Concurrent rheumatoid arthritis and ankylosing spondylitis in one patient: the importance of new classification criteria

Valderilio Feijó Azevedo[1], Pedro Grachinski Buiar[2]

ABSTRACT

We report the case of concomitant ankylosing spondylitis and rheumatoid arthritis in a 65-year-old Caucasian male, who had symmetric polyarthritis with erosion of the metacarpophalangeal joint on conventional X-ray, inflammatory low back pain with HLA-B27 positivity, and sacroiliitis. Laboratory analysis showed high levels of rheumatoid factor and anti-cyclic citrullinated peptide antibody (anti-CCP). Clinical features of previously reported cases were compared with those of our case. This is the first case report on the coexistence of both diseases in the same patient, for whom anti-CCP testing and the latest versions of axial ASAS criteria and ACR/EULAR criteria for the classification of ankylosing spondylitis and rheumatoid arthritis, respectively, were used.

Keywords: rheumatoid arthritis, spondylitis ankylosing, disease classification, rheumatoid factor, HLA antigens.

INTRODUCTION

Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are chronic and progressive inflammatory joint diseases that lead to joint damage and functional disability. In the past, AS was included in the RA spectrum and considered an axial variant of that. Since the 1950s, when the rheumatoid factor (RF) 'appeared', several different characteristics have been established to differentiate those two rheumatologic disorders.[1] Currently, each disease has its own well-defined diagnostic criteria. To such criteria, laboratory tests that identify antibodies and genes related to each disease, such as HLA-DR4 and HLA-B27, have been added. The anti-cyclic citrullinated peptide antibody (anti-CCP), currently used in the diagnosis of RA, has been the main focus of studies. Coexistence of RA and AS in the same patient is rare. Of the almost 50 cases described in the literature, a large number was reported more than 30 years ago, when specific laboratory tests were not available and the classification criteria of both diseases were still largely debated.

Many of those cases have been published as an extremely rare occurrence.[2–4] In 1979, Major et al.[2] reported 2 cases and commented on 21 others that had already been described in the English literature. In 1995, Toussirot et al.[3] reported 3 more cases and, reviewing the literature, found 44 previous cases. Since then, some more cases have been added, but the frequency of their report has decreased. In this article, we report the diagnosis of RA and AS in the same patient by using the ASsessment in Ankylosing Spondylitis (ASAS) group criteria for axial AS and the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria along with anti-CCP testing for RA, which had not been performed in previous reports. Among the updated 2010 ACR/EULAR criteria for RA, anti-CCP testing is worthy of note.[5]

CASE REPORT

The patient is a 65-year-old retired Caucasian male, long-time smoker and alcohol drinker, who was admitted due to polyarthralgia and weight loss (5 kg in approximately 1.5 month).

Received on 05/14/2011. Approved on 11/26/2012. The authors declare no conflict of interest.
Universidade Federal do Paraná – UFPR.
1. Assistant Professor of Rheumatology, Universidade Federal do Paraná – UFPR
2. Medical school student, UFPR; Academic Coordinator, Scientific Initiation in Spondyloarthritis
Correspondence to: Valderilio Feijó Azevedo. Rua Lamenha Lins, 1110, ap. 11 – Rebouças. CEP: 80220-080. Curitiba, PR, Brazil. E-mail: valderilio@hotmail.com

The patient reported low back and chest pain initiated approximately 1 year and 4 months before, which worsened at night and improved with physical activities, in addition to morning stiffness for approximately 40 minutes. He also complained of mild pain in his right tarsal joints and right knee, with no edema associated, and that, two months before admission, moderate pain initiated on mobilization of both elbows and metacarpophalangeal joints. He denied cough, night sweating and fever in the period. He also denied any similar previous history, urethritis, intestinal symptoms or even a previous diagnosis of rheumatic disorder.

On physical examination, the patient was lucid and oriented, with a facial expression of pain. His general state of health was good. His cervical spine was stiff and had bilateral limited mobility (< 45º). On palpation, his lumbar spine was painful at the L3-L5 level. Schöber's tests, 10.0–11.6 cm; chest expandability, 2.1 cm; occipital-wall distance, 0 cm. His shoulders and elbows evidenced, bilaterally, an increase in volume and temperature, and limited mobility (extension). Both hands showed Bouchard and Herberden nodules, and atrophy of the interosseous muscles. His knees were tender on palpation and clicked with motion. A small erythematous cutaneous lesion was identified on the right knee, and was biopsied. No nodules were identified. His blood pressure was 145x95 mm Hg, heart rate, 125 bpm, and respiratory rate, 20 rpm. His laboratory exams were as follows: erythrocyte sedimentation rate (ESR), 111 mm/1h (up to 32.5 mm/1h); C-reactive protein (CRP), 9 mg/dL (normal: 0.5 mg/dL); hematocrit, 36.2%; hemoglobin, 11 g/dL; platelets, 429,000/mm^3; leukocytes, 8120/mm^3; RF, 633 IU/mL. Radiographies of the sacroiliac and lumbar spinal joints evidenced sclerosis of the sacroiliac joints bilaterally without erosions (grade 2), more evident on the right side, and syndesmophytes on L4 and L5 (Figure 1a). The biopsy of the skin lesion of the right knee revealed superficial perivascular chronic dermatitis, whose cause was not established, and not compatible with a psoriatic lesion. The exam was positive for HLA-B27. The patient was discharged following improvement after treatment with non-steroidal anti-inflammatory drugs and sulfasalazine. His scores were as follows: BASFI = 6.5; BASDAI = 5.8; DAS-28 = 5.5.

The patient returned only after one year, reporting general improvement of the pain in his knees, shoulders and hands. He also reported mild pain on the left second and third fingers two months before. The physical examination then showed the following: edema of the right second metacarpophalangeal joint, left second and third metacarpophalangeal joints and left elbow; pain on bone palpation of all metacarpophalangeal joints; edema and pain on palpation of the left acromioclavicular joint; increased volume and pain of the left second, third and fourth metacarpophalangeal joints; and increased volume of the right second metatarsophalangeal joint. His laboratory findings were as follows: RF, 526 IU/mL; CRP, 4.64 mg/dL; and ESR, 42 mm/1h. Radiography of his hands showed mild erosion of the right first metacarpophalangeal joint, reduced joint space, and reduced juxta-articular bone density (Figure 1b). The anti-CCP antibody titer was 525 (strong positivity > 60 Au).

His 2010 ACR/EULAR score for RA was 8 (positive diagnosis). At the time, the patient was diagnosed with RA and AS, and the following drugs were prescribed: diclofenac (150 mg/day), prednisone (7.5 mg/day) and methotrexate (15 mg/week). Currently, the patient is being followed up on the outpatient clinic, with indication for treatment with a biologic agent (tumor necrosis factor inhibitor – anti-TNF).

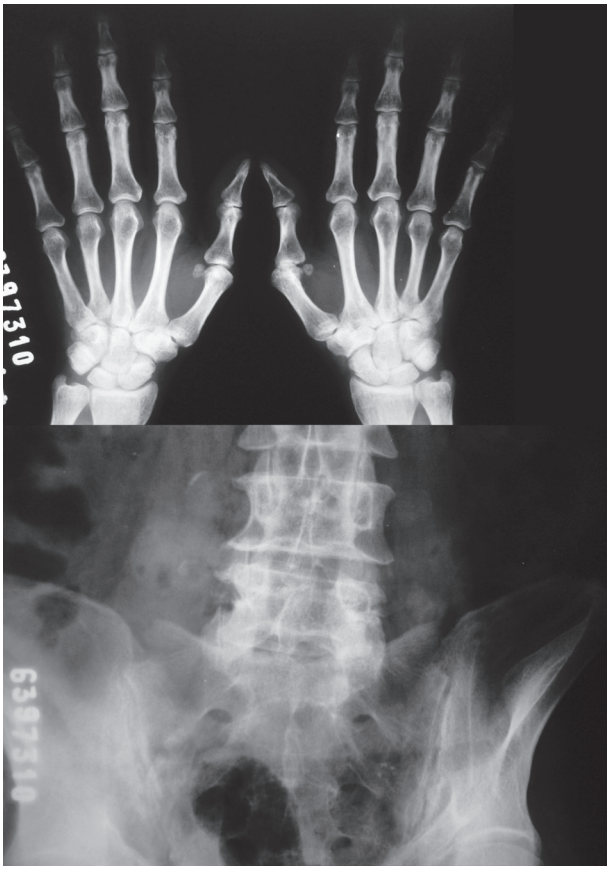

Figure 1
(A) Discrete erosion of the right first metacarpophalangeal joint, reduced joint space, and decreased juxta-articular bone density. **(B)** Sclerosis of the sacroiliac joints bilaterally without erosions, more evident at the right side (grade 2), and syndesmophytes on L4 and L5.

DISCUSSION

Physiopathological, clinical and diagnostic differences between RA and AS have been well established. Rheumatoid arthritis has prevalence of 1%–2% in the Caucasian population and is associated with the HLA-DR4 or DR1 genes (present in 60% of the patients).[6] Its incidence peaks between the ages of 40 and 70 years, and RA is more prevalent in the female sex. Ankylosing spondylitis has prevalence of 0.2%–0.9% in the Caucasian population and is associated with the HLA-B27 gene (present in approximately 95% of individuals with AS).[7–9] Although our patient can be considered elderly, AS has an incidence peak between the ages of 20 and 45 years, showing male predominance.[7] Rarely it occurs at more advanced ages. Although HLA-B27 has gained importance, in the genetic group with that histocompatibility antigen, the risk of developing AS is lower than 50%.[9]

Rheumatoid arthritis usually manifests as symmetric polyarthritis that affects the small joints of the hands and feet, metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal joints, rarely affecting entheses. It can affect the cervical spine. However, AS occurs most often as an inflammatory low back pain, which can be accompanied by enthesitis and asymmetrical oligoarthritis, preferably of axial and large joints, such as shoulders, hips and knees, its major characteristic being the involvement of the sacroiliac joints, and, at advanced stages, vertebral ankylosis at all levels.[10]

The most common extra-articular manifestations of RA are subcutaneous nodules, keratoconjunctivitis sicca, pleural and pericardial involvement, and vasculitis. Ankylosing spondylitis, however, can manifest as psoriasis, acute anterior uveitis, fibrosis of the pulmonary apex, inflammatory bowel disease, heart valve problems, and heart electrical conduction disorders.[11] Aggravation of gastrointestinal lesions and peptic ulcers with the use of non-steroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs (DMARDs) is common in both diseases.[12]

In RA, there is evidence of bone resorption in the form of erosions. In AS, there is bone erosion associated with bone neoformation in the form of syndesmophytes. It is worth noting that finding bilateral sacroiliitis is highly suggestive of AS. In our patient's case, the radiologic findings of juxta-articular osteopenia, erosion of the right first metacarpophalangeal joint, and bilateral sacroiliitis with syndesmophytes on L4 and L5 supported both diagnoses.

The CRP and ESR levels are parameters frequently used to show inflammatory activity, being also criteria for the clinical activity monitoring of both diseases, being elevated in most patients with active RA, but also in 50%–60% of the patients with active AS.[13] The RF is almost always present in patients with RA (around 70%–90%), and their levels can be directly correlated with disease severity. Nevertheless, the RF is not specific, being also present in a series of other clinical conditions. Although 10%–15% of the patients with spondyloarthritis might have RF, their titers are usually lower,[6] unlike this case, whose titers were elevated. A extremely specific test developed at the end of the 1970s is anti-CCP antibody testing. Although present in only 67% of the patients with RA, according to the meta-analysis carried out in 2005 by Visser,[14] a positive result is highly specific (> 96%) for the diagnosis of RA. It is currently considered the most specific marker for the diagnosis of RA, as recently reported by Zhao et al.[15] Anti-CCP antibodies and RF are not usually found in patients with AS.[6] Our patient had high titers of RF and anti-CCP antibodies associated with the arthritis of the hands, feet and elbows, indicating RA concomitant with AS, HLA-B27 positive, with inflammatory low back pain and sacroiliitis.

The classification criteria for RA have been recently reviewed by the ACR and the EULAR.[5] According to the new ACR/EULAR classification (2010) for RA, patients have to add 6 points of some characteristics, considering that they have at least one synovitis not explained by another disease.

According to such classification criteria for RA, our patient had the involvement of 2 large and 3 small joints, high titers of RF and anti-CCP antibodies, abnormal CRP and ESR levels, and symptoms for over 6 weeks. Considering all that, his total score was 8, and he could be classified as having RA.

According to the modified New York criteria for AS, our patient had bilateral sacroiliitis (grade 2, right side), characteristic inflammatory low back pain, and reduced low back mobility and chest expandability. Furthermore, according to the ASAS classification criteria for axial spondyloarthritis, our patient had his diagnosis confirmed by being HLA-B27 positive and having sacroiliitis, in addition to inflammatory low back pain and high CRP levels.

Based on the criteria cited, our patient can be classified as having both diseases: RA and AS. According to the literature, 45 cases of the concomitance of both diseases have been reported.[3]

Most of the previous reports have used clinical data and not all have assessed the presence of either HLA-B27 to support the hypothesis of AS or RF to support the hypothesis of RA (Table 1). Toussirot et al.[3] have reported a prevalence of 6.6% of HLA B27-positive patients with RA and of 8.3% of RF-positive patients with AS versus a prevalence of 9.8% of controls, although the results had no statistical significance.

Table 1
Review of the reports about patients with concomitant rheumatoid arthritis and ankylosing spondylitis

Reference	First symptom (n of cases)	Nodules	PEA	RF	HLA-DR4	Anti-CCP	Low back pain	Sacroiliitis	Syndesmophytes	HLA-B27
Rosenthal et al.	Low back pain (1)	+	ND	+	ND	ND	+	+	+	ND
Rotés Querol et al.	Low back pain (7)	2+	3+	7+	ND	ND	7+	7+	2+	7+
Luthra et al.	Low back pain (2)	2+	2+	2+	ND	ND	2+	2+	2+	2+
Good et al.	Low back pain (3)	0+	3+	3+	ND	ND	3+	3+	3+	3+
Fallet et al.	Low back pain (5) Polyarthritis (7) Oligoarthritis (1) Cervical pain (1) Iritis (1)	6+	14+	15+	7+	ND	11+	15+	11+	15+
Clayman et al.	Low back pain (1)	+	+	+	ND	ND	+	+	+	+
Espinoza et al.	Low back pain (1)	+	+	+	ND	ND	+	+	+	+
Major et al.	Low back pain (2) Low back pain (1) Polyarthritis (1) ND (3)	1+; 5 ND	7+	7+	3+; 2 ND	ND	2+; 5 ND	7+	2+; 3 ND	5+
Lavery et al.	Low back trauma (1)	+	+	+	ND	ND	+	+	+	+
Alarcón-Segovia et al.	Low back pain (1)	+	+	+	+	ND	+	+	+	+
Sattar et al.	Polyarthritis (1)	–	+	+	+	ND	+	+	+	+
Helfgott et al.	Low back pain (1)	+	+	+	+	ND	+	+	+	+
Martinez et al.	Oligoarthritis (1)	–	+	+	+	ND	+	+	+	+
Toussirot et al.	Polyarthritis (2) Cervical pain (1)	1+	2+; 1 ND	2+	0+	ND	3 +	+	1+	1+; 2 ND
Genc et al.	Polyarthritis (1)	–	+	–	–	ND	+	+	+	+
Our report	Low back pain (1)	–	+	+	ND	+	+	+	+	+
Total: 47 cases	Low back pain (18) Low back pain (8) Polyarthritis (12) Oligoarthritis (2) Cervical pain (2) Low back trauma (1) Iritis (1) ND (3)	21+	40+	45+	10+	1+	38+	45+	31+	42+

