Case Report
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Granulomatosis Polyangiitis Presented with Diabetes Insipidus

Granülomatöz Polianjitisin Nadir Bir Tutulumu: Diabetes İnsipidus Olgusu

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Abstract

The pathogenesis of granulomatosis polyangiitis (GPA), systemic vasculitis of small and medium-size vessels, is not completely understood. GPA mainly affects the upper and lower respiratory tract. However, it may involve the central nervous system (CNS) as well. The most common manifestation of CNS involvement is necrotizing vasculitis, leading to peripheral neuropathies or cranial nerve palsy. CNS disorder is less common. CNS involvement in GPA can manifest itself in three ways: Vasculitic involvement, granuloma spread from adjacent anatomical areas, and new granuloma formation in brain tissue. We present a case of GPA presented with diabetes insipidus.

Keywords: Diabetes insipidus; pituitary insufficiency; granulomatosis polyangiitis; vasculitis

Özet

Granülomatöz polianjitis (GPA), küçük ve orta ölçekli damarların sistemik bir vaskülitidir. Patogenezi tam olarak anlaşılamamıştır. Başlıca üst ve alt solunum yollarını etkiler. Ancak, sinir sistemi tutulumu da söz konusudur. En sık olarak, periferal nöropatilere veya kraniyal sinir felcine yol açan nekrotizan vaskülit olarak kendini gösterir. Santral sinir sistemi (SSS) bozukluğu daha az sıklıkta görülür. SSS tutulumu 3 şekilde olabilir: Vaskülitik tutulum, komşu anatomik alanlardan granülom yayılımı ve beyin dokusunda yeni granülom oluşumu. Biz bu olgumuzda, diabetes inspidus ile prezante olan bir GPA vakası sunduk.

Anahtar kelimeler: Diabetes insipidus; pituiter yetmezlik; granülomatöz polianjiitis; vaskülit

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Introduction

Granulomatosis polyangiitis (GPA) is a systemic disease characterized by small vascular vasculitis of unknown etiology. GPA is involved in the class of vasculitis associated with antineutrophil cytoplasmic antibodies (ANCAs). It generally involves the upper and lower respiratory tract, kidneys, ear, nose, and throat. However, GPA may affect any organ or tissue (1).

Diabetes insipidus (DI) is a rare, water homeostasis disorder characterized by abnormal hypotonic urinary excretion. Polyuric symptoms start developing if >90% of the

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vasopressinergic neurons in the supraoptic and paraventricular nuclei of the posterior pituitary get damaged (2).

Pituitary dysfunction is one of the rare findings of GPA. DI is the most common presentation of pituitary involvement in GPA (3). Ahlstrom et al. reported the first case in 1953 (4). Since then, only case reports or small case series have been published (5-10). In this case report, we review pituitary involvement, which is an extremely rare presentation of GPA.

Case Report

In March 2017, a 24-year-old woman was admitted to the Mugla Sitki Kocman University Department of Endocrinology and Metabolism Disorders with complaints of headache, polydipsia, and polyuria for about 3 years. Her vital signs were as follows: temperature 36.7°C, heart rate 90/min, and arterial blood pressure 100/80 mmHg. Her physical examination was normal. Her serum sodium level was 141.9 mmol/L and urine density was 1003 g/L. A water deprivation test was performed and the results were consistent with central DI. Table 1 shows the patient's levels of the anterior pituitary hormone. Her adrenocorticotropic hormone (ACTH) level was 24.4 pg/mL (7.2-63.3 pg/mL) and cortisol level was 4.49 µg/dL (6.2-19.4 µg/dL). The results of the Synacthen stimulation test showed that cortisol values at 30 and 60 min were 17.27 and 11.94 µg/dL, respectively (<18-20 µg/dL is significant for diagnosis). Sella magnetic resonance imaging (MRI) showed a complex cystic lesion, 13×15×10 mm, with a 7x5 mm cystic part, extending to the suprasellar region. There was no compression of the optic chiasm and a bright spot of the neurohypophysis was not observed (Figure 1, Figure 2). Trans-sphenoidal pituitary surgery was performed and histopathological examination revealed granulomatous necrotizing vasculitis. For the differential diagnosis of granulomatous necrotizing vasculitis; the following tests were performed: C-reactive protein 39.6 mg/L (normal; <5 mg/L) and first hour sedimentation value 26 mm/h (<17 mm/h). Antinuclear antibody, anti dsDNA, anti-centromere antibody, antiJo-1, anti-Scl-70, anti-Sm, anti-SSA and -SSB, rheumatoid factor, antiphospholipid antibodies, anticardiolipin antibodies, and lupus anticoagulant were all negative. Moreover, her angiotensin-converting enzyme level for sarcoidosis was 25.40 U/L, which was in the normal range of 8-52 U/L, and purified protein derivative (PPD) test for tuberculosis was also negative. Her cytoplasmic antineutrophilic cytoplasmic antibodies (c-ANCAs) were positive (70.4 and 98.4 U/mL, normal <20 U/mL) and perinuclear antineutrophilic cytoplasmic antibodies (p-ANCA) were neg-

