

Penile granulomatosis with polyangiitis



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INTRODUCTION

Granulomatosis with polyangiitis (GPA) is a systemic form of vasculitis that predominantly affects small and medium-sized vessels. The organs often involved are the kidneys and respiratory tract. Diagnosis can be established based on the histologic findings of necrotizing granulomatous inflammation and vasculitis and positive test results for anti-neutrophil cytoplasmic antibodies (ANCA).

Male urogenital manifestations are found in fewer than 1% of cases in large cohorts, and often the upper respiratory tract (90%-100%), lungs (81%-87%), and kidneys (45%-60%)¹ are also involved.

Myasthenia gravis is a condition characterized by weakness and fatigue of various muscles in the body. It is caused by autoantibodies directed against certain components of the muscle membrane at the neuromuscular junction. Diagnosis is made via the detection of acetylcholine receptor antibodies or antibodies against muscle-specific tyrosine kinase (MuSK).

We present a case of penile ulceration and induration as the main manifestation of GPA in a patient for whom ocular myasthenia gravis was diagnosed simultaneously.

CASE REPORT

The patient is a 70-year-old man who presented with a painful penile ulcer and induration for 3 months. His medical history showed type 2 diabetes mellitus, hepatic steatosis, and dyslipidemia.

He was first treated unsuccessfully with ceftriaxone and pristinamycin. Three months later, with the presumptive diagnosis of a neoplastic tumor, surgical treatment with posthectomy was carried out.

Abbreviations used:

ANCA: anti-neutrophil cytoplasmic antibodies
GPA: granulomatosis with polyangiitis

Postsurgical examination showed a 6-cm induration of the penis and pubis area, with a reduction in the size of the penis, and a painful glans ulceration (Fig 1). He also complained of polyarthralgia, and on physical examination arthritis of the right knee was found.

Histopathologic analysis of posthectomy showed necrotizing epithelioid granuloma and chronic vascular lesions (Fig 2). Results of biological investigations for sexually transmitted infections, tuberculosis, and sarcoidosis were negative. Immunologic assessment found positive cytoplasmic ANCA at a titer of 1/160, with a cytoplasmic pattern and anti-PR3 antibodies at 468 IU, suggesting the diagnosis of urogenital and rheumatologic granulomatosis with polyangiitis. Full-body computed tomography results were normal and ruled out any pulmonary or sinus involvement of GPA. Renal function was normal, and proteinuria results were negative.

Furthermore, complete physical examination also showed intermittent binocular diplopia, which worsened at the end of the day, and left eyelid ptosis.

Ophthalmic examination could not identify the type of diplopia. Cerebral magnetic resonance imaging was not contributive. Testing for acetylcholine receptor antibodies was performed and showed positivity, with a value of more than 13 nmol/mL (standard value, <0.2 nmol/L).

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Fig 1. Clinical photograph before treatment: glans ulceration and penile induration



Fig 3. Clinical photograph one month after treatment (corticosteroids and trimethoprim-sulfamethoxazole): healing of the ulceration is evident.

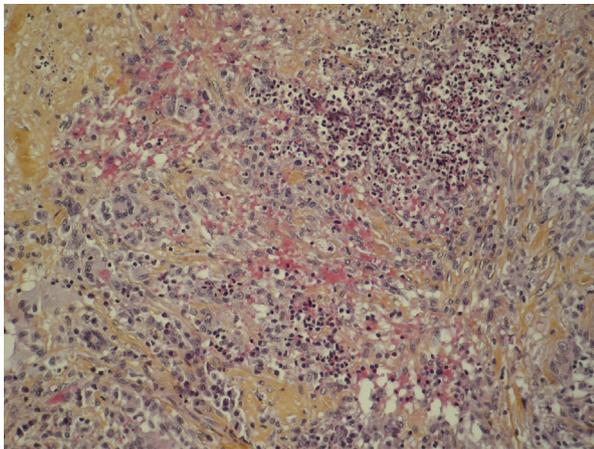


Fig 2. Histology: Necrotizing epithelioid granuloma and vascular infiltration. Hematoxylin, Eosin and Safran (HES) staining, Magnification $\times 200$.

The patient was treated with prednisone 1 mg/kg per day by mouth and trimethoprim-sulfamethoxazole to prevent relapses of this localized form of GPA. The treatment proved to be effective after 1 month: the pubis induration decreased to 1 cm in size, and the ulceration of the penis healed (Fig 3). Plasmatic levels of ANCA were still at 1/160 after 6 months, but ant-PR3 decreased to 74 IU, and prednisone was gradually decreased (removing 10 mg every 15 days for 2 months and then 5 mg every month). For his myasthenia gravis condition, treatment with pyridostigmine induced quick and total recovery.

DISCUSSION

Usually, GPA affects lungs, kidney, and sinuses. Genitourinary involvement is rare and occurs in fewer than 1% of cases, of which 20 cases with penile involvement were described in the literature.¹ Moreover, our patient exhibited an isolated manifestation, which is uncommon, and it was associated

with myasthenia. To our knowledge, this association has not been described to date.

We studied 32 case reports of male urogenital manifestations of GPA. In 15 cases, GPA diagnosis included manifestations of the sinuses, lungs, and/or kidneys that precede or occur at the same time as the urologic symptoms.²⁻⁵ Because of these severe manifestations, patients are generally treated with corticosteroids and immunosuppressive therapies (mostly cyclophosphamide), with expected adverse effects.

Urogenital symptoms were the first evidence of GPA in 8 of the 32 case reports, followed months later by more severe organ involvement.²⁻⁶ Diagnosis was made secondarily with the appearance of classical localizations of vasculitis, which led to the use of corticosteroids and immunosuppressive therapy.

The 9 cases of isolated urogenital involvement were treated differently.^{1,4,5,7-10} In particular, 2 cases of orchitis were treated only surgically,^{7,9} leading to good response and diminution of the ANCA titer. Other cases were managed medically with corticosteroids, cyclophosphamide, azathioprine, and/or methotrexate, depending on the severity and the treatment response of the area involved.

In our case, considering the absence of any kidney, lung, or sinus involvement of GPA, we decided to treat the patient with corticosteroids 1 mg/kg per day with gradual decrease in dosage. Trimethoprim-sulfamethoxazole was added as an adjunct treatment and has been proven to reduce relapses of the disease.¹¹ After 6 months of follow-up, no disease relapse was noted, and symptoms were controlled with trimethoprim-sulfamethoxazole and oral prednisone at a dose of 0.3 mg/kg/d.

To our knowledge, the association of GPA with myasthenia has never been described. The occurrence of 2 autoimmune diseases suggested the

possibility of neoplasia. However, investigations (full-body computed tomography, prostate-specific antigen, blood count, protein electrophoresis) ruled out any signs of neoplasia, particularly thymoma.

Isolated urogenital manifestations of GPA may represent a difficult diagnostic challenge because it can simulate neoplasia or infection and has nonspecific histologic findings. However, early diagnosis can result in quicker introduction of immunosuppressive therapy, leading to a better response and, potentially avoiding surgical treatment. This diagnosis should be evoked in patients presenting with unexplained chronic urogenital manifestations with histologic granuloma.

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