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Case Report

Development of Granulomatosis with Polyangiitis in a Patient with Psoriatic Arthritis in Treatment with Ustekinumab

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Keywords

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Abstract

Granulomatosis with polyangiitis (GPA) is a systemic, multiple-cause vasculitis that affects small and medium vessels. It is characterized by the affectation of the respiratory system and the kidneys, although it can affect other organs. Antineutrophil cytoplasmic antibodies (ANCA) are frequently positive and the most relevant histological feature is the presence of necrotizing granulomas. The diagnosis is based on the clinical manifestations, the biopsy of the affected organs and the presence of ANCA. We report a clinical case of a patient diagnosed with granulomatosis with polyangiitis probably related to the use of ustekinumab. The vasculitis can be idiopathic or secondary, being caused by different causes such as infections, medications, systemic diseases or malignant tumors. All of these possible causes should be considered in the differential diagnosis, such as drug-induced vasculitis, since it is essential to identify and stop the guilty medication. In drugs such as ustekinumab, some rare events, including vasculitis, may not be evident until their wider use and rigorous post-marketing surveillance, the key element is the suspicion for a diagnosis and early and adequate treatment. The histological diagnosis is definitive, which allows us to establish an adequate treatment early, improving the prognosis.

ABBREVIATIONS

ANCA: Antineutrophil Cytoplasmic Antibodies; GPA: Granulomatosis with Polyangiitis; NSAIDs: Nonsteroidal Anti-inflammatory Drugs; p-ANCA: Perinuclear Anti-Neutrophil Cytoplasmic Antibodies; c-ANCA: Cytoplasmic Antineutrophil Cytoplasmic Antibodies; DLCO: Diffusion Pulmonary Carbon Monoxide; GFR: Glomerular Filtration Rate; TNF: Tumor Necrosis Factor; APV: ANCA-Positive Vasculitis

INTRODUCTION

Granulomatosis with polyangiitis, previously known as Wegener's granulomatosis, is a systemic, multiple-cause vasculitis that affects small and medium vessels [1]. It is characterized by the involvement of the respiratory system and the kidneys, although it can affect other organs [2]. ANCA is observed in more than 90% of patients with GPA and the most relevant histological feature is the presence of necrotizing granulomas. The diagnosis is based on the clinical manifestations, the biopsy of the affected organs and the presence of ANCA [3]. Then, we report a clinical case found in our usual practice of a patient diagnosed with granulomatosis with polyangiitis probably related to the use of ustekinumab.

CASE PRESENTATION

A 61-year-old man with history of hypertension, psoriatic arthritis in treatment with ustekinumab on a quarterly dose and methotrexate for 3 years and persistent microhematuria in study by urology who came to the hospital with extensive joint affectation, in treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), diazepam and corticosteroids with subsequent hospital discharge. After one month, the articular symptoms persisted with the appearance of nausea, vomiting and oligoanuria with coluric urine. Initial exam revealed local inflammatory signs in joints, blood pressure 148/76 mmHg, no edema and the rest of the exploration was normal.

The first complementary tests performed showed an acute renal failure with creatinine 7.3 mg / dl, urea 157.7 mg / dl, potassium 6.2 mEq/ l, hemoglobin 8.9 g/dl, C-reactive protein 77 mg / l, and abdominal ultrasound without interesting findings. Initially, an acute renal failure was suspected, possibly secondary to the taking of NSAIDs, but after starting treatment there was no adequate evolution. Progressively, renal function deteriorated rapidly to creatinine 9.5 mg / dl and urea 280 mg / dl. The study was completed with serology, proteinogram, light chains, immunoglobulins, and complement, all with normal results.

The autoimmunity study revealed antinuclear antibodies negative, Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (p-ANCA) negative and cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) positive with a titer of 99 Ui/ml. During admission, the patient began with hemoptysis, so a chest x-ray

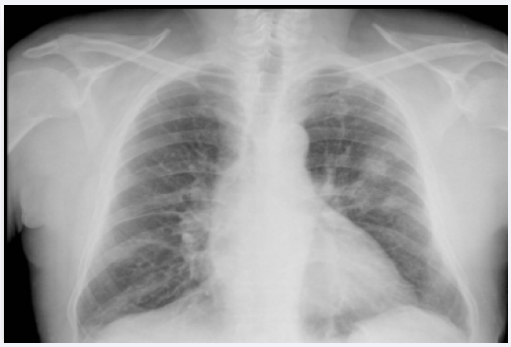

Figure 1 Chest x-ray with bilateral pulmonary infiltrates in middle fields, although predominantly left.

was performed that revealed bilateral pulmonary infiltrates in middle fields, although predominantly left (Figure 1). Consequently, the Department of Pneumology was asked to realize a respiratory functional study with diffusion pulmonary carbon monoxide (DLCO) that showed an increase of 114%, confirming the diagnosis of pulmonary hemorrhage.

