Immunoglobulin A Nephropathy in Rheumatic Diseases

Nefropatía IgA en las enfermedades reumáticas

To the Editor,

Immunoglobulin A nephropathy (IgAN) is a glomerulopathy characterized by the presence of mesangial deposits of IgA, either alone or showing predominance over other immunoglobulins. The pathological study enables the diagnosis and evaluation of the disease activity. Its association with rheumatic diseases has been reported; however, the pathophysiological relationship is still not clear. For the purpose of establishing the prevalence, clinical features, analytical findings, treatment and outcome of IgAN in a cohort of patients with rheumatic disease, we conducted a retrospective study (1984–2014) in a university hospital serving a population of 850,000. We reviewed the pathological diagnoses of 27,215 patients being treated in the rheumatology department and selected those with a histological diagnosis of IgAN. We excluded the patients in whom the only rheumatic disease diagnosed was gout, osteoporosis or noninflammatory disease. We identified 6 patients (0.025%), all men. Of 1110 patients with rheumatoid arthritis, 2 (0.009%) had been diagnosed with IgAN. Of 287 patients with ankylosing spondylitis, 2 (0.69%) had IgAN. Only 1 (0.17%) of the 558 patients with psoriatic arthritis had received a diagnosis of IgAN, as was the case of 1 of the 13 patients (0.7%) with undifferentiated connective tissue disease. The mean age at the diagnosis of IgAN and of the rheumatic disease was 46.7 and 37 years, respectively (range: 34–54 and 18–67 years). The mean duration of the rheumatic disease prior to the diagnosis of IgAN was 15.4 years. Hematuria (100%), renal failure (100%) and nephrotic syndrome (8.6%) were the signs that led to the suspicion of the presence of IgAN. All 6 patients had hypertension and 8.6% had nephrotic-range proteinuria. The mean values of serum creatinine and 24-h proteinuria at the time of the diagnosis of IgAN were 1.85 mg/dL (range: 1.5–2.5) and 1.94 g (range: 0.8–4.12), respectively. Over the course of the disease, 3 patients (50%) required hemodialysis after a mean period of 5.6 years since the diagnosis (range: 2–11); all 3 underwent renal transplantation within an interval of 9–25 months after starting hemodialysis. One patient (16.6%) died at the age of 60 years (7 years after the diagnosis of IgAN) due to sepsis of pulmonary origin. During follow-up, the mean creatinine levels of the patients who did not receive dialysis was 1.4 mg/dL (range: 1.1–1.6); they were treated medically (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers).

The prevalence of IgAN in the general population is 25–50 cases per 100,000 population and, although in the majority of patients with chronic inflammatory arthropathy, renal involvement is secondary to amyloidosis or an adverse drug reaction, there are reports that indicate the possible relationship between rheumatic diseases and IgAN. Given the prevalence of IgAN in the general population, in some cases, its coexistence with a rheumatic disease may be coincidental. In patients with spondyloarthropathies, the relationship would be explained by the reported change in the catabolism of glycoprotein receptors and IgA-specific receptors (FceRI and CD89) found in tissue and peripheral blood.

The results of the present study do not differ from previous findings reported in the literature. The prevalence is higher in men and the clinical presentation is characterized by proteinuria, hypertension and hematuria. The cohort of patients of Azevedo et al. showed a higher frequency of calcaneal enthesis and anterior uveitis. In accordance with our observations, in clinical practice, the diagnosis of IgAN should be considered in patients with a rheumatic arthropathy who develop hematuria, proteinuria, renal failure and hypertension during the course of their disease.

References
Septic Arthritis by *Streptococcus equi*<sup>5</sup>

**Arthritis infecciosa por Streptococcus equi**

To the Editor,

*Streptococcus equi* is a Gram-positive, Lancefield group C cocal bacterium that has a close genetic link to *Streptococcus zooepidemicus*,<sup>1</sup> of which it is thought to be a direct ancestor, and is the cause of less than 2% of all the group C streptococcal infections.<sup>2</sup> It is a common pathogen in horses, cows and dogs, and can be isolated from the serous discharge of wounds.<sup>3</sup>

*Streptococcus equi* infection has been documented in humans who are in direct or indirect contact with animals, especially horses, although in most cases, the route of transmission has not been clarified.<sup>4</sup>

We report a case of septic arthritis caused by *Streptococcus equi* in a person who may have acquired the infection through a relative who was in contact with horses. The patient was a 72-year-old woman who presented with a 4-day history of pain, swelling and functional limitation in right knee. She had had no injuries. Her granddaughter was a veterinarian at a racetrack. She had a temperature of 38.5 °C, increased knee volume, fixed flexion of 30°, erythema and local warmth. There was no evidence of tegmental damage either in or around the knee. Ultrasound showed degenerative changes in the knee, a compressible anechoic area in both suprapatellar recesses associated with a marked proliferation of homogeneous synovial fluid (SF) (Fig. 1) and the power Doppler signal was 1+/3+. In the other knee, only similar degenerative changes were observed.

Arthrocentesis yielded 90 mL of synovial fluid with inflammatory features.

The results of laboratory tests included a leukocyte count of 16,000/mm<sup>3</sup> (90% neutrophils), C-reactive protein level of 210 mg/L and procalcitonin level of 1.70 ng/mL. In SF, there were no signs of microorganisms, the cell count was 20,000 cells/mL, and the glucose and protein concentrations were 30 mg/dL and 2.3 g/dL, respectively.

The patient underwent surgical lavage and was admitted to the hospital, and empirical treatment with ceftriaxone 2 g/day and cloxacillin 500 mg/6 h was begun.

As SF and peripheral blood cultures were positive for *Streptococcus equi*, treatment was changed to 1,200,000 U/day of penicillin G. As the patient’s fever and pain persisted, surgical lavage was repeated 10 days after her admission. The outcome was favorable and she was discharged after 5 weeks of intravenous therapy.

*Streptococcus equi* is a pathogen that causes “strangles”, a lymphoproliferative disease that can affect horses, donkeys and cattle, although subclinical infection has also been documented in dogs.<sup>1,2</sup> This disease produces enlargement of the cervical lymph nodes and is associated with upper airway symptoms in animals. The lymphocyte proliferation can produce skin necrosis and neck abscesses. Both the serous discharges from abscesses and saliva of the diseased animal are sources of transmission to other animals or to humans.<sup>3,4,5,6</sup> Infection in humans mediated by the consumption of dairy products from infected animals has also been documented.<sup>5,6</sup>

Although a number of cases of *Streptococcus equi* infection have been reported in humans,<sup>2,10-13</sup> septic arthritis is a highly uncommon finding.<sup>5,11,14-16</sup> Information on the epidemiological burden of this pathogen as the causative agent is not available.

A history involving a connection to horses, as occurred in our patient, has not been demonstrated in most of the case reports.<sup>17</sup> However, despite this link, it was not possible to determine the mechanism that produced the infection.

*Streptococcus equi* infection responds favorably to treatment with penicillins, although cases of drug resistance have been reported and the clinical course is variable.<sup>17</sup>

Another interesting finding was the marked synovial proliferation, which could hardly be attributed to the similar degenerative changes in both knees.

*Streptococcus equi* is an uncommon cause of arthritis due to group C streptococci that should be considered in the differential diagnosis of arthritis in a single joint in patients who are in contact with animals, especially horses. The clinical course is variable and, although, theoretically, it is sensitive to beta-lactams, antibiotic resistance has been documented. Our patient also had a marked synovial proliferation and an increased procalcitonin level, but the cellularity in SF was not consistent with joint infection. This protein is a precursor of calcitonin, and has been included as a key test in the diagnosis of inflammatory processes mediated by bacterial agents. Its concentration increases within the first 6 h of the production of bacteremia, and its specificity ranges between 91% and 93%, depending on the disease.<sup>18</sup> A recent study demonstrated the value of procalcitonin in cases in which the suspicion of septic arthritis overlapped that of gout.<sup>19</sup> It was this finding that, despite

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