Majorensis 2013; **9**: 31-34 www.majorensis.es

Majorensis
ISSN 1697-5529

Polyarticular involvement in a patient with Hashimoto's disease

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Recibido 11-Diciembre-2013; revisado 16-Diciembre-2013; aceptado 19-Diciembre-2013

Summary
Polyarticular involvement in a patient with Hashimoto's disease.
Polyarthritis that occurs in patients with Hashimoto's thyroiditis can be due to an associated autoimmune disorder such as rheumatoid arthritis or it can be a direct manifestation of myxedema. We report the case of a patient with Hashimoto's thyroiditis who presented with a seronegative symmetrical polyarthritis that was probably secondary to hypothyroidism. This manifestation has been uncommonly reported
Key words: Arthritis. Autoantibodies. Autoimmune thyroiditis. Hashimoto disease. Hypothyroidism. Myxedema
Resumen
Afectación poliarticular en un paciente con enfermedad de Hashimoto
La poliartritis que ocurre en pacientes con tiroiditis de Hashimoto puede ser debida a enfermedades autoinmunes como la artritis reumatoide o puede ser una manifestación directa del mixedema. Se comenta el caso de un paciente con tiroiditis de Hashimoto que presentó una poliartritis seronegativa simétrica probablemente secundaria al hipotiroidismo. Esta manifestación ha sido descrita muy raramente.
Palabras clave: Artritis, Autoanticuerpos, Autoinmune, Tiroiditis, Enfermedad de Hashimolto, Hipotiroidismo, Mixedema.

Introduction

Hashimoto's thyroiditis is a common autoimmune entity which mainly affects elderly individuals, usually leading to hypothyroidism. Due to its autoimmune nature, it is frequently accompanied by other autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus, vitiligo, type 1 diabetes mellitus, celiac disease, Addison's disease, myasthenia gravis, and pernicious anemia [2]. In this sense, it is not exceptional to find signs of polyarthritis in patients affected by Hashimoto's thyroiditis.
LeRiche and Bell studied patients with Hashimoto's thyroiditis and polyarthritis, and described a subset that was rheumatoid factor-positive and another subset that had seronegative inflammatory polyarthritis [6]. This case series differed from that described by Bland and Frymoyer in which polyarthritis without inflammatory features was the principal manifestation of myxedema and it resolved with thyroid replacement therapy. These authors cite studies of experimental hypothyroidism in which the deposition of hyaluronic acid in skeletal and smooth muscle leads to muscle necrosis and synovial effusions [1].
We have recently treated a patient with hypothyroidism who presented with a relatively indolent symmetrical polyarthritis. His clinical evolution suggested that the polyarthritis could be a direct manifestation of myxedema in Hashimoto's disease. This association has been rarely described.

Case report

A 65 year old patient was admitted to our hospital with a 15-day history of painful swelling of multiple joints, particularly wrists, proximal interphalangeal joints of both hands, and his right shoulder. He also complained of joint stiffness in the morning that lasted approximately 1 hour and improved after mobilization. On focused anamnesis he denied drowsiness, constipation, weight gain, and other symptoms of hypothyroidism besides cold intolerance. On physical examination, a striking feature was a relative lack of inflammatory signs besides slight warmth on some of the affected joints (Fig.1). His heart rate was around 60 bpm. No further remarkable signs were found.
Laboratory evaluation was consistent with an intense inflammatory reaction. His blood count revealed leukocytosis (total white blood cell count 13400/mm3 with 78.4% neutrophils) and a C-reactive protein greater than 90 mg/l. Rheumatoid factor and antibodies to cyclic citrullinated peptide were negative. The only relevant findings on autoimmunity testing were a positive ANA (1/80 titre, homogenous pattern) that was later negative on a follow-up visit, and a positive p-ANCA (although MPO and PR3 antibodies were negative). A bone scintigraphy using 99mTc showed increased uptake in bilateral metacarpophalangeal, proximal, and distal interphalangeal joints (Fig 2). It also revealed uptake in the lower dorsal and lumbar spine compatible with osteoarthritis.

