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Case Report Open Access

Primary Sjogren's Syndrome Presenting as Osteomalacia

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Abstract

Background: The most common renal disease in Sjogren's syndrome (SjS) is tubulo-interstitial nephritis, which is responsible for renal tubular acidosis type 1 (RTA-1) in around 20% of patients. Osteomalacia rarely occurs as the first manifestation of a renal tubule disorder due to a connective tissue disease such as SjS.

Results and conclusion: We report a 47-year-old woman with tubular acidosis induced osteomalacia. The tubular acidosis was a result of renal involvement in SjS. Improvement was obtained with vitamin D, calcium, and high-dose steroid therapy. These findings suggest that evidence for SjS should be sought in adult patients with unexplained osteomalacia and renal tubular acidosis, even in the absence of subjective sicca syndrome. Conversely, in patients with SjS, early investigation and treatment of renal tubular dysfunction may prevent future complications, such as osteomalacia.

Keywords: Sjogren's syndrome; Osteomalacia; Renal tubular acidosis

Introduction

Sjögren's syndrome (SjS) is an autoimmune disorder involving exocrine glands. Latent renal tubular diseases are common in SjS. The Renal dysfunction is dominated by Tubulointerstitial nephritis. A renal tubular acidosis type 1 (RTA-1) is the usual pattern. Rarely, the secondary renal tubular acidosis to the SjS can be revealed by an osteomalacia. Here, we describe a case of primary SjS presenting as osteomalacia secondary to renal tubular acidosis.

Case report

A 47-year-old woman, without particular pathological antecedents complained from bilateral thigh pain for 1 year, which followed a limitation of her walking ability. She had not any extra-articular complaint. At admission, she had no fever and her march was waddling. The neurological exam found a motor deficit of the pelvic belt. There was no joint pain or evidence of arthritis. Musculoskeletal radiography (pelvis, spine, ribs and long bones) were normal. An isotope bone scan showed increased uptake at the seventh and eight right ribs, on the left femoral neck and in the pubic rami. The MRI showed a fissure on the left femoral neck. Laboratory tests showed severe inflammation (erythrocyte sedimentation rate, 105 per hr; and polyclonal hypergammaglobulinemia, 20 g/L). Decreases were found in urinary and serum calcium (2 mmol/24 hr and 2 mmol/L), suggesting the diagnosis of osteomalacia. The etiologic appraisal was negative first-line. Serum alkaline phosphatase was normal and parathyroid hormone was 77 mmol/L. Therefore, serum electrolyte assays showed metabolic acidosis with low potassium (2.9 mmol/L), however, urinary PH was inappropriate (6.5), confirming the diagnosis of renal tubular acidosis. Besides, proteins were found in the urine (0.94 g/24 hours) and renal function was satisfactory. Findings were negative from urine cytology and microbiology. Although she has not sicca syndrome, the lip salivary gland biopsy revealed Chisholm stage 3 lesions; and an ophtalmological examination revealed diminished tear secretion by the Schirmer test (0 mm for both eyes). Antinuclear antibodies (AAN) were present in a titer of 1/1600 and regarding the typing; only Anti - SSA and anti - SSB were positive. Rheumatoid factor was well positive. A renal biopsy showed chronic tubulointerstitial nephritis with an important lymphocyte infiltration. The survey in immunofluorescence was negative. Thus the diagnosis was osteomalacia caused by renal tubular acidosis complicating tubulointerstitial nephritis as part of Sjögren's syndrome. A corticosteroid (0.5 mg/kg), vitamin D (Ergocalciferol: 8000 IU/day), and calcium supplements (1 g per day) were given. A month later, the clinical features were improved (she described an improvement of pain and capacity to walk again). The high dose of both, corticosteroid and vitamin D was maintained until the normalization of the laboratory test. Then a gradual degression had started.

Discussion

Renal involvement appears to represent one of several systemic changes occurring SjS [1]. Their frequency isn't rare although rates vary widely across studies. Chronic tubulointerstitial nephritis (TIN) is the usual pattern, although it's generally accepted that glomerulonephritis (GMN) is uncommon [2]. Distal renal tubular acidosis (RTA-1) is the most common clinical manifestation of TIN related to SjS (20% - 70%). However, the proximal renal tubular acidosis (RTA-2), whether associated to Fanconi syndrome or not, is rare [1,3]. RTA-1 is a condition characterized by an inability of the distal nephron to acidify the urine [4]. The pathogenesis of RTA-1 as noted in SjS patients is thought to be closely related to the development of TIN. Some cases of RTA-1 are associated with genetic abnormalities of the collecting tubule anion exchanger (band 3) [5] or of the hydrogen-adenosine triphosphatase pump [6]. Other patients have had hyperglobulinemic autoimmune disorders, often SjS, and still other cases are due to a toxin such as amphotericin [7]. The patients with RTA-1 have significantly higher baseline levels of serum total gamma-globulin, serum protein, and serum beta-2 microglobulin compared to

those with normal acidification capacity. In those with subsequent proteinuria, the levels of serum beta-2 microglobulin were almost significantly higher at baseline compared to those with normal urinary protein excretion. Based on these facts, it was been suggested that the high levels of serum total gamma-globulin, serum protein and serum beta-2 microglobulin were the best predictors of the development of RTA-1 during SjS [8].

Osteomalacia rarely occurs as the presenting manifestation of SjS. Its incidence in SjS patients with RTA- 1 has been reported to range from 25% to 45% [9]. RTA-1 is often latent [1,2]. It's rarely appears by a defect of urine concentration and a hyperchloremic metabolic acidosis with an alkali urinary pH, superior to 5.3 as found in our case. A symptomatic hypokaliemia with cramps or paralysis can complicate The RTA-1. Unusually, the osteomalacia can reveal a secondary RTA-1 to the SjS. To our knowledge, only 19 cases have been previously described in the literature [2,3,9,10,12].

Pathophysiological mechanisms remain unclear. We undertook this survey to try to elucidate the relations among RTA1, SjS, and osteomalacia in adults. The pathogenesis of osteomalacia based on RTA-1 is considered to be as follows: 1) a low production of activated vitamin D3 by renal tubular impairment, 2) activated osteoclasts in the bones due to a high excretion of parathyroid hormones, 3) an acceleration of calcium transition from the bones in highly acidic conditions, and 4) a reduction of calcium reabsorption in the uriniferous tubules [13].

The standard therapy for RTA-1 consists of an alkali supplement with sodium bicarbonate, supplemental vitamin D and a correction of the electrolyte levels. Correcting the acidosis may be sufficient [10,14]. In cases with strong lymphocyte infiltration based on the histological findings of biopsied renal samples, as it was proved in our patient, steroids might be indicated [15]. High-dose Corticosteroid therapy has been used successfully in patients with osteomalacia related to renal tubular acidosis [16].

SJS should be considered as an etiology of osteomalacia, especially when first explorations are negatives and even without sicca syndrome like in our case.

In conclusion, during SjS, osteomalacia can complicate the RTA-1. In spite of the rare cases of osteomalacia revealing SjS, this auto-immune disease must appear in the aetiologies osteomalacia list. Conversely, in patients with SjS, early investigation and treatment of renal tubular dysfunction may prevent future complications, such as osteomalacia. Through treatment with alkali supplement, vitamin D or steroids, RTA-1 and osteomalacia were remarkably improved, although far larger numbers of patients would be needed to confirm this.

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