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Case Report

Dacryoadenitis as the Initial Manifestation of Granulomatosis with Polyangiitis in a 7 Year Old Girl: A Case Report

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ABSTRACT

Granulomatosis with polyangiitis, previously known as wegener's granulomatosis, is a systemic granulomatous disease. It is histologically characterized by necrotizing vasculitis of medium and small vessels. We present the case of a seven-year-old girl patient who presented unilateral, non-painful dacryoadenitis as the first manifestation of this disease. An incisional biopsy of the lacrimal gland was performed for diagnosis. Evidence of active small-vessel vasculitis was found in the histologic study. Systemic treatment was initiated immediately after, with an excellent initial response. Subsequently, the patient developed pulmonary and renal involvement, and systemic treatment was started with a multidisciplinary team for her treatment.

A literature review was carried out regarding the most relevant aspects of pediatric characteristics of GPA, as it is a rare and often overlooked pathology when it presents itself as a lacrimal gland inflammation.

Keywords: Dacryoadenitis; Wegener's granulomatosis; Vasculitis; polyangiitis; Pediatric

INTRODUCTION

Granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis was first described in 1937 by the German pathologist Friedrich Wegener [1]. It is a necrotizing small and medium vessel systemic vasculitis. It belongs to a broad spectrum of disorders called Anti-Neutrophil Cytoplasmic Antibody (ANCA) associated vasculitis, which also includes microscopic polyangiitis and eosinophilic granulomatosis with polyangiitis. These diseases were grouped at the Chapel Hill consensus conference in 2012 [2,3].

The exact etiology of GPA is unknown, and its incidence is relatively low. It presents itself more in caucasians and rarely in African ethics. The prevalence is 3/100,000 people, with an annual incidence of 8-10 cases per million. The most common age of presentation is between the seventh and eighth decade of life, with a lower incidence rate in the pediatric age group, being less than 15% in children under 19 years of age, as in the present case.

Clinical manifestations can be very diverse, and the affected organs and severity vary greatly. According to the extent of the disease, it can be divided between the limited and systemic variants, the latter being defined as that in which only the upper and lower respiratory tract is affected; however, in the systemic form, kidneys, respiratory tract, and other organs are affected [4,5].

Periocular and ocular involvement is found in half of the cases. It can present as palpebral edema, dacryoadenitis, proptosis, ulcerative conjunctivitis, scleritis, peripheral ulcerative keratitis, anterior and posterior uveitis, retinal vascular occlusions, oculomotor nerve damage, with varying severity in each case [6].

Most laboratory studies are not always helpful or even favorable to a correct diagnosis, with a few exceptions, making a biopsy especially useful in many cases to orient or even confirm the diagnosis. An early diagnosis and multidisciplinary care for treatment are recommended to reduce morbid-mortality and disease progression.

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In this article, our team will present a case of a seven-year-old child with dacryoadenitis as the first manifestation of GPA, followed by a brief review of the current literature concerning the manifestations of GPA in children.

CASE PRESENTATION

A 7-year-old girl attends the ophthalmology department because of a sudden-onset, non-painful superior eyelid edema of the right eye. It was characterized by a purplish color, with multiple episodes lasting for days to weeks and a partial improvement lasting for approximately five months, without apparent triggering stimuli. The patient was treated multiple times with oral and topical antibiotics. Some of them were ertapenem, amoxicillin/clavulanate, and metronidazole for two weeks each. Oral non-steroidal anti-inflammatory drugs were also used without improvement. Previous disease history, including systemic and ophthalmological diseases, was excluded. Other symptoms were not present, such as coughing, myalgia, arthralgia, headaches, and general malaise.

Intraocular pressure was 16 mmHg for the right eye and 14 on the left eye. Visual acuity of 20/50 (logMAR 0.3979) was found for the right eye, and visual acuity of 20/30 (logMAR 0.1760) was found for the left eye. No abnormalities were found in the eye movement examination.

On biomicroscopy, purple-colored, non-painful eyelid edema was found on the upper lid of the right eye, which caused mild mechanical ptosis. Eyelashes had no abnormalities, and the tarsal conjunctiva presented multiple papillae, with a more intense reaction on the lateral upper lid. Discrete enlargement of the right lacrimal gland was found, with mild erythema of the gland. The bulbar conjunctiva presented marked hyperemia. The rest of the anterior segment had no other abnormalities (Figures 1 and 2).

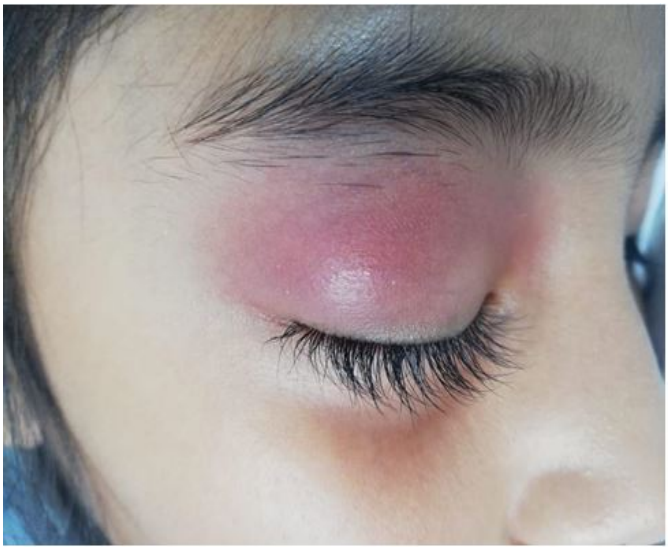

Figure 1: The bulbar conjunctiva presented marked hyperemia.

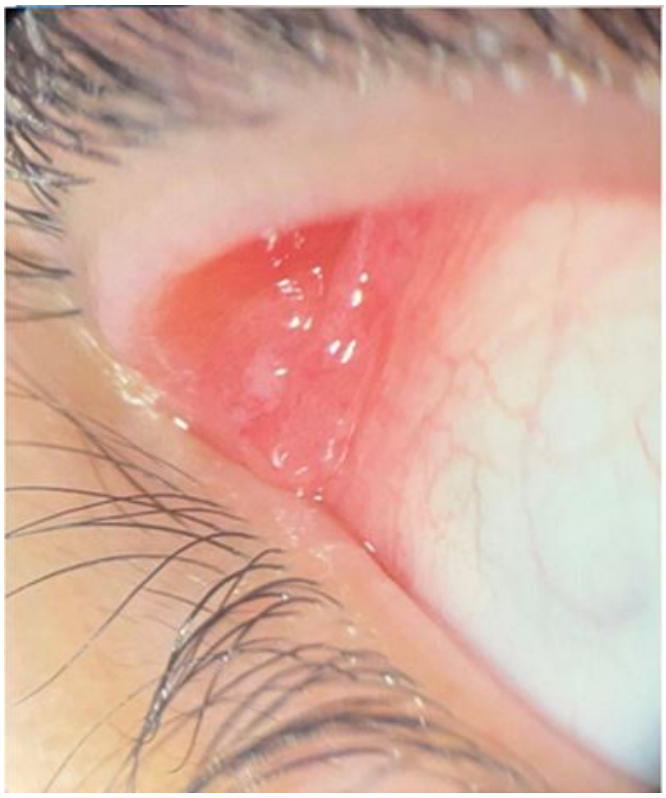

Figure 2: Discrete enlargement of the right lacrimal gland was found, with mild erythema of the gland.

There were no significant abnormalities in the left eye. Both eyes had a normal vitreous and retina on exploration.

Computed tomography of the orbits was done, where enlargement of the lacrimal glands was found, with a more prominent enlargement of the right lacrimal gland. The affected tissues presented no enhancement with contrast. The rest of the study had no alterations (Figure 3).

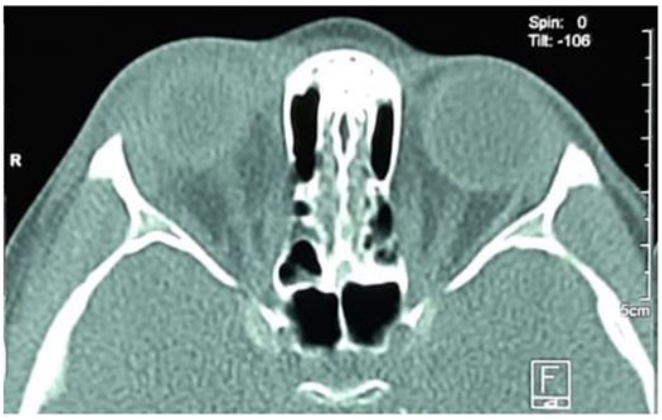

Figure 3: Incisional biopsy of the right lacrimal gland.

An incisional biopsy of the right lacrimal gland was performed *via* lid sulcus, without complications. The pathology study reported an active phased small vessel vasculitis (Figure 4).

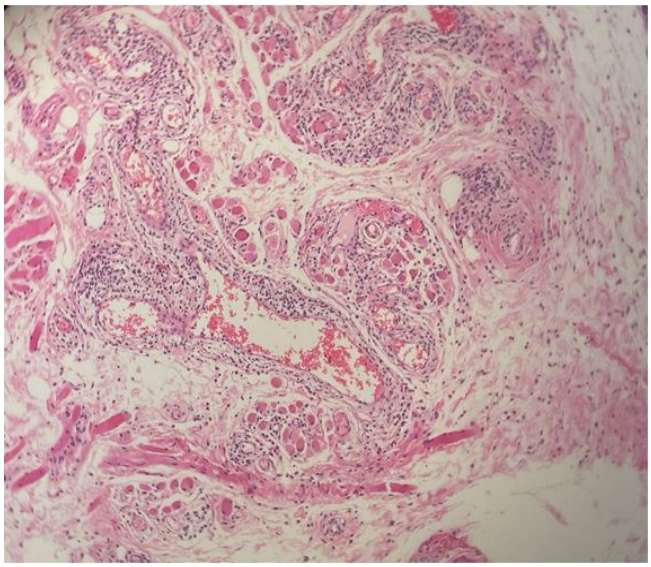

Figure 4: Pathology study reported active-phased small vessel vacuities.

A multidisciplinary approach was initiated in coordination with pediatric rheumatology. Laboratory studies were carried out with the following results (Table 1).

Table 1: Laboratory studies were carried out with the following results.

Variables	Results
Globular sedimentation rate	26 mm/h (Increased for age)
Reactive C protein	0.330 mg/dL (Negative)
p-ANCA	1:40 (Positive)
MPO	41.3 IU/ml (Positive)
PR3	<2 IU/ml (Negative)
Antinuclear antibodies	1: 320 (Positive) Patron de moteado fino
PPD	0 mm (Negative)

A thorax computed tomography was requested, and multiple pulmonary nodules and a ground glass pattern in the pulmonary tissues. Despite these findings, the patient presented no respiratory symptoms. Due to previous findings, our group emitted the diagnosis of GPA. Treatment was initiated by pediatric rheumatology with systemic steroids and mycophenolate mofetil, with a later change of therapeutics to rituximab.

Two months after treatment with rituximab, the patient presented great effort induced dyspnea, accompanied by cough, fever, and tachycardia. Radiologic findings corresponded to pneumonia and mild pulmonary hypertension, and the pediatric neurology department carried out treatment.

One month later, the patient presented macroscopic hematuria and abdominal pain. An abdominal tomography revealed right stage I hydronephrosis due to renal lithiasis with right urethral obstruction. The nephrology department started treatment, and the complication was successfully addressed.

To minimize the risk of infection, our team decided to start prophylaxis against opportunistic microorganisms with antibiotics. Up to this date, the patient is stable and under treatment by a multidisciplinary team comprising rheumatologists, neurologists, nephrologists, and ophthalmologists.

DISCUSSION

GPA is a small and medium vessel necrotizing systemic vasculitis, with an annual incidence in adults that varies between studies from 8-13 cases per million patients a year [7,8]. In children, the incidence is much lower, around 2.75 cases per million persons a year [9].

The incidence, prevalence, and the most frequent characteristics in Mexico are still uncertain due to the lack of large-scale studies; thus, the information available is mostly because of a few reference center cohorts. [10] In adults, GPA presents itself more frequently in males, with 50%-62% of total cases being of this gender. The highest incidence is in the fifth and sixth life decades [11-13]. Contrary to this finding in adults, patients younger than 18 years have a larger proportion of females affected (64%) and the age with the highest incidence is 14 years.

In the study carried out by Cabral et al. of the children with GPA, the most frequent symptoms, organs, and systems affected by percentage were general malaise in 88%, renal damage in

83%, pulmonary involvement in 74%, upper respiratory symptoms in 70%, musculoskeletal damage in 65%, gastrointestinal symptoms in 58% and skin manifestations in 52%. In this cohort, the cases of GPA presenting any ocular symptom represented 43% of the population. The most common symptoms in this study were conjunctivitis (11%), non specified red eye (10%), episcleritis (8%), and proptosis (2%) [14].

In a prior publication by our group, we described patients with GPA who had different orbital manifestations of the disease. In this study, only 14.8% of patients with GPA presented orbital diseases. Only 33% had lacrimal gland involvement in their CT scan, and 26% had dacryoadenitis as their primary clinical manifestation. [15].

Another series describing pediatric patients found that out of 6 patients with ocular or periocular manifestations as the first symptom, four presented eyelid edema and erythema. One of them had dacryoadenitis as the first symptom. All patients in this series had symptom improvement after treatment [16].

Clinical and pathology findings for diagnosing GPA by the EULAR/PRINTO/PRES in 2008 in Ankara include the main symptoms and target organ damage. The main diagnostic criteria include upper respiratory system involvement, laryngeal, tracheal or bronchial stenosis, pulmonary involvement, renal involvement, and antineutrophil cytoplasmic antibodies. These findings have a high sensitivity and specificity for diagnosis, thus requiring 3 out of 6 of these criteria. Characteristic histopathologic findings of the disease are granulomatous inflammation inside the vascular wall, or in the perivascular or extravascular area in the affected tissues, with a specificity of up to 99.6%. Other findings can be pauci-immune necrotizing glomerulonephritis [17].

Some series compare clinical findings between children and adults. Most organs and systems affected are similar in children and adults, but the initial presentations vary between these two groups. In children, the initial symptoms are general malaise, followed by respiratory symptoms. In contrast, adults present hearing loss as the most common initial symptom. Dacryoadenitis as the first symptom is a very infrequent presentation of the disease, and some cases have been reported. On some occasions, it has been the only symptom of the disease [18]. GPA is a rare cause of dacryoadenitis since it only represents 15% of all non-infectious dacryoadenitis. Other common causes are idiopathic dacryoadenitis, sarcoidosis, IGG4 related disease, and sjogren's syndrome [19].

There are, to date, no specific guidelines for treating this disease in children; therefore, the guidelines for treatment are based on adult studies and expert consensus [20]. The primary treatment consists of immune system modulating drugs and is divided into two stages: The induction of remission and the maintenance phase. Cyclophosphamide combined with glucocorticoids is the most efficient treatment in the induction of remission phase with severe disease that threatens life or organ function. Patients with mild to moderate disease can be treated with methotrexate with glucocorticoids. In the maintenance phase, other drugs can be used to prevent new disease activity. Methotrexate, azathioprine, or rituximab can be effective in achieving these goals.

Morbidity remains high in children with GPA, not only because of the disease but also because of the adverse effects caused by medications. Generally, in patients with ANCA-related diseases, reactivation of the disease is higher than in adults and requires a more prolonged maintenance therapy than adults to achieve disease remission. Furthermore, despite early treatment, less than 50% of patients of this age group respond well and achieve remission of the disease in less than 12 months [21].

We present a case of a patient who presented unilateral dacryoadenitis as the first symptom of GPA, an infrequent presentation in the pediatric population. Once the diagnosis was established, multidisciplinary treatment was initiated, and complications and symptoms followed the usual pattern of this disease. Nevertheless, a critical factor in the early treatment of this disease was an early biopsy, which can potentially improve prognosis significantly by starting opportune treatment.

CONCLUSION

An early lacrimal gland biopsy is essential in cases of chronic dacryoadenitis in children since it can lead to an early diagnosis of numerous systemic diseases. In many cases, early treatment can be critical to a better prognosis of those diseases. This case is an excellent example of how early intervention can lead to a better prognosis and treatment of a disease that, although infrequent, can have potentially high morbidity.

Data availability

All data can be verified with the corresponding author.

Consent

Informed consent was given to use images and patient information by the patient's parents.

Conflicts of interest

The authors declare no conflicts of interest.

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