Majorensis
ISSN 1697-5529

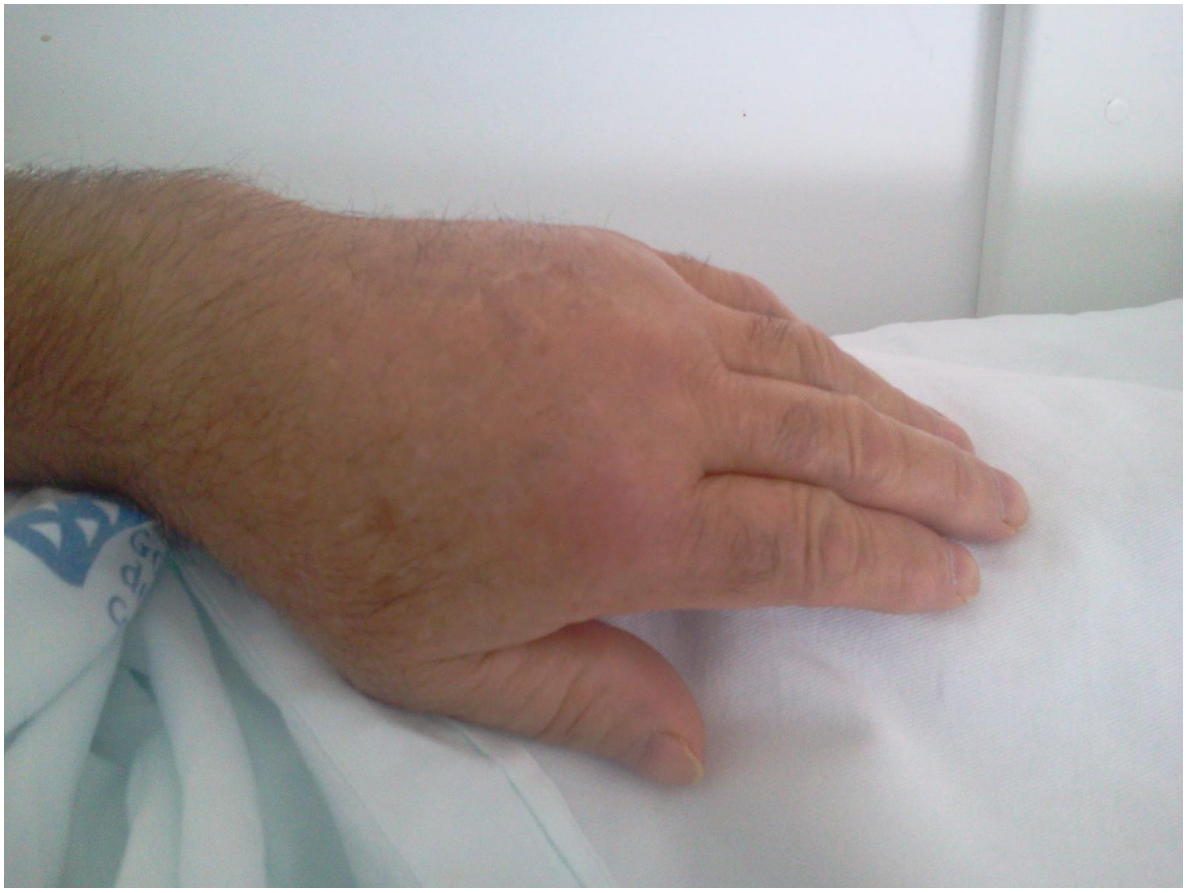

Figure 1. Arthritis of multiple hand joints with a relative lack of inflammatory signs.

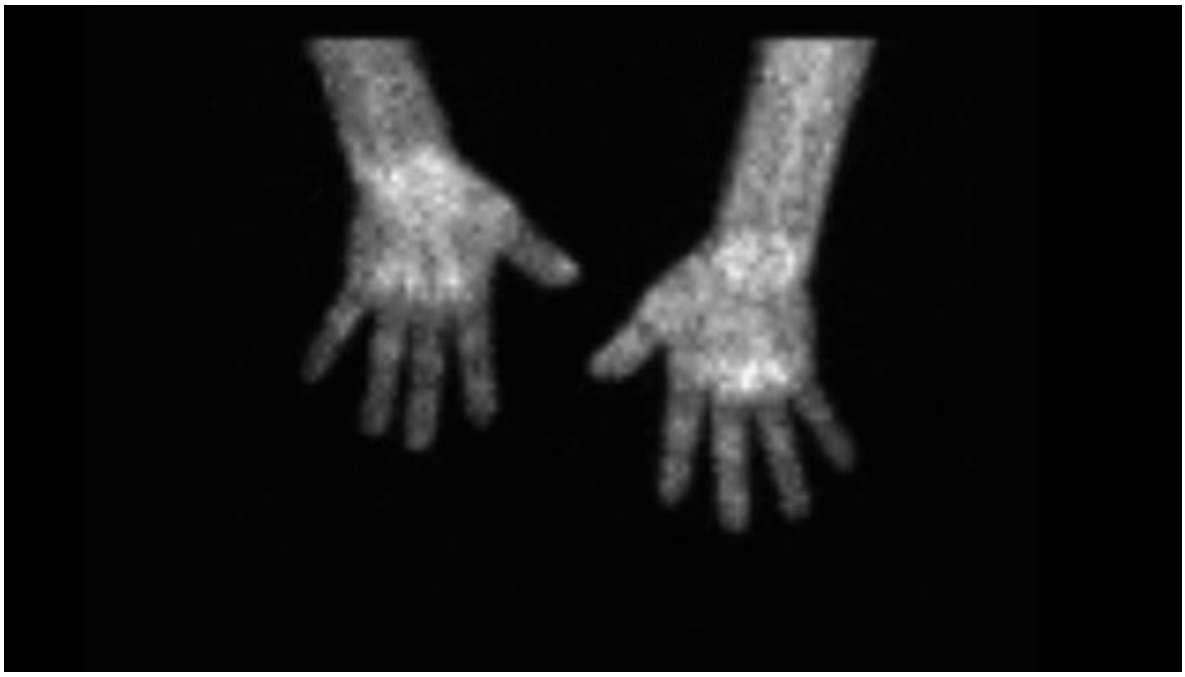

Figure 2. Bone scintigraphy using 99mTc that shows uptake of the radioactive tracer in wrists and metacarpophalangeal joints.

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ISSN 1697-5529

Thyroid function tests revealed serum thyroid stimulating hormone (TSH) levels over 100 mUI/ml and free thyroxine (T4) levels of 0.39 ng/ml. Free triiodothyronine (T3) levels were slightly below the normal range while reverse T3 levels were 0.15 ng/ml. It is worth of note that the patient lacked significant symptoms of hypothyroidism despite the very low levels of free thyroxine. We also found positive thyroid peroxidase (TPO) antibodies. Thyroglobulin levels were normal and thyroglobulin antibodies were negative. Ultrasound studies revealed a heterogeneous thyroid with low echogenicity. A hypoechoic solid nodule that measured 12 mm in diameter was observed in the right thyroid lobe. A fine-needle aspirate revealed findings compatible with an adenomatoid nodule. Cytology studies also showed a chronic lymphocytic thyroiditis.

Hormonal therapy was then instituted, with a progressive escalation of the thyroxine dose to 100 µg. The patient was also placed on 60 mg of prednisone. The signs and symptoms of arthritis disappeared the next day and the patient's general status improved. Prednisone was progressively tapered during the following 15 days. Currently –one month after discharge- the patient no longer receives corticosteroids but he continues to take 100 µg/day of thyroxine. His arthritis has resolved and his general status remains excellent.

Discussion

We describe a patient with a marked derangement of thyroid function tests (without overt clinical signs and symptoms of hypothyroidism) who presented with polyarthritis that lacked significant inflammatory signs.

The polyarthritis described was seronegative: we ruled out the presence of rheumatoid factor, anti cyclic citrullinated peptide antibodies and other immune markers of connective tissue disease. As mentioned above, we found a questionable positive p-ANCA that normalized on a second visit. Even though the patient had improved significantly once he was placed on corticosteroids, this improvement persisted when steroids were already discontinued. This strongly suggests that joint involvement was secondary to hypothyroidism itself, and not an association of rheumatoid arthritis with Hashimoto's disease.

Given the autoimmune nature of Hashimoto's disease, it has been associated with several autoimmune diseases. Some authors have reported that these diseases are present in 14.3% of patients with Hashimoto's thyroiditis and 9.67% of patients with Graves' disease [2]. Rheumatic conditions such as recurrent apthous stomatitis, and osteoarthritis have been described in as many as 62% of patients with autoimmune thyroid diseases [8].

Punzi and Betterle mention several mechanisms that could explain the association between Hashimoto's thyroiditis and autoimmune diseases [7]. One of the mechanisms cited is the effect of autoantibodies on other end-organs besides the thyroid. In fact, antinuclear antibodies (ANA) have been reported in up to 35% of patients with autoimmune thyroid diseases [9]. Autoimmune thyroiditis can also be part of an overlap syndrome that includes other autoimmune disorders. As mentioned earlier, Hashimoto's thyroiditis can be associated with a constellation of autoimmune diseases and when symptoms from two or more of these conditions are present in a single patient, they are categorized as having an overlap syndrome [5]. What underlies all autoimmune disorders is the disruption of immune system homeostasis that is in charge of preventing the development of autoimmunity [3]. Interestingly, Punzi and Betterle also discuss the possibility that autoimmune diseases could be a manifestation of a systemic inflammatory reaction secondary to thyroiditis [7]. These associations highlight the importance of ruling out autoimmune diseases in patients with Hashimoto's thyroiditis, as was done in this patient.

However, in addition to rheumatic diseases associated with Hashimoto´s thyroiditis, there are also polyarticular manifestations which do not derive from co-existing autoimmune conectivopathies, but represent unusual manifestations of hypothyroidism.

A striking feature in this patient was the relative lack of inflammatory signs despite the positive uptake of radiocolloid in the affected joints. This is characteristic of the rheumatic manifestations of myxedema described by Bland and Frymoyer about 40 years ago in which the deposition of hyaluronic acid in the synovium and ligaments leads to polyarthritis without inflammatory features. Some authors have also proposed that TSH can activate adenylate cyclase in synovial membranes, leading to synovial effusions [1].

Golding has followed up patients with Hashimoto's disease that presented with a benign form of seronegative polyarthritis that resembled early rheumatoid arthritis [4]. He found that among the seronegative group, the disease course was mild, they tended to have HLA-DR2, and there was significant improvement after initiating thyroid hormone replacement therapy. In this patient, the diagnosis of polyarthritis secondary to hypothyroidism is supported by the relative lack of inflammatory signs, the negative immune markers, the quick resolution of symptoms after initiating thyroid hormone replacement therapy, and the clinical improvement that persisted long after discontinuing corticosteroids.

Majorensis
ISSN 1697-5529

Conclusion

When treating patients with Hashimoto's thyroiditis who present polyarthritis that resembles rheumatoid arthritis, it is not only necessary to rule out associated autoimmune conditions, but it is also important to keep in mind that some forms of polyarthritis may respond positively to thyroid hormone replacement therapy. A favorable response to thyroid hormone replacement may make further diagnostic tests unnecessary.

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