Table 1. Results of the endocrine tests.

Blood Test	Result	Normal Range
ACTH (pg/mL)	24.4	7.2-63.3
CORTISOL (µg/dL	4.49	6.2-19.4
TSH (µIU/mL)	1.61	0.27-4.2
fT4 (pmol/L)	20.87	12-22
fT3 (pmol/L)	5.44	3.1-6.8
FSH (mIU/mL)	5.43	3.5-12.5
LH (mIU/mL)	13.15	2.4-12.6
ESTRADIOL (pg/mL)	125.5	12.4-233
PROLACTIN (ng/mL)	55.63	4.79-23.3
GH (ng/mL)	<0.03	0.126-9.88

ACTH: Adrenocorticotropic hormone, TSH: Thyroid-stimulating hormone, fT4: Free t4, fT3: Free T3, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, GH: Growth hormone.

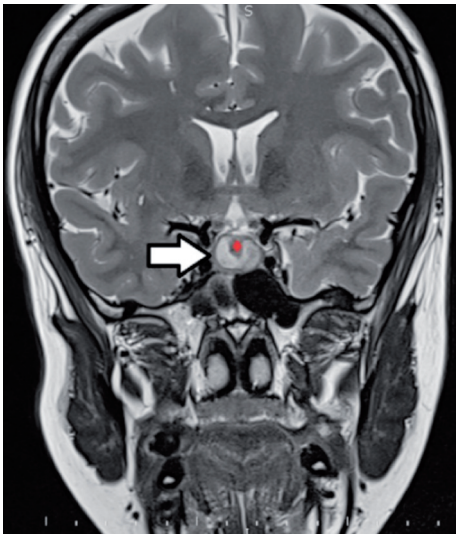

Figure 1: T2-weighted coronal image shows a complex cystic mass with a 1.5 cm diameter and a hypointense solid component with a diameter of 7 mm in the sellar cavity. The area marked with an arrow indicates the lesion and the red star shows solid component.

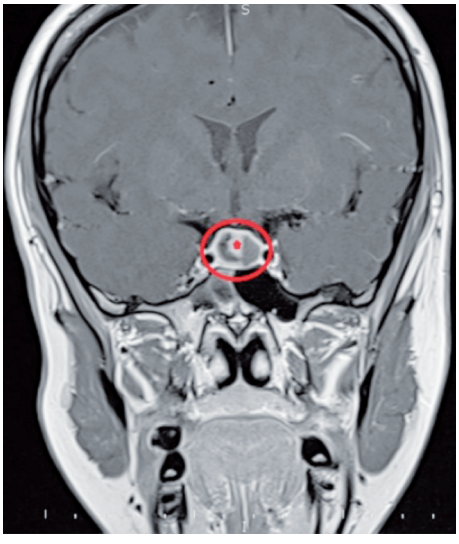

Figure 2: The T1-weighted coronal dynamic image shows a hyperintense solid component that contrasts in the central part of the suprasellar cystic lesion. The red ring shows the entire lesion, while the red star shows the enhanced solid component.

ative. In the paranasal sinus tomography, mucosal thickening in the ethmoid cells in the right maxillary sinus, erosions in the inferior part and the sellar region of the sphenoid sinus, soft tissue formation filling the sphenoid sinus, and focal defect in the central section of the nasal septum were observed (Figure 3, Figure 4). Thoracic tomography showed an asymmetric ice-glass density of 8 mm in diameter in the right upper lobe apical, focal thickening of the left upper lobe posterior fissure, and subpleural nodular density of 2 mm in the posterior lobe of the left lung. The patient was started on 1 mg/kg/day prednisolone and 15 mg/week methotrexate. One month after the beginning of the treatment, there was a considerable improvement in the symptoms of polyuria and polydipsia. Sedimentation value (5 mm/h) and C-reactive protein level (0.4 mg/L) were in the normal range after the treatment.

Discussion

GPA is a rare autoimmune disease characterized by necrotizing granulomatous vasculitis. Although it may frequently involve the upper and lower respiratory tract and kidneys, GPA may affect any other organ or tissue (1). Neurological involvement is seen in one-third of patients with GPA, mainly as a peripheral neuropathy due to small vessel vasculitis, and specifically, CNS involvement is seen in 7-18% of all GPA cases (2). Pituitary involvement in GPA, identified in 1953, is a rare condition and can be seen in about 1% of all GPA cases (3,4). There are some other diseases in the differential diagnosis of the granulomatous pituitary lesions such as idiopathic giant cell granulomatosis, sarcoidosis, Crohn's disease, tuberculosis, and Takayasu vasculitis (11).

The pathophysiology of pituitary involvement in GPA and all related mechanisms have not been accurately described, but three primary reasons seem responsible. The most common reason is the direct intracranial extension of granulomatous process from the nose or paranasal granuloma to the pituitary gland. The second prevailing reason is the vasculitis of pituitary vessels and the third is granuloma development in the pituitary gland (5,12). Symptoms of pituitary insufficiency uncommonly co-occur with GPA but these symptoms are

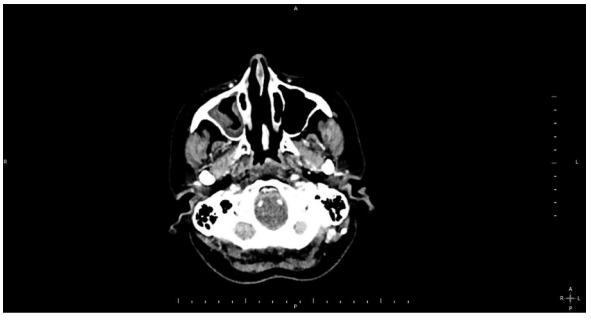

Figure 3: Peripheral mucosal thickening of right maxillary sinus.

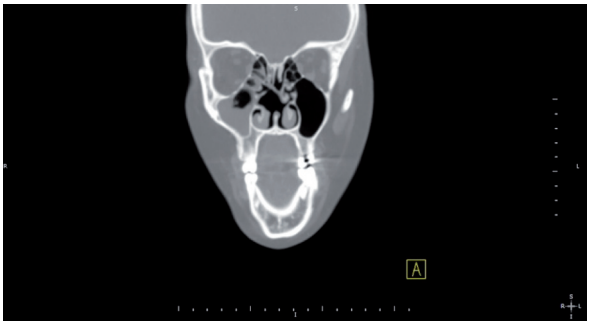

Figure 4: Peripheral mucosal thickening of right maxillary sinus and soft tissue density obliterating almost all of the right maxillary sinus.

generally combined with the clinical symptoms, months or years after diagnosis. These symptoms may be nonspecific, such as fatigue, weakness, or headache, and this may lead to a delay in diagnosis (1). Our case, unlike the literature, was diagnosed with GPA with the observation of pituitary insufficiency symptoms. Out of the 23 cases of pituitary involvement in GPA that were reviewed, in 8 cases, clinical features related to pituitary involvement were present at onset and preceded other organ involvement in 3 patients (13). Of these 8 cases, only one had isolated pituitary involvement at presentation, while in the other 7 cases, at least one other organ was involved (13). In one of the studies reviewed, the mean age at the time of diagnosis of pituitary insufficiency was 38 years and 74% of the patients were women (13). In the French Vasculitis Study Group cohort, nine patients with GPA had a mean age of 51 years (24-77 years) at the time of diagnosis, and 5 of these patients were women (1). Kapoor et al. found that the male to female ratio was equal and the average age at the time of diagnosis was 48 years among 8 cases (3).

A clinical manifestation usually occurs in the form of DI or isolated anterior pituitary insufficiency (6-10). De Parisot et al. reported that the most common endocrinopathy in GPA is secondary hypogonadism (78%) followed by DI (71%) (1). A decrease in gonadotropin-releasing hormone secretion can be related to other pathophysiological mechanisms such as malnutrition, hyperprolactinemia, acute illness, or use of drugs (1). The mechanisms behind hypogonadism are still unclear. Treatment with glucocorticoids and cyclophosphamide suppresses the hypothalamic-pituitary-gonadal axis (14). Other hormonal pathologies in GPA-associated pituitary dysfunction are not as common as hypogonadism and DI. Some other hormone diseases may be reported as follows: central hypothyroidism in 54% of patients, secondary adrenal insufficiency in 39%, hyperprolactinemia in 37%, and growth hormone deficiency in 20% (1).

The most common finding in MRI is pituitary gland enlargement. Other findings seen in MRI include cystic changes, infundibular thickening, and increased contrast enhancement. Another significant finding is the lack of characteristic hyperintense signal in T1 imaging (13). In our case, there was a 13×15×10 mm noncontrast lesion in the sellar cavity with a 7×5 mm complicated cystic nodule in the cranial part of the lesion. The remission induction therapy in GPA involves high- dose glucocorticoids combined with oral or intravenous cyclophosphamide (3). In the literature review of De Parisot et al., 69% of the patients were treated with conventional treatment and after five years of follow-up and 11% had a recurrent systemic disease (1). Induction therapy without using cyclophosphamide is related to recurrence in
50% of patients (3). Patients who are resistant to conventional treatment can be effectively treated with rituximab (15). GPA patients treated with rituximab achieve complete remission more frequently than those treated with cyclophosphamide but the experience of treatment with rituximab in GPA is limited (16). The follow-up of patients should include the evaluation of pituitary imaging and pituitary deficiency. In spite of the remission of systemic disease and the regression of radiological findings, the regeneration capacity of the pituitary function is limited because of the irreversible damage caused by necrotizing granulomatous lesions (1,3,13).

GPA is a vasculitic disease that may cause multiple organ dysfunction. Pituitary involvement is rarely seen in GPA. In the case of anterior or posterior pituitary insufficiency in a patient with a histopathological diagnosis of granulomatous necrotizing vasculitis of the pituitary masses, pituitary GPA should be considered in the differential diagnosis of the disorder.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the sci-

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Authorship Contributions

Idea/Concept: Emine Koca, Emine Figen Tarhan, Neşe Çınar; Design: Emine Koca, Emine Figen Tarhan, Neşe Çınar; Control/Supervision: Emine Koca, Emine Figen Tarhan, Neşe Çınar; Data Collection and/or Processing: Emine Koca, Emine Figen Tarhan, Neşe Çınar, Funda Dinç Elibol; Analysis and/or Interpretation: Emine Koca, Emine Figen Tarhan, Neşe Çınar; Literature Review: Emine Koca, Emine Figen Tarhan, Neşe Çınar; Writing the Article: Emine Koca, Neşe Çınar; Critical Review: Emine Koca, Neşe Çınar; References and Fundings: Emine Koca, Emine Figen Tarhan, Neşe Çınar.

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