



## Case Report

# Good Response to Surgical Treatment and Mycophenolate in Woman With Inflammatory Pseudotumor Secondary to ANCA Positive Vasculitis<sup>☆</sup>



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## ABSTRACT

We present the case of a young woman with ANCA positive vasculitis and inflammatory pseudotumor as a granulomatous manifestation, who had a good response to surgical removal and mycophenolate mofetil.

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## Buena respuesta al tratamiento quirúrgico y micofenolato en mujer con pseudotumor inflamatorio secundario a vasculitis ANCA positivo

## RESUMEN

Presentamos el caso de una mujer joven con vasculitis ANCA positivo y pseudotumor inflamatorio como manifestación granulomatosa, que cursó con buena repuesta a la exéresis quirúrgica y micofenolato mofetilo.

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### Palabras clave:

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## Introduction

*Antineutrophil cytoplasmic antibody* (ANCA) positive vasculitides are disease that can be difficult to diagnose and classify because of the different ANCA patterns found, which do not correspond to the most common ones. However, the course of disease helps to approach them. In this clinical case, we present a patient with ANCA positive vasculitis with an alternating antibody pattern and

a rare granulomatous manifestation in the orbital region, with a good response to mycophenolate mofetil and not to other, more common, drug used in this group of diseases.

## Clinical Presentation

The patient is a 36-year-old woman from Colombia, with no known allergies or any other history of interest.

In March 2006 she went to the emergency room of another hospital with fatigue, an evanescent rash, afternoon fever, sweating (which had lasted for weeks) and hemoptysis which had started 48 h prior. Laboratory tests showed anemia (hemoglobin 8.3 g/dl), thrombocytosis (525 000/ml), ESR 97 mm/h, CRP 2.47 mg/dl and microhematuria. A chest X ray showed an abnormal pattern in the lower right lobe, which was confirmed with a thorax

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CT, with a diffuse, ground glass pattern. All microbiology tests were negative except Mantoux. Autoimmunity tests showed ANA 1/640, P-ANCA 1/160 and antimitochondrial antibodies by indirect immunofluorescence (IIF). A skin biopsy showed toxicodermia, and a transbronchial biopsy showed iron laden macrophages in the lung parenchyma, suggesting alveolar hemorrhage. There was no additional data found in her file. Faced with the possibility of microscopic polyangiitis (MPA), methylprednisolone was administered in bolus (1 mg/kg/day for 3 days) and, later was switched to oral treatment. A renal biopsy showed mesangial glomerulopathy with scarce electron-dense deposits. Treatment with azathioprine was started (100 mg/day) with progressive clinical improvement. Upon discharge, the patient was receiving daily methylprednisolone 36 mg, ASA 100 mg and azathioprine. In addition, sulphamethoxazol was added as prophylaxis for *Pneumocystis jirovecii* and bisphosphonates were added due to steroid induced osteoporosis. The apgient never showed up to follow-up.

In June 2011 she came to our center presenting fatigue, joint pain, fever, palpebral edema, chest pain and pain upon paranasal sinus palpation, with an ESR of 67 mm/h. A sinus CT was performed showing no alterations. After this she received azathioprine 150 mg and methylprednisolone 10 mg daily. She was examined after a month in the outpatient clinic with no signs of activity.

In November 2011 she presented with right eye proptosis, diplopia and angioedema and a doubtful palsy of the VII cranial nerve. An orbital CT scan was performed which showed diffuse thickening of the rectus superior and an enhancement of the periorbital fat. A cranial MRI confirmed these findings. A high-resolution chest CT ruled out lung affection. These findings suggested Wegener's granulomatosis (WG). We suspended azathioprine, administering 3 boluses of methylprednisolone for 3 days, continuing with oral steroids in a reduction dose. Treatment with methotrexate (MTX) was started for the granulomatous manifestations. After disappearance of the diplopia and angioedema, the patient was discharged.

In December 2011 she presented headache and worsening of diplopia, with an ESR of 56 mm/h, CRP 2.3 mg/dl, anti-PR3 1/80 and positive anti-MPO antibodies. A new MRI was performed which showed increased thickening of periorbital fat. This was surgically treated with improvement of proptosis, eye movements and headaches. Pathological study did not show signs of infection, sarcoidosis or lymphoma. Histologically, there was a great loss of structure of the lacrimal gland due to lymphocyte infiltrate on a hyaline stroma. The patient was diagnosed with an inflammatory pseudotumor (IP). MTX was suspended due to gastric toxicity (even subcutaneously) and treatment with mycophenolate (MMF) was started 500 mg every 12 h, starting with this dose to avoid gastric intolerance and insure compliance with treatment. In addition, she received 16 mg a day of methylprednisolone.

The last review of the patient was in August 2012, finding her asymptomatic and with steroid dose reduction to 4 mg/day.

## Discussion

The Chapel Hill consensus defines WG as «necrotizing and granulomatous vasculitis which affects the respiratory tract and can be associated to necrotizing glomerulonephritis». It is very commonly associated with ANCA, with PR3 being specific. Our patient showed anti-MPO/p-ANCA, which suggested MPA, although this is not 100% specific. Between 82% and 94% of patients with WG or MPA are ANCA positive, relating to the severity of the disease.<sup>1,2</sup> WG is associated to PR3 and MPA with MPO. However, 20% of patients with WG or MPA have an alternating ANCA pattern and, at least 10% are ANCA negative.<sup>3–5</sup>

Lung affection is one of the main manifestations of WG. It is the initial manifestation in 45% of patients and up to 87% develops it

over the course of the disease (cough, hemoptysis and pleuritis are the most common symptoms).<sup>6</sup> In our case, alveolar hemorrhage was the initial manifestation, making our first diagnostic possibility MPA, where this is the initial manifestation in up to 30% of patients. However, the course of the disease fits better with WG due to the granulomatous manifestations, uncommon in MPA.

Ocular manifestations occur in 28%–58% of patients with WG and are the initial manifestation in 8%–16% of cases.<sup>7,8</sup> Any part of the eye may be affected. It may also occur as a complication of treatment. Lymphoma and sarcoidosis were ruled out due to the absence of clinical and histological characteristics. There was no data regarding infection in the pathology or microbiology tests. Thyroid associated ophthalmopathy was not possible as the patient had normal thyroid hormone levels and that disease is usually bilateral. IP is a benign lesion of unknown etiology. It is frequently found in the lung, but the orbits and paranasal sinuses may be affected. There may be swelling of the muscle insertions and a palpable mass, commonly associated with ophthalmoplegia and diplopia. It typically occurs unilaterally and is recurrent. Oral steroids are the treatment of choice and improvement with these is considered a diagnostic characteristic. Improvement occurs in the first 48 h. It is less frequently associated to ANCA positive vasculitis (less than 10.7% of eye manifestations).<sup>9</sup> Our patient had a relapse when starting treatment with azathioprine, leading to the switch to MTX. This was suspended due to gastrointestinal toxicity and, because of the need for high steroid doses, we opted for MMF. No relapses, as defined by the *Birmingham Vasculitis Activity Score* (BVAS), were seen up until October 2012 (the last patient visit to the clinic). Her headaches disappeared after surgery.

Several studies support the use of azathioprine, MTX and rituximab as treatment for granulomatous manifestations of WG. On the contrary, MMF is shown to be less effective in «head to head»<sup>10</sup> trials. However, in our patient, MMF was started after a lack of response to other treatments, holding rituximab for possible future events and obtaining the same clinical remission with low doses of MMF.

## Conclusions

Our patient developed IP as a granulomatous complication, without evidence of new lung or renal alterations, changing our diagnosis to WG and treated initially in accordance with current treatment recommendations. Finally, MMF was shown to be superior in maintaining our patient in remission. No new granulomatous manifestations or IP recurrences were found up to 9 months after surgery, when she failed to show up to the outpatient clinic.

Although no clinical trials have been published proving the efficacy of MMF as a treatment of granulomatous manifestations in WG, this case suggests that MMF may be a well tolerated and effective drug for this type of manifestations.

## Ethical Responsibilities

**Protection of people and animals.** The authors state that for this study, no experiments were performed on people or animals.

**Data confidentiality.** The authors state that all of the protocols of their center regarding the publication of patient data and all patients included in the study have received sufficient information and have given their informed consent to participate in the study.

**Right to privacy and informed consent.** The authors have obtained the informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

## Conflicts of Interest

The authors report no conflicts of interest.

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