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Eosinophilic Granulomatosis with Polyangiitis and Bowel Perforation: Case Report

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Resumo: A vasculite de pequenos e médios vasos incluída no grupo das vasculites associadas a anticorpos anticitoplasma de neutrófilos, é uma doença rara, caracterizada pela presença de vasculite em associação com asma e eosinofilia. O objetivo deste trabalho é descrever um caso de início típico de granulomatose eosinofílica com poliangite - GEPA, que evoluiu com manifestações atípicas graves sendo necessária intervenção cirúrgica. Face a uma patologia potencialmente grave e de prognóstico infortúnio, cabe discutir a epidemiologia, as manifestações clínicas e os achados dos exames complementares. Justificando a evolução clínica e compreendendo a resposta terapêutica do paciente em questão, com embasamento científico na literatura médica publicada.

Palavras-chave: Granulomatose com Poliangeíte, Vasculite, Asma, Eosinofilia, Abdome Agudo.

Abstract: The small and medium sized vessels vasculitis included in the group of vasculitis associated with anti-neutrophil cytoplasmic antibodies, is a rare disease characterized by the presence of vasculitis in association with asthma and eosinophilia. The objective of this report is to describe a case with a typical initial presentation of eosinophilic granulomatosis with polyangiitis - EGPA, that evolved with atypical clinical manifestations and findings in complementary exams. Justifying the clinical evolution and comprehending the therapeutic response of the patient in question, with scientific embasement on published medical literature.

Key words: Granulomatosis with polyangiitis, Vasculitis, Asthma, Eosinophilia, Acute abdomen.

1. Introduction

The Eosinophilic Granulomatosis with Polyangiitis (EGPA) syndrome, also called Churg-Strauss syndrome, is a necrotizing systemic vasculitis that targets medium and small-sized vessels. Caused by immune-mediated phenomena that suggest immediate hypersensibility reactions considering the coexistence of rinitis, asthma, eosinophilia and increased serum IgE levels [1].

The disease epidemiology is still uncertain, due to its diagnostic difficulties. But it's believed that EGPA is present in around 10% of all patients with anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis. Apparently the incidence similar between men and women, with mean age of diagnosis around 40 and 50 years [2].

The main symptom that precedes the disease, in most cases, is asthma; and the shorter its presence as an only symptom before the vasculitis manifestations, the worse the prognosis. Allergic rhinitis and sinusitis symptoms are also common, and also a pulmonary involvement with interstitial infiltrates or transitory alveolar, with possible association to nodules without cavitation and pleural effusion, possibly present in 70% of the cases. Furthermore, in up to 70% of the cases, there is also cutaneous involvement with the presence

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of palpable purpura and, very typically, subcutaneous nodules with or without ulceration.

The disease diagnosis is based on criteria established by the American College of Rheumatology, in 1990. The criteria is the following:

1) asthma
2) eosinophilia higher than 10% in blood count
3) presence of mononeuropathy or polyneuropathy
4) migratory pulmonary infiltrates in radiographic images
5) paranasal sinuses abnormalities
6) extravascular eosinophils in biopsies

The fundamental treatment of EGPA is the use of systemic glucocorticoids. The application of immunosuppressive drugs is indicated in the disease remission stage associated with corticoids. Treatment with plasmapheresis and anti-tumor necrosis factor agents still does not have sufficient scientific evidence for its usage in clinical practice [3].

2. Case Report

Male patient, 39 years old, brown skin, natural from Horizonte-CE, started presenting in December/2019 paresthesia on right leg associated to hypoesthesia in first and second distal interphalangeal joints of his right hand, progressing, in January of 2020, with neuropathic patterned pain in the same limb. The patient also reported postprandial abdominal pain associated with episodes of emesis and hyporexia, leading to weight loss during the period. Furthermore, reported frequent asthmatic crises in the last six months, demanding attendance to emergency services for treatment.

Due to an aggravation of his clinical condition, went to an emergency service, being consequently interned. The physical examination found a bad general state, skinny (body mass index = 19 kg/m²), hypocorated and adynamic.

His cardiac and respiratory rates were 109 per minute and 24 respiratory incursions per minute respectively, and his temperature was 36.8 ℃. Pulmonary auscultation evidenced expiratory wheezing in both lungs apexes and the abdominal examination evidenced pain induced by palpation of the mesogastrium, but no peritonitis signs. He was also presenting purpuric, not palpable lesions on his first and second distal interphalangeal joints on the right hand (Figure 1). Neurological examination evidenced polyneuropathy on C6/C7 dermatomes of his upper right limb, and S1 of his lower right limb.

Fig. 1 Purpura occurred in the first and second distal interphalangeal joints of the patient's right hand.

The admissional blood tests showed: Hemoglobin 8.4 mg/dL, Leukocytes 28.343/μL with 14% of Eosinophils, also showing higher inflammatory indicators (VHS and PCR). Moreover, the urinary analysis presented proteinuria and haemoglobinuria. Renal function, hepatic function, and thyroid function biochemical tests showed no alterations and HIV, syphilis, and hepatitis serologies were negative.

A thoracic radiography evidenced peri-hilar opaque images bilaterally with a characteristic interstitial lesion (Figure 2). Blood electrophoresis presented increased polyclonal of gamma globulins, associated with a consumed complement (CH50) and P-ANCA reagent, being established the diagnosis of Eosinophilic granulomatosis with polyangiitis, according to the American College of Rheumatology criteria (ACR-1990).

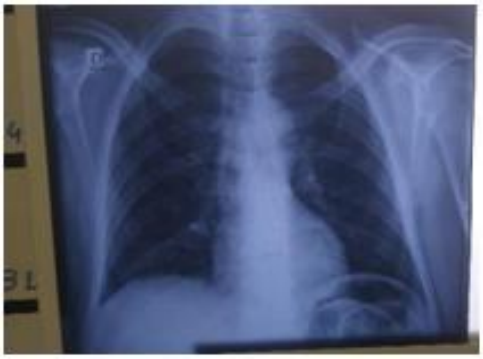

Fig. 2 Patient chest film display.

Prednisone at a dose of 60 mg/day orally was initiated for 8 weeks, presenting an initial lowering of the eosinophils level and an improvement of the respiratory pattern. The patient received hospital discharge to continue as an outpatient. However, in the following 6 weeks, persisted the abdominal pain after meals and the weight loss, being interned again for immunosuppression.

During the new internment, methylprednisolone at a 500 mg/day dose was administered IV for 3 straight days, with a posterior maintenance dose of 40 mg/day. But on the fourth day of treatment, the patient presented intense abdominal pain again, with peritonism signs, being submitted to an emergence surgery, which evidenced an ascendent colon perforation next to the ileocecal valve, leading to the execution of enterectomy with confection of a protective colostomy (Figure 3).

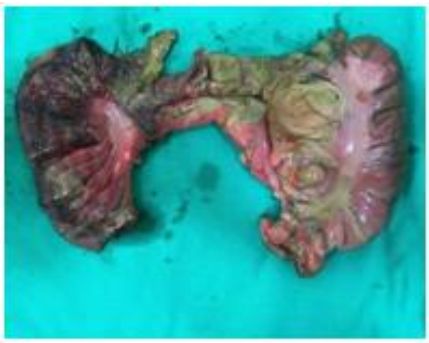

Fig. 3 Enterectomy.

After the surgical approach, sedation and invasive mechanical ventilation were needed because of haemodynamic instability, staying in the intensive care unit for 7 days. This leads to a refractory septic shock associated with renal injury that led to dialysis. So it was decided to maintain only proportional care due to the severity of the clinical condition. In the following 96 hours of intensive support, the patient showed a good hemodynamic response, evolving extubation without intercurrences and, then, being sent to a general ward to continue clinical treatment. The antibiotics were maintained with the expectancy of an

improvement of the clinical and infectious condition to start immunosuppression again.

In May/2020, the first cycle of immunosuppression was administered with 800 mg of cyclophosphamide, which induced agranulocytosis, leading to soft tissue infection in the peristomal region with the necessity of antibiotics and "Granulokine". During the same hospitalization, received the second immunosuppression cycle with 750 mg of cyclophosphamide in June/2020, this time with no events. He received hospital discharge in August/2020 with a follow-up program with a multidisciplinary team and an outpatient plan for immunosuppression.

3. Discussion

This report describes a case of Eosinophilic granulomatosis with polyangiitis (EGPA), with a severe manifestation, almost always fatal, the bowel perforation, seen in less than 10% of the cases. The diagnosis is hard due to the isolated occurrence of the symptoms through the years, making it hard to connect them as an only condition. The symptoms tend to start after exposition to some trigger factors, like infectious agents, drugs, vaccines, and others.

EGPA symptoms are divided between the vasculitis and eosinophilic ones. Usually the disease course follows a sequence: prodromal stage, eosinophilic stage, then the vasculitis stage. Patients positive for ANCA assays tend to present a symptomatology with a vasculitis pattern, with neuropathy, glomerulonephritis and purpura. As for the ANCA-negative patients, the eosinophilic symptoms are more evident, like myocardial, respiratory and gastrointestinal involvement. In the case described, the patient started with a common prodromal stage, first presenting asthma, that occurs in most patients, suggesting eosinophilic infiltration, followed by neurologic involvement on his right lower limb and right hand, now suggesting auto-antibodies activity, also present. At the moment of the internment, gastrointestinal symptoms were evidenced, reinforcing the eosinophilic component and the disease progression [4].

As for the histopathologic analysis, there were typical findings, like a tissular infiltrate with a considerable amount of eosinophils, necrotizing vasculitis and extravascular granulomas. However, these characteristics are hardly found in biopsies, and are not specific for this condition. According to medical literature, the antibodies ANCA (antineutrophil cytoplasmic antibodies) play a fundamental role on vascular manifestations, possibly through neutrophil activation and consequent production of oxygen reactive species and proteolytic enzymes. It is believed that this mechanism contributes to cause the necrosis and tissular hemorrhage seen in the condition, starting with the skin showing palpable purpura and nodules, and also with a severe involvement of the gastrointestinal tract, which mesenteric vasculitis unleashes obstructive or haemorrhagic symptoms [4, 5].

Furthermore, the gastrointestinal involvement usually occurs due to the eosinophilic infiltration in the system's organs mucosa, and affects the small bowel more frequently. Ulceration, perforation, stenosis, are all possible results for the ischemia caused by the vasculitis, increasing morbimortality in patients who develop these complications. Besides that, acute ulcers or perforations normally occur in association with long-term corticosteroid treatment [1, 6].

Corticosteroids are first-line therapy for EGPA in patients without severe organ involvement, and can be used as long-term treatment after a satisfactory clinical response, generally after some weeks, with gradual reduction of the doses. In some cases, human immunoglobulin may be used for patients with residual neuropathy in clinical remission or to induce it in infected patients, refractory to therapy with corticosteroids and cyclophosphamide. For patients that do not have a satisfactory clinical response to the habitual remission therapy, cyclophosphamide and

rituximab can be interchanged for a more adequate result. For remission maintenance, corticosteroid doses must be reduced to the minimum possible, according to the patient tolerance, and association with azathioprine must be done [1-3].

EGPA can be mistaken for other diseases that also increase eosinophil levels, especially in cases where there is pulmonary repercussion, with infiltration. Some examples are: Parasitosis and the hypereosinophilic syndrome; but principally other vasculitis associated with ANCA or like polyarteritis nodosa, which causes mononeuritis multiplex, joints and muscular lesions, and gastrointestinal symptoms [7].

In the described case, the considerable eosinophilia in the blood count leads to some diagnostic possibilities, but asthma in an adult patient, the interstitial pulmonary and gastrointestinal involvement, direct the diagnostic to EGPA.

To evaluate prognosis, the Five-Factor Score is used, and it includes the following topics: Increase in serum creatinine (> 1.58 mg/dL), proteinuria (> 1 g/day), gastrointestinal involvement, cardiomyopathy, and central nervous system involvement. Each item is worth a point. Patients with 0 points show a surviving chance of 100% in 1 year and 88.1% in 5 years. Those with 2 or more points have a surviving expectancy of 54.1% in 5 years [8, 9].

4. Conclusions

Here we report an EGPA case that evolved with a severe complication: a perforative acute abdomen. The early diagnosis and intervention made possible the prevention of various complications that could eventually lead to death, reinforcing how important it is to standardized and thoroughly analyze patients with similar clinical presentations.

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