

## A rare cause of nasal obstruction: giant invasive nonfunctioning pituitary adenoma

Nadir bir burun tıkanıklığı nedeni: Dev invaziv nonfonksiyonel hipofiz adenomu

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Nasal obstruction is a very rare symptom caused by a pituitary adenoma. A 57-year-old man admitted to our clinic with bilateral nasal obstruction for the last six months. Endoscopic examination revealed soft pinkish pulsatile tissues in both nasal cavities. Radiologic investigation revealed a suprasellar mass extending to the frontal lobes, sphenoid sinuses and nasal cavities. He had bitemporal superior quadrant hemianopsia. Pituitary hormone levels were normal. Biopsies were taken from the patient endonasally. Pathological evaluations and laboratory findings were compatible with nonfunctioning pituitary adenoma.

**Key Words:** Biopsy; nasal obstruction; pituitary adenoma.

Burun tıkanıklığı hipofiz adenomunun neden olduğu çok nadir bir semptomdur. Elli yedi yaşında erkek hasta altı aydır süren iki taraflı burun tıkanıklığı ile kliniğimize başvurdu. Endoskopik muayenesinde her iki burun boşluğunda yumuşak pembemsi, pulsatil doku izlendi. Radyolojik incelemelerinde frontal loba, sfeno-etmoidal sinüslere ve burun boşluklarına uzanım gösteren suprasellar kitle izlendi. Hastada bitemporal üst kadran hemianopsi vardı. Hipofiz hormon düzeyleri normal idi. Biyopsiler hastadan endonazal yol ile alındı. Patolojik değerlendirilmesi ve laboratuvar bulguları nonfonksiyonel hipofiz adenomu ile uyumluydu.

**Anahtar Sözcükler:** Biyopsi; burun tıkanıklığı; hipofiz adenomu.

Pituitary adenomas account for 10-20% of all intracranial tumors.<sup>[1]</sup> Small pituitary tumors have a prevalence of 14.4% in autopsy studies and 22.5% in radiologic studies.<sup>[2,3]</sup> They arise from suprasellar hypophyseal adenoid tissue in the suprasellar space. They appear as an expansion of the sella turcica in lateral cephalic radiograms or are directly visualised as a soft tissue mass in computed tomography (CT) or magnetic resonance images (MRI). They can cause anterior pituitary hormonal imbalance, structural problems related to inva-

sion of surrounding structures, or syndromes of hormone excess.<sup>[4]</sup> Sometimes pituitary adenomas extend to the suprasellar region, cavernous sinuses, paranasal sinuses, nasopharynx and nasal cavity. Locally infiltrating adenomas are called invasive pituitary adenomas.<sup>[1,5,6]</sup> These tumors must be distinguished from other malignant aggressive tumors with an invasive behavior.

The frequency of nasopharyngeal extension of a pituitary tumor is estimated to be approximately 2% of all the pituitary adenomas.<sup>[6]</sup> By contrast,

ectopic pituitary adenomas located in the sphenoid sinus and nasopharynx region are extremely uncommon. They may arise from the embryonal remnant of the extrasellar pituitary tissue in the sphenoid sinus or nasopharyngeal regions during the migration process of Rathke's pouch.<sup>[7]</sup>

Pituitary tumors were classified as basophilic, acidophilic, or chromophobic on the basis of whether or not they took up the stains hematoxylin and eosin. This classification has fallen into disuse. At present, classification of pituitary tumors is based on radiologic findings, immunohistochemical staining and plasma hormone levels.<sup>[4]</sup> Corticotrophic adenomas, thyrotrophic adