Is it worth investigating coeliac disease in patients with rheumatic disorders?

Sirs, Gastrointestinal complaints are common in patients with rheumatic diseases, and some authors have related inflammatory response in the gut of patients to rheumatic diseases [1–3]. Although many of these complaints may be due to the use of medications such as NSAIDs, MTX or LEF [4], they may also be caused by the disease itself. Patients with spondyloarthritis suffer from inflammatory process in the intestinal mucosa [1]; the same happens with RA although to a lesser degree [2]. Individuals with scleroderma may have motility disorders, bacterial overgrowth, diarrhoea and malabsorption [3]. The knowledge of the cause of gastrointestinal complaints in the patients is important in order to treat them properly.

There is evidence that patients with an autoimmunity disorder may be predisposed to other concomitant autoimmune disease [5]. This association may be due to a shared genetic predisposition or exposure to a common triggering event [5]. Some of these associations are quite common and often the diagnosis of a first disease is followed by the search for a second simultaneously. Coeliac disease (CD) is a chronic inflammatory and immunologically mediated intestinal disease that causes life-long sensitivity to gliadin, a protein found in barley, wheat, rye and oat [6]. It affects nearly 1% of Western populations [7], and in Brazil it affects ~0.2% of the population [8]. The classical presentation of CD includes diarrhoea, abdominal pain and nutritional deficiencies due to malabsorption. However, clinical symptoms could be misleading in most of the patients, mainly adults presenting subclinical forms, with only minor gastroenterological symptoms, such as dyspepsia [6].

Screening for CD in patients with autoimmune disease such as thyroiditis, diabetes mellitus type 1 and autoimmune liver diseases is always recommended [7]. There are few studies describing the association of CD with rheumatic autoimmune systemic diseases. The occurrence of these autoimmune diseases concomitantly may cause inadequate interpretation of the aetiology of gastrointestinal symptoms. Furthermore, the intestinal damage caused by CD could be disrupting to treatment, as it may lead to incomplete absorption of prescribed drugs or lack of compliance with the therapeutic regimen.

Although intestinal biopsy is still considered the gold standard for CD diagnosis, serological tests have been widely used in screening because of their high sensitivity and specificity and because it is not an invasive procedure [9]. Anti-endomisial (IgA-EmA) antibody has over 90% specificity and sensitivity for CD diagnosis [9].

In this study, we investigated the association of CD in Brazilian rheumatic patients after receiving approval from the Ethics Committee of the Evangelical University of Paraná and with the patients’ formal written consent. A total of 380 individuals from a single rheumatic outpatient clinic were included: 156 with RA; 105 with scleroderma (59 with limited form, 36 with diffuse form, 1 sine scleroderma and 9 with scleroderma associated with myositis); 70 spondyloarthritis patients (41 with AS, 19 with undifferentiated form, 4 with reactive arthritis and 6 with PsA); 49 adult patients with JIA (2 with enthesis-related arthritis form, 16 with oligoarthritis, 2 with systemic onset, 6 with RF-positive polyarthritis and 23 with RF-negative polyarthritis). One hundred healthy individuals from the same geographical area were included as controls. The rheumatic patients sample comprised 297 females and 83 males. The mean age was 45.5±15.8 years. In the control group, the mean age was 47.6±15.8 years (P = 0.35), and there were 18 males and 82 females (P = 0.70).

All the samples were screened for IgA-EmA through indirect immunofluorescence assay, using human umbilical cord as substrate and fluorescein-conjugated anti-human IgA (DAKO, Copenhagen, Denmark) as conjugate, as previously described [10]. Positive and negative controls were included in each test battery. The slides were examined by fluorescence microscopy (Olympus, Tokyo, Japan) by two experienced observers. All patients and controls evaluated were negative.

The data obtained in this study differ from those of other authors, however, in that most of the studies used ELISA kits to investigate anti-gliadin or anti-tissue transglutaminase antibodies [11–13]. In those reports, the positivity of autoantibodies is higher than observed in the present study; however, in general, CD was not confirmed in the duodenal biopsy. These authors suggest that this positivity probably is non-specific for the presence of CD among autoimmune rheumatological disease patients. Therefore, the differences observed may be caused by the methodology used and the influence of genetic background of the studied population, allied to differences in geographical and environmental conditions.

Therefore, based on our investigations, we suggest that the presence of rheumatic disease such as RA, JIA, spondyloarthritis or scleroderma does not increase the risk of CD in Brazilian individuals.

Rheumatology key message

- Patients with systemic rheumatic disorders do not have a higher risk of coeliac disease.
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Fulminant course of osteonecrosis of the jaw in a rheumatoid arthritis patient following oral bisphosphonate intake and biologic therapy

Sir, Bisphosphonate-associated osteonecrosis of the jaw (BONJ) is a serious adverse event of bisphosphonate (BP) therapy. BONJ affects exclusively the maxillofacial bones and is defined as exposed necrotic jaw bone lasting longer than 8 weeks in patients under BP treatment and lacking a history of radiation therapy [1]. BPs are given intravenously in metastatic bone disease [2] and increasingly in oral preparations for the treatment of osteoporosis [3]. BONJ aetiology has been linked to infection [4] and immunosuppressive drugs are common in the treatment of RA. Therefore, BP therapy might be an important co-factor in the proper selection of medication for patients with RA. Here we report about a fulminant course of BONJ in an oral BP patient under treatment with IL-6 receptor antagonist tocilizumab for RA.

A 74-year-old female presented in January 2007 with a left-sided perimandibular abscess. Previously tooth 35 had been extracted. Her general medical history revealed osteoporosis and severe RA. The patient had received a 20-month course of oral BP therapy (risedronate, 35 mg/week) from February 2005 until October 2006 (cumulative dose 3080 mg) for the treatment of osteoporosis. The patient was treated for RA with infliximab, an anti-TNF-α antibody (200-400 mg i.v. every 6-8 weeks from July 2005 until October 2008), in combination with MTX (15 mg/week from May 2004 until December 2008), folic acid (10 mg/week), prednisolone (5 mg/day from May 2004 until December 2008, cumulative dose 4850 mg), ibuprofen (1800 mg/day), pantoprazol (40 mg/day) and calcium plus vitamin D3 (500 mg/10 µg 2×/day). Treatment consisted of incision and drainage of the abscess under general anaesthesia and high-dose i.v. antibiotic treatment with clindamycin requiring 5 days of inpatient care. Three months later the patient presented with signs of advanced BONJ showing exposed bone and extra-oral fistula formation located in the left mandible. A panoramic radiograph showed persistent extraction sockets surrounded by periapical hypermineralized lines in the left mandible. Her anti-rheumatic medication was as stated above. The previous dose of infliximab had been given 8 weeks before. Surgical treatment including sequestrectomy was followed by gastric tube feeding for 10 days. After discharge, the woman was followed up bimonthly in our outpatient clinic. In