral hyperintense and contrast-enhanced sacral and iliac areas consistent with bone marrow oedema (arrowheads), and subchondral iliac sclerosis (arrow) in the bilateral sacroiliac joint. Coronal oblique fat-suppressed T2-weighted (C and D) and contrast-enhanced fat-suppressed T1-weighted axial (E) MRIs of the sacroiliac joints obtained after therapy show loose bilateral sacral and iliac areas consistent with bone marrow oedema, and subchondral iliac sclerosis (arrow) in the bilateral sacroiliac joint.

revealed that she consumed non-pasteurised milk and dairy products. Examination disclosed a positive brucellosis Rose Bengal test and positive brucellosis Coombs test with a titre of 1/640. The patient was diagnosed with brucellosis, and a course of treatment with rifampicin at 600 mg/day and doxycycline at 200 mg/day was begun. Antibiotic treatment was stopped after 8 weeks. After treatment, the patient's back and hip pain resolved completely. However, her visual impairment continued, although at a decreased level.

DIFFERENTIAL DIAGNOSIS

Because our patient's primary diagnosis was uveitis, she was evaluated in relation to other diseases that can cause uveitis. With regard to Behçet's disease, which is common in Turkey, there was no history of recurrent oral aphtha, genital ulcers, papulopustular lesions, or erythema nodosum. A pathergy test was negative. In consideration of granulomatous diseases such as tuberculosis and sarcoidosis, the serum calcium and 24 h urine calcium levels, lung graph and purified protein derivative test were performed; all results were normal. In terms of infectious causes, HBsAg, anti-HCV, anti-HIV, EBV and CMV IgM antibodies were all negative. With respect to inflammatory intestinal diseases, the patient did not have diarrhoea, there was no blood or parasites in her stools, and she tested negative for the *Clostridium difficile* toxin. The patient's joint symptoms began 5 years previously, while the visual symptoms started 4 years previously. An eye examination showed that she had experienced uveitis attacks on many occasions. We recalled that the patient had been experiencing AS for a long period of time and considered that the uveitis attacks might therefore be due to the AS. We also considered that the brucellosis infection that was later included in the diagnosis had accelerated the course of the disease.

TREATMENT

The patient was given a course of treatment comprising of doxycycline at 200 mg/day, rifampicin at 600 mg/day and acemetacin at 60 mg/day for 8 weeks for the brucellosis infection and sacroiliitis. Additional treatment with infliximab at 300 mg (5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks thereafter) was started once it was clear that the uveitis attacks were not under control.

OUTCOME AND FOLLOW-UP

The patient's inflammatory backache completely recovered after doxycycline, rifampicin and acemetacin treatment. The ESR and CRP levels returned to normal at the end of the 8 weeks. Although the patient's vision improved compared with that at the onset of treatment, it remained poor. At the time of writing, the patient was undergoing maintenance treatment with infliximab at 300 mg every 8 weeks.

DISCUSSION

Extra-articular manifestations (EAM) play an important role in the diagnosis of SpA, because they change the treatment choices, and affect the patient's quality of life and ability to work. EAM can be observed before or after the diagnosis of AS. Acute anterior uveitis (AAU) is seen in almost 20–30% of patients with AS.⁶ In their study, Stolwijk *et al* identified AAU before a diagnosis of AS in 12% of patients. They also showed that the prevalence of AAU was associated with the length of the disease and that the cumulative incidence increased following the first attack.⁷ Patients with chronic backache should be carefully examined in terms of EAM while making a diagnosis.

AS should be considered particularly if uveitis is present. Rudwaleit *et al*⁸ found that the prevalence of uveitis was 20.9% (with an average symptom period of 5.2 years) in 462 patients with axial SpA. In a French cohort study of patients with inflammatory backache, the prevalence of AAU was found to be 11.1% in 181 newly diagnosed AS patients (with an average symptom period of 1.6 years).⁹ Our patient, for example, showed signs of previous uveitis attacks and panuveitis.

