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Case Report

Orbito-nasal Fistula, A Therapeutic Challenge Against an Uncommon Manifestation in Granulomatosis with Polyangiitis

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Abstract

Granulomatosis with Polyangiitis (GPA) is a clinical-pathological condition that presents with granulomatous inflammation of the upper and lower respiratory tract, focal necrotizing glomerulonephritis and necrotizing vasculitis of small and medium-sized vessels (capillaries, venules, arterioles and arteries). Orbital GPA involvement ranging from 7-45%. The lacrimal gland can occasionally be affected in isolation and be the initial manifestation of the disease. We present the case of a patient with GPA and nasolacrimal fistula.

Keywords: Granulomatosis Con Polyangiitis; Orbito-Nasal Fistula; Corneal Erosion; Nasal Septum Perforation

Introduction

Granulomatosis with Polyangiitis (FPG) is a clinical-pathological picture that presents with granulomatous inflammation of the upper and lower respiratory tract, focal necrotizing glomerulonephritis and necrotizing vasculitis of small and medium-sized vessels (capillaries, venules, arterioles and arteries) [1].

The prevalence of FPG ranges from 2.3 to 146.0 cases per million people, with an incidence of 0.4 to 11.9 cases per million person-years [2].

The incidence of GPA varies widely depending on geography. It mainly affects regions of the world where the population is predominantly of European descent and is rarely seen in East Asia. Studies of multiethnic populations in France and the United States report at least twice the incidence of GPA among white populations compared to other ethnicities [3,4].

In the FPG, antineutrophil cytoplasmic antibodies with cytoplasmic pattern, directed against proteinase 3 (c-ANCA/antiPR 3), are detected in 65 to 75% of cases, this being a very specific, although not pathognomonic, marker of the disease [2,5].

Approximately 82 to 94% of patients with GPA have a positive ANCA, depending on the severity of the disease [6].

The disease tends to be chronic and relapsing, with a broad spectrum of clinical manifestations ranging from granulomatous disease restricted to the respiratory tract (localized disease), to severe necrotizing disease with multisystem involvement and predilection for the lung and kidney. To establish a correct diagnosis and treatment, it is usually necessary to perform a biopsy, as well as to assess the extent and severity of the disease in each organ [2,5].

Humoral and cellular immunity participate in its pathogenesis, tissue damage occurs as a result of an inflammatory process that is manifested by the formation of granulomas and the infiltration of polymorphonuclear, macrophages and lymphocytes into the walls of blood vessels, as well as by the synthesis of autoantibodies (ANCA) directed against antigens present in polymorphonuclear and monocytes [1].

Up to 70% of patients with FPG have otorhinolaryngological manifestations, being frequently the form of presentation of the disease [7]. The involvement at the nasal level (64-80%) is characterized by inflammatory rhinitis, mucosal ulceration, with epistaxis (11-32%), and may evolve to ulceration of the septum with perforation and deformity (9-29%). Maxillary and frontal sinus involvement occurs in 90% of cases. Subglottic stenosis occurs in up to 16% of patients [8,9].

Orbital involvement of GPA is less frequent, ranging from 7-45% according to the literature reviewed [10-12]. This can present with proptosis in 69% of cases, ocular inflammation, loss of orbital walls in 38%, epiphora in 52%, diplopia in 52%, edema and eyelid erythema in 31%, orbital pain in 24%, decreased VA in 17%, sinus involvement and loss of nasal septum. The lacrimal gland can occasionally be affected in isolation and be the initial manifestation of the disease [10-12].

Treatment will depend on the severity of the clinical manifestations. In severe cases, treatment with Rituximeb 375 mg/m^2 every week for 4 weeks or 1000 mg on days 1 and 15 is recommended for induction of remission [13].

Although most patients achieve remission, a high percentage will relapse and a few patients will be refractory to treatment. This last group represents a great therapeutic challenge. In recent years, great advances have been made in the knowledge of the physiopathogenesis of the disease, and with this, new and attractive therapeutic targets have emerged expanding the possibilities of treatment of this pathology. B-cell depletion with rituximab has been shown in multiple reports to be a beneficial alternative in the treatment of patients with refractory FPG and other ANCA-associated vasculitis [14-17].

However, in those cases where the patient's life is not at risk, drugs such as oralmethotrexate, 20-25 mg/week, mycophenolate mofetil up to 3 g/day and azathioprine 2 mg/kg/day are used [13].

Destructive midline lesions (LDLM) of the upper airway (VAS) present a diagnostic dilemma due to overlapping signs and symptoms and their various etiologies (traumatic, infectious, neoplastic, autoimmune or unknown). For this reason, it was decided to present the following clinical case due to the low frequency of the disease and the particular organ damage produced in this patient. In addition, it entails a therapeutic challenge since it requires multidisciplinary work and is a pathology that presents very varied responses to available treatments.

Clinical Case

In the present study, the case of a 24-year-old patient with a history of hypertension (HTN) and a diagnosis of FPG of 4 years of evolution is reported. Upon questioning, he denied any history of drug abuse or other substance use. Physical examination revealed saddle deformity, mucogonal secretion along with crusty lesions in both nostrils, blurred vision in the right eye and intermittent bilateral hearing loss. Interconsultation with Infectology was performed to rule out concomitant fungal or bacterial infections and an immunological laboratory was requested that reports negative HAB, PR3 -ELISA positive, positive PCR (C-reactive protein), ERS (erythrocyte sedimentation) within normal values.

The tomographic study reports the absence of the right medial orbital wall, nasal septum and cornet, presence of right nasal orbitalfistula with frontal sinus and occupied ethmoid cells, continuity solution at the level of the papyraceae laminae with apparent communication with orbits, predominantly right (Figure 1).

Figure 1: Computed tomography of facial massif. Mucous and bony involvement of the paranasal sinuses.

Ophthalmological evaluation revealed recurrent corneal erosion, inferior corneal leukoma reaching the pupillary axis, right superficial keratitis.

Scheduled washes and antibiotic prophylaxis are performed, and after ruling out associated infectious pathology, the picture is interpreted as secondary to progresión of basic disease and the patient receives induction treatment with Cyclophosphamide 1gr every month for 6 months, continuing maintenance stage with Mycophenolator 2 gr/day and low-dose corticosteroid therapy. After one year of treatment, he relapses of his underlying disease, manifesting with episodes of epistaxis, severe right eye pain and sudden hearing loss. A tomographic study was carried out in which an inflammatory process involving the mastoid cells and the rest of the cavities of both middle ears was evidenced, absence of the nasal septum with nasal tear fistula (Figure 2), for this reason, it was decided to indicate infusion of Rituximab 1gr (day 0 and 15), this being an option indicated in cases of new activity of the disease or relapse. The patient did not present new signs of activity for approximately two years, persisting with sequelae of the disease, in maintenance treatment with azathioprine 50 mg day, triweekly antibiotic prophylaxis with trimethoprim-sulfamethoxazole 800-160 mg, and topical treatment with antibiotics indicated by otorhinolaryngology service.

Figure 2: Absence of nasal septum with nasal lacrimal fistula.

Discussion

GPA is a granulomatous and necrotizing vasculitis that affects small and medium-sized vessels. It usually involves the VAS and inferior, and the kidneys. In general, FPG is a multisystem disease, with varied manifestations according to the organ involved.

Local manifestations, such as breast involvement, with facial pain, edema, nasal obstruction or purulent discharge are common signs and symptoms in this picture.

The orbital manifestation is usually unilateral and may be due to the perforation of neighboring structures such as the sinuses, the nasal cavity or being originating from the orbit itself, can potentially lead to visual loss and facial deformation [7]. Lacrimal gland involvement is rare, usually unilateral, and occurs primarily as enlargement of the lacrimal gland.

Extensive questioning is required to rule out associated systemic disease. The history of endemic area, contacts, immunodeficiencies, drug addiction, toxic and trauma are important. The general clinical examination should include an in-depth ophthalmological and VAS study.

Conclusion

According to the present clinical case described and the literature consulted, we highlight the severe orbital involvement observed in this patient, given its less frequent presentation and potential complications. The sequelae of the disease can severely compromise the quality of life of those who present it, since they are exposed to multiple infections which require prolonged antibiotic treatment. In addition, intense immunosuppression increases susceptibilityto serious, life-threatening infections.

Summary

The granulomatosis with polyangiitis (GPA) is a clinical-pathological condition that occurs with granulomatous inflammation of the upper and lower respiratory tract, focal necrotizing glomerulonephritis and necrotizing vasculitis of small and medium-sized vessels (capillaries, venules, arterioles and arteries). Involvement of orbital GPA ranges from 7% to 45%. Occasionally, the lacrimal gland can be affected in isolation and be the initial manifestation of the disease. We present the case of a patient with GPA and nasolacrimal fistula.

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