

Complete pituitary regression with immunosuppressive treatment in a patient with Granulomatosis Polyangitis

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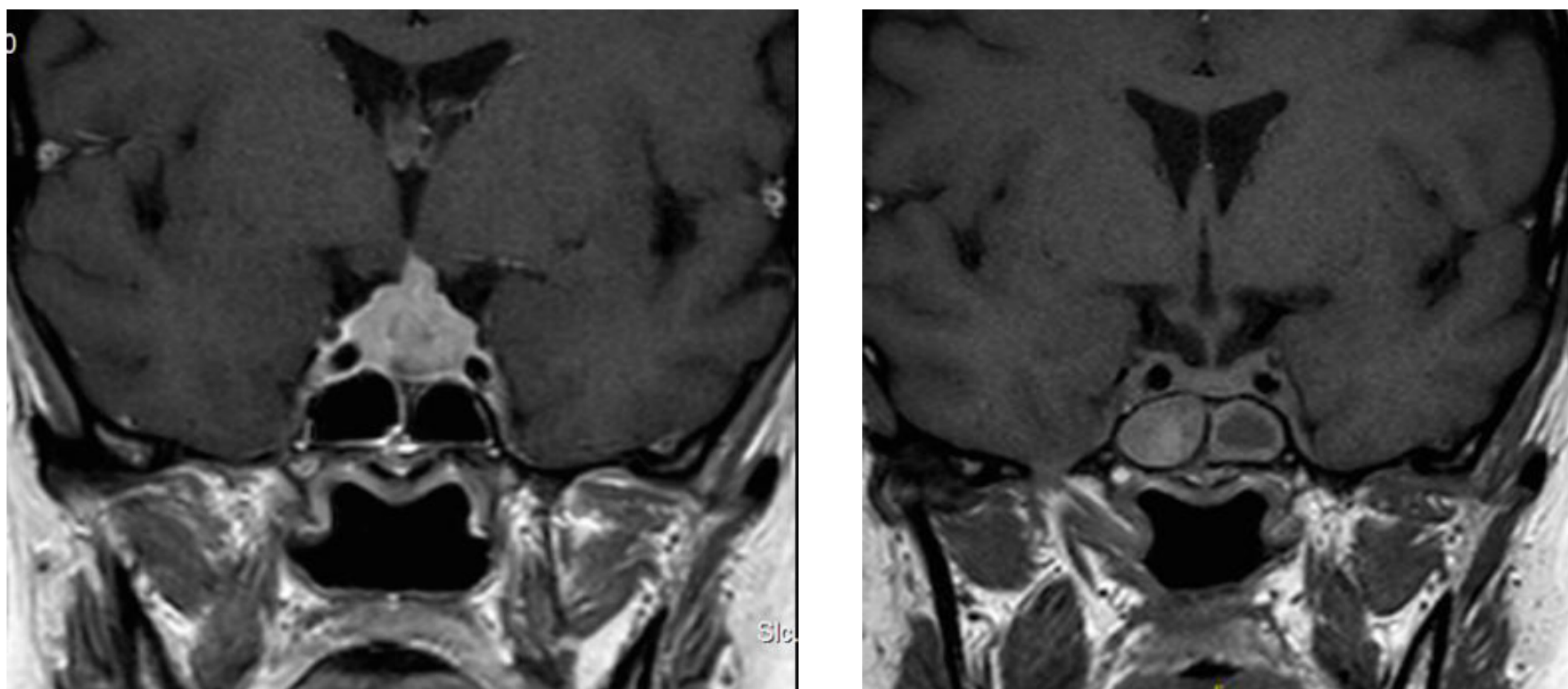
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Context: Granulomatosis polyangitis (GPA), formerly known as Wegener granulomatosis, is a necrotizing granulomatous small-vessel vasculitis. Antineutrophil cytoplasmic antibodies (ANCA) are the serological hallmark of GPA but 30% of patients with GPA were negative (1). It typically affects the upper respiratory tract, lungs, and kidneys but can involve virtually any organ including the pituitary (2). Pituitary involvement in GPA is very rare. It can cause anterior pituitary dysfunction, diabetes insipidus or pituitary mass. Pituitary dysfunction and/or sellar mass may persist after treatment (3). Here in we report a case of complete resolution of pituitary mass after cyclophosphamide and methylprednisolone treatment in patients with GPA.

Case description: A 50-year-old woman was admitted to the hospital with severe dyspnea for 2 years and stridor for a month. During her hospitalization, her sodium level was noted to be persistently high. A further workup revealed a consistently low urine osmolality in the presence of high serum osmolality suggesting diabetes insipidus. Her baseline laboratory data showed Na 164 mEq/L (135-145 mEq/L), serum osmolality 351mOsm/kg, and urine osmolality 232mOsm/kg. Water deprivation test results were consistent with CDI. Her serum sodium level was corrected with desmopressin. MRI revealed enlargement of the whole pituitary, including the stalk, with heterogeneous gadolinium enhancement and a disappearance of the high signal intensity of the posterior pituitary (Figure1). Anterior pituitary functions were normal at presentation. Basal and stimulated of FSH, LH, GH, cortisol and TSH levels were normal.



Computed tomography showed thickened mucosa of the nasal sinus and multiple small nodular lesions in the lung. A nasal sinus biopsy revealed a pauci-immune focal segmental necrotizing sinusitis. She was diagnosed with GPA. Serology revealed the presence negative ANCA, and that the C-reactive protein was elevated. No abnormalities were noted in urine examination. Intravenous pulse methylprednisolone 1000 mg was administered for 3 days and then cyclophosphamide was given at a dose 1000 mg monthly for 3 months. A repeat pituitary MRI 4 months later showed complete resolution (Figure2).

Conclusions:

We report a patient presenting severe dyspnea leading to diagnosis of GPA. One week later she complained of polyuria and diagnosed diabetes insipidus but adenohipophysis functions is normal. Pituitary involvement was shown by MRI as pituitary mass. A nasal sinus biopsy diagnosed GPA. She responded cyclophosphamide and corticosteroid therapy well. Four months later, post treatment pituitary MRI showed a complete resolution.

Pituitary involvement in GPA have long been linked with three different pathogenic mechanisms: vasculitis having a direct effect on the pituitary vessels, contiguous involvement of the pituitary from granulomatous masses in locations such as the ear, nose or throat tract, and/or granulomatous inflammation in situ (4).

In the related literature, two case series including eight and nine patients, respectively (5,6) and total fifty one patients were published about pituitary involvement in patients with GPA (2-10). These studies show that pituitary involvement in patients with GPA was estimated as %1.3, %1.1, respectively, with 1:1 male to female ratio.

Pituitary involvement in GPA is usually accompanied by the disease with other organ involvement. While pituitary involvement can exist at the time of the diagnosis, the symptoms almost always emerge in the course of previous GPA within a time lapse, ranging from several months to several years after diagnosis. In general, although other sites in the body may show signs of active disease, pituitary involvement can be isolated from other manifestations. Initial isolations of the lesions may make it difficult to diagnose pituitary GPA, as seen in the 3 patients study reported in the literature (7-9). In our case, pituitary involvement was detected 2 weeks later when she was admitted to clinic and she had posterior pituitary and sinusoidal involvement.

Granulomatosis with polyangitis can alter partial or total pituitary endocrine function to widely ranging degrees (10). Central diabetes insipidus has been more commonly observed with or without concurrent anterior pituitary insufficiency resulting from a preponderance of posterior pituitary involvement. In addition, secondary hypogonadism is common endocrinopathy in patients with pituitary GPA (5,6). In our case, we detected only diabetes insipidus. It is shown that the patients have a variable recovery of pituitary function with treatment (5,6). Previous experience has indicated residual deficits in 48% of the patients despite remission of systemic disease (10). Surprisingly, posterior pituitary disease was reversible in 83% of patients affected by DI, as brought out by resolution of symptoms and/or discontinuation of vasopressin therapy (5). The current patient was started on methylprednisolone and cyclophosphamide treatment, which led to improve of posterior pituitary gland function.

Pituitary disease is often diagnosed through pituitary imaging aiming to detect diabetes insipidus, headache and visual symptoms. There are some MRI abnormalities in patients with pituitary involvement of GPA. MRI findings of pituitary involvement in GPA include enlargement of the gland, thickening of the pituitary stalk, loss of the hyper intensity of the neurohypophysis and loss of the intensity of the adeno hypophysis (5,10). These MRI abnormalities may vary with disease activity. Patients may exhibit a predominantly small vessel vasculitis, and only minimal changes would be visible on MRI after treatment. There were only nine patients showing complete regression after treatment and all of them had ANCA positive test results (2,5,6,8,9). Our patient has also showed complete regression of pituitary involvement after treatment; in addition, she has ANCA negative with GPA. To date, in the related literature, there are fifty-one involved pituitary patients who had GPA. Thirty-two out of total fifty one patients are reported in the related literature with follow-up ranges changes from 2 months to 21 years, and only one patient died from GPA.

Treatment of GPA can be used corticosteroid, cyclophosphamide and rituximab, an anti-CD20 monoclonal antibody, which dramatically decreases B lymphocytes. Our patient responded cyclophosphamide and corticosteroid therapy well. The lack of pituitary recovery may be attributable to advanced tissue necrosis caused, in part, by delayed diagnosis and treatment. Because of this situation, the treatment should be started as early as possible. Pituitary deficiency in our patient did not developed.

In summary, this case demonstrates that pituitary mass can be seen on pituitary MRI of patient with GPA and this symptom can disappear after treatment. For this reason, endocrinologists should not be misled by laboratory and imaging finding which may point towards a pituitary adenoma. GPA should be considered in the differential diagnosis of pituitary enlargement.

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