Axial skeleton involvement and uveitis can be observed in brucellosis infections and is widely defined in the literature. Humans are infected via the consumption of raw meat and non-pasteurised dairy products that have been contaminated with brucellosis.⁵ Our patient had a history of consuming non-pasteurised milk and other dairy products. Brucellosis can mimic a great number of infections with an atypical course. In particular, when there is musculoskeletal involvement, the patient's history, serological test results and imaging findings should be assessed carefully. Osteoarticular disease is seen in 10–85% of patients and is the most common complication. Bone and joint lesions are present in patients with arthritis, bursitis, tenosynovitis, sacroiliitis, spondylitis and osteomyelitis. While sacroiliitis and peripheral arthritis are seen in children and teenagers, spondylitis is observed in older people. Brucellosis sacroiliitis has been reported with a rate of 0–72% in brucellosis infections that involve the musculoskeletal system. When diagnosing sacroiliitis, particularly during the early period of the disease, MRI should be the preferred method for evaluating bone marrow oedema and periarticular involvement. Subchondral sclerosis in the long term, and erosion and ankylosis in joints, can be seen. Our patient's MRI showed irregularities, cortical erosion and an obvious increase in subchondral sclerosis on the iliac wings. Brucellosis can present with various rates of ocular findings. Güngür *et al*¹⁰ reported ocular findings in 38 (26%) of 147 patients, and in those 38 patients, they reported anterior uveitis with a rate of 4.1% and posterior uveitis with a rate of 0.7%. Puig Solanes *et al*¹¹ found ocular symptoms in 60 (14.5%) of 413 patients. In the aetiological classification of 12 patients with ocular brucellosis, Rolando *et al*¹² reported that 6 (50%) had panuveitis, 2 (16.7%) had posterior uveitis, 3 (25%) had intermediate uveitis and 1 (8.3%) had anterior uveitis. In another study of 52 patients with ocular brucellosis, 21 (40%) had posterior uveitis, 9 (17%) had panuveitis, and 8 (15%) had anterior and intermediate uveitis.¹³ Our patient also had panuveitis; however, it was non-granulomatous. Because the patient's inflammatory joint symptoms and eye symp had been ongoing for approximately 4 years, and because the pattern of eye involvement brought spondylitis to mind, the uveitis was considered to be dependent on AS—AS reactivation induced by brucellosis.

Learning points

- ▶ In patients with uveitis, especially if there is chronic inflammatory backache, spondyloarthritis and particularly ankylosing spondylitis (AS) should be considered.
- ▶ In patients with uveitis and sacroiliitis, if there is history of consumption of unpasteurised milk and other dairy products, brucellosis infection in the endemic areas should be considered.
- ▶ An awareness of extra-articular manifestations is important in the diagnosis and treatment of patients, and in providing a good quality of life. Because the frequency of uveitis is associated with the period of the underlying disease, early diagnosis and treatment are of great importance.
- ▶ In the treatment of AS-induced chronic or refractory uveitis, antitumor necrosis factor agents such as infliximab can be used successfully.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Ali A, Samson CM. Seronegative spondyloarthropathies and the eye. *Curr Opin Ophthalmol* 2007;18:476–80.
- 2 Selmi C. Diagnosis and classification of autoimmune uveitis. *Autoimmun Rev* 2014;13:591–4.
- 3 Levy-Clarke G, Jabs DA, Read RW, *et al*. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. *Ophthalmology* 2014;121:785–96.e3.
- 4 Akgul O, Ozgocmen S. Classification criteria for spondyloarthropathies. *World J Orthop* 2011;2:107–15.
- 5 Sathyanarayanan V, Razak A, Saravu K, *et al*. Clinical profile of brucellosis from a tertiary care center in southern India. *Asian Pac J Trop Med* 2011;4:397–400.
- 6 Rudwaleit M, van der Heijde D, Khan MA, *et al*. How to diagnose axial spondyloarthritis early. *Ann Rheum Dis* 2004;63:535–43.
- 7 Stolwijk C, Essers I, van Tubergen A, *et al*. The epidemiology of extra-articular manifestations in ankylosing spondylitis: a population-based matched cohort study. *Ann Rheum Dis* 2015;74:1373–8.
- 8 Rudwaleit M, Haibel H, Baraliakos X, *et al*. The early disease stage in axial spondylarthritis: results from the German Spondylarthritis Inception Cohort. *Arthritis Rheum* 2009;60:717–27.
- 9 Dougados M, d'Agostino MA, Benessiano J, *et al*. The DESIR cohort: a 10-year follow-up of early inflammatory back pain in France: study design and baseline characteristics of the 708 recruited patients. *Joint Bone Spine* 2011;78:598–603.
- 10 Güngür K, Bekir NA, Namiduru M. Ocular complications associated with brucellosis in an endemic area. *Eur J Ophthalmol* 2002;12:232–7.
- 11 Puig Solanes M, Heatley J, Arenas F, *et al*. Ocular complications in brucellosis. *Am J Ophthalmol* 1953;36:675–89.
- 12 Rolando I, Vilchez G, Olarte L, *et al*. Brucellar uveitis: intraocular fluids and biopsy studies. *Int J Infect Dis* 2009;13:e206–11.
- 13 Rolando I, Olarte L, Vilchez G, *et al*. Ocular manifestations associated with brucellosis: a 26-year experience in Peru. *Clin Infect Dis* 2008;46:1338–45.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow