Exceptional association of a common variable immunodeficiency and ankylosingspondylitis: A case report

Abstract :

We report a new observation of an unusual association of CVID with ankylosing spondylitis (AS). Osteoarticular involvement associated with CVID occurs in approximately 5 to 40% of cases, most commonly in the form of septic arthritis, or non-septic arthritis, which is part of the joint manifestations of autoimmune and rheumatic diseases associated with CVID. A 53-year-old patient with a history of recurrent bronchopulmonary infections complicated by bronchial dilatation since the age of 38, pelvic-axial syndrome and peripheral inflammatory arthralgia affecting the large and medium-sized joints and enthesitis (talalgia), who has presented since the age of 40 with a digestive disorder consisting of chronic liquid diarrhoea with 6 stools a day, developing in the context of a deterioration in her general condition, without any mention of medication. Regarding biotherapy, in particular anti-TNF alpha, this is the first-line biotherapy for APS. It has been shown to be effective in patients with CVID with joint involvement in the course of granulomatous disease, which would be beneficial for our patient.

Keywords: ankylosing spondylitis, granulomatous diseases, immunoglobulins, autoimmune manifestations

Introduction:

Common variable immunodeficiency (CVID) is a rare disease. It is the most common constitutional humoral deficiency of CVID in adults, characterised by polymorphic manifestations, in particular a decrease in the serum concentration of most circulating immunoglobulins (Ig), and by the occurrence of recurrent bacterial infections, autoimmune manifestations, malignant tumours or malabsorption.

Osteoarticular involvement associated with CVID occurs in approximately 5 to 40% of cases, most commonly in the form of septic arthritis or non-septic arthritis, which is part of the joint manifestations of autoimmune and rheumatic diseases associated with CVID. Bone involvement is less common.

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The discovery of hypogammaglobulinemia in inflammatory rheumatism is a rare event.

We report a new observation of an exceptional association of CVID with ankylosing spondylitis (AS)

Case presentation :

A 53-year-old male patient with a history of recurrent bronchopulmonary infections since the age of 38, complicated by bronchial dilatation, pelvic-axial syndrome and peripheral inflammatory arthralgia of the large and medium-sized joints and enthesitis (talalgia), who presented with a digestive disorder since the age of 40, consisting of chronic liquid diarrhoea with 6 stools per day, developing in the context of a deterioration in his general condition, without any mention of medication. On clinical examination, the patient was in relatively good general condition, with bilateral snoring and achromatic patches on the anterior surfaces of both legs, consistent with vitiligo. Paraclinical investigations revealed an inflammatory syndrome with a CRP of 27mg/l, and the CBC showed a hyperleukocytosis of 14400/mm3 with a predominance of PNN (70%). Stool tests for bacteria and parasites were negative. HIV serology was negative. Protein electrophoresis showed a significant hypogammaglobulinemia of 0.6 g/l and low levels of IgG1 (<0.15), IgG2 (<0.02 g/l) and IgA (<0.007 g/l) by weight. Examination of lymphocyte subpopulations showed no qualitative or quantitative abnormalities. Rheumatoid factor, anti-CCP and ANA were negative. IgG and IgA anti-transglutaminase antibodies were negative, gastric fibroscopy and biopsy showed partial duodenal villous atrophy, chest CT showed bilateral bronchial dilatation, HLA b27 was negative, and CT of the sacroiliac joints showed bilateral stage III sacroiliitis. A diagnosis of digestive CVID with systemic autoimmune manifestations such as vitiligo associated with ankylosing spondylitis (AS) was accepted.

The treatment regimen consisted of a monthly immunoglobulin infusion of 0.8 g/kg, antibiotic prophylaxis, and corticosteroid therapy of 10 mg/d with a slow taper of the corticosteroids, maintaining a low dose of 5 mg/d as maintenance treatment in conjunction with the monthly intravenous infusion.

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The therapeutic progress was notable, particularly in the osteoarticular and digestive areas.

Discussion:

Primary immune deficiencies (PIDs) are defined as functional and/or quantitative abnormalities in one or more components of the immune system, including T or B lymphocytes, natural killer cells, phagocytic cells, complement proteins, and others.

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that primarily affects the axial skeleton and the sacroiliac joint, but can also involve peripheral joints and entheses. Following the discovery of the human leukocyte antigen B27 (HLA-B27), several hypotheses have been put forth to elucidate the precise etiology of AS. The tendency of HLA-B27 to form unusual structures leads to the recognition and activation of crucial components of the innate immune system. In recent years, SpA has been classified as a polygenic autoinflammatory disease, in which innate immune abnormalities may play a significant role..(1)(2)

These PIDs are manifested by repeated infections, which typically occur during childhood. However, other clinical manifestations are also possible. Some are highly specific and rare, while others are more frequent, particularly osteoarticular complications. These are caused by a wide variety of mechanisms, and are observed in different types of DIP, mainly humoral (3). The prevalence of osteoarticular involvement in CVID is estimated to range from 5 to 40%. (4).

Although bone manifestations are relatively uncommon, arthritis is a more prevalent condition. These are arthralgias, which may be genuine septic or aseptic. They may resemble rheumatoid arthritis but never ankylosing spondylitis. (5).

The occurrence of hypogammaglobulinemia in the context of inflammatory rheumatism is a relatively uncommon phenomenon, which presents a diagnostic challenge that is frequently challenging to resolve. In practice, several hypotheses have been proposed to explain this phenomenon.

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The condition may be the result of an inflammatory rheumatism that has been complicated by an immune deficiency secondary to background treatment or corticosteroid therapy. This is the most common occurrence. However, this was not the case in our observation, as the patient had not previously received any treatment that caused CVID, and the diagnosis of SPA was made at the same time as that of immune deficiency.

An alternative hypothesis is that the patient may be suffering from a genuine humoral DIP. However, this is a rare or even exceptional situation, given that these arthropathies are not associated with enthesopathy and do not, apart from exceptional cases, progress to an APS picture. Furthermore, there is no established link with HLA-B27. (6).

Alternatively, it may be a lymphoproliferative syndrome complicated by an immune deficiency, which is revealed by joint manifestations.

This presents a significant challenge in the treatment of ankylosing spondylitis. We were hesitant to prescribe anti-inflammatory drugs due to the patient's digestive involvement, in order to avoid exacerbating the condition.

Nevertheless, efficacious pharmaceutical agents have yet to be developed, and a significant proportion of patients encounter difficulties or become incompatible with existing pharmacological treatments(7).

Although corticosteroid therapy can induce moderate hypogammaglobulinemia, it was the only treatment the patient received that demonstrated a statistically significant improvement in joint damage at a rate of 5 mg/d. It would appear that the infectious consequences are low.(8)

In contrast to immunosuppressive drugs such as methotrexate, which induce neutropenia and therefore indirectly facilitate bacterial infections, corticosteroids do not appear to have this effect.

With regard to biotherapy, in particular anti-TNF alpha, this is the recommended first-line biotherapy for APS. It has been demonstrated to be efficacious in patients presenting with CVID and joint involvement in the context of granulomatous diseases, a scenario that would be advantageous for our patient. Nevertheless, this form of treatment should be employed with

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caution, given the increased risk of infectious complications, the most significant of which is the reactivation of tuberculosis. (9).

It is therefore advisable to exercise caution when considering the use of these therapies, provided that antibiotic prophylaxis has been initiated.

Intravenous immunoglobulin (IVIg) has been demonstrated to be efficacious in the treatment of aseptic arthritis in patients with common variable immunodeficiency (CVID), although there is no consensus on this matter. Moreover, there is a paucity of studies in the field of AS. (10, 11).

Conclusion:

In conclusion, the occurrence of hypogammaglobulinemia associated with inflammatory rheumatism is a relatively uncommon scenario, often difficult to diagnose, and may occur secondary to immunosuppressive therapies. However, our observation represents a unique case of a true common variable immunodeficiency disorder (CVID) associated with ankylosing spondylitis (AS), a combination not previously reported in the medical literature.

The therapeutic management of such cases is complicated by the limited treatment options available due to the increased risk of infection in individuals predisposed to hypogammaglobulinemia.

Abreviations ; AS: ankylosing spondylitis

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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