Given these findings and given the bad evolution of the patient, a renal biopsy was performed showing an extra capillary and pauci-immune necrotizing glomerulonephritis in relation to ANCA and signs of tubular ischemia in evolution. Therefore, it was concluded that the patient presented a renopulmonary syndrome compatible with a granulomatosis with polyangiitis. Regarding the treatment, several sessions of hemodialysis, plasmapheresis and immunosuppressive regimen were initiated with cyclophosphamide and corticosteroids.

Finally, the patient remains with impaired renal function. Currently, its estimated glomerular filtration rate (GFR) is 20ml / m / 1.73m2.

DISCUSSION

Vasculitis can be idiopathic or secondary, being caused by different etiologies such as infections, medications, systemic diseases or malignant tumors, etc [4]. The determination of ANCA in clinical practice has increased the suspicion capacity of this disease. Despite the discovery of ANCA and the description of certain effector mechanisms that underlie the development of GPA [5], the pathogenesis of this disease is still poorly understood. Among the elements that predispose to the appearance of GPA, there are genetic factors, such as some HLA haplotypes or gene polymorphisms coding of proteins involved in the immune response (IL-10, CTLA4 or PTPN22) [4]. However, environmental factors play a vital role, whether this exposure to certain environmental toxins such as silica, or a vasculitis triggered by an infection or drug [4]. In this sense, tumor necrosis factor (TNF) inhibitors, propylthiouracil, hydralazine, and minocycline have been previously reported to induce ANCA-positive vasculitis (APV) [6], which may present with high ANCA titers [7]. Therefore, a drug etiology must also be considered [6]. The mechanism for autoantibody formation in drug-induced APV persists undetermined. Different positive auto antibodies have been described in previous cases of APV induced by drugs [6], although they are of unknown predictive value and were not observed in our case. It is also not known if very high c-ANCA titers are characteristic of the etiology of the drug, as is the case with p-ANCA titers [8]. Since in patients exposed to drugs, p- ANCA titers can be more than 12 times the average titer of patients with APV without exposure to the drug [8]. Our case suggests that drug triggers may be more numerous than previously appreciated and we could raise suspicion for drug etiology.

After a review of the literature, ustekinumab has never been reported as a medication that can induce c-ANCA positive vasculitis but, we report ustekinumab as another possible culprit in drug-induced APV. Our case reinforces the need to consider drug etiology for APV and cautions about the surveillance of drugs when these types of events appear. The suspicion and identification of the drug is essential to identify and suspend the guilty medication [5]. In drugs such as ustekinumab, some rare events, including vasculitis, may not be evident until their wider use and rigorous post-marketing surveillance. For this reason, the key element is the suspicion for a diagnosis and early and adequate treatment.

The histological diagnosis is definitive and therefore the early renal biopsy could be indicated to establish an adequate treatment early, improving the prognosis [4]. In terms of treatment, classical immunosuppressive schemes used in GPA combine high-dose corticosteroids and cyclophosphamide, although recent trials have shown that rituximab offers a similar efficacy with probably less cytotoxic side-effects [5].

REFERENCES

1. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum. 1994; 37: 187-192.
2. Hoffman GS, Kerr GS, Leavitt RY, Hallahan CW, Lebovics RS, Travis W, et al. Wegener granulomatosis: an analysis of 158 patients. Ann Intern Med. 1992; 116: 488-498.
3. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum. 1990; 33: 1101-1107.
4. Brogan P, Eleftheriou D. Vasculitis update: pathogenesis and biomarkers. Pediatr Nephrol. 2018; 33: 187-198.
5. Chen M, Kallenberg CG. ANCA-associated vasculitides-advances in pathogenesis and treatment. Nat Rev Rheumatol. 2010; 6: 653-664.
6. Grau R. Drug-Induced Vasculitis: New Insights and a Changing Lineup of Suspects. Curr Rheumatol Rep. 2015; 17: 71.
7. Pendergraft W, Niles J. Trojan horses: drug culprits associated with antineutrophil cytoplasmic autoantibody (ANCA) vasculitis. Curr Opin Rheumatol. 2014; 26: 42-49.
8. Choi H, Merkel P, Walker A, Niles J. Drug-associated antineutrophil cytoplasmic antibody–positive vasculitis: Prevalence among patients with high titers of antimyeloperoxidase antibodies. Arthritis Rheum. 2000; 43: 405-413.

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