(+): presence of the item/symptom; (–): absence of the item/symptom; (ND): presence/absence of the item not specified by the author; PEA: peripheral erosive arthritis; RF: rheumatoid factor.
*For this review table, only articles published in English were considered.
This is the first case report using the last updates of the ACR/EULAR and the ASAS classification criteria for RA and AS, respectively, and anti-CCP antibody testing. We consider appropriate that future reports about the concomitance of RA and AS use anti-CCP testing in addition to the latest criteria for the diagnosis and classification of that rare association.

1. Benedek TG. How did ankylosing spondylitis become a separate disease? Clin Exp Rheumatol 2009; 27(4 Suppl 55):S3–9.
2. Major P, Resnick D, Dalinka M, Kline P. Coexisting rheumatoid arthritis and ankylosing spondylitis. AJR Am J Roentgenol 1980; 134(5):1076–9.
3. Toussirot E, Acquaviva PC. Coexisting rheumatoid arthritis and ankylosing spondylitis discussion of 3 cases with review of the literature. Clin Rheumatol 1995; 14(5):554–60.
4. Fallet GH, Mason M, Berry H, Mowat A, Boussina I, Gerster JC. Coexistence of rheumatoid arthritis and ankylosing spondylitis-report of 10 cases. J Rheumatol Suppl 1977; 3:70–3.
5. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010; 62(9):2569–81
6. van der Horst-Bruinsma IE, Lems WF, Dijkmans BA. A systematic comparison of rheumatoid arthritis and ankylosing spondylitis. Clin Exp Rheumatol 2009; 27(4 Suppl 55):S43–9.

7. van der Linden SM, Valkenburg HA, de Jongh BM, Cats A. The risk of developing ankylosing spondylitis in HLA-B27 positive individuals. A comparison of relatives of spondylitis patients with the general population. Arthritis Rheum 1984; 27:241–9.
8. Will R, Edmunds L, Elswood J, Calin A. Is there a sexual inequality in ankylosing spondylitis? A study of 498 women and 1202 men. J Rheumatol 1990; 17:1649–52.
9. Maksymowych WP, Brown MA. Genetics of ankylosing spondylitis and rheumatoid arthritis: where are we at currently, and how do they compare? Clin Exp Rheumatol 2009; 27(4 Suppl 55):S20–5.
10. Khan MA. Ankylosing spondylitis: clinical aspects. The spondylarthritis. A. Calin, Taurog J (eds.). Oxford University Press, 1998.
11. Heeneman S, Daemen MJ. Cardiovascular risks in spondyloarthritides. Curr Opin Rheumatol 2007; 19(4):358–62.
12. de Leest H, van Dieten H, van Tulder M, Lems WF, Dijkmans BA, Boers M. Costs of treating bleeding and perforated peptic ulcers in The Netherlands. J Rheumatol 2004; 31:788–91.
13. Spoorenberg A, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, et al. Relative value of erythrocyte sedimentation rate and C-reactive protein in assessment of disease activity in ankylosing spondylitis. J Rheumatol 1999; 26(4):980–4.
14. Visser H. Early diagnosis of rheumatoid arthritis. Best Pract Res Clin Rheumatol 2005; 19(1):55–72.
15. Zhao J, Liu X, Wang Z, Liu R, Li Z. Is it necessary to combine detection of anticitrullinated protein antibodies in the diagnosis of rheumatoid arthritis? J Rheumatol 2010; 37(12):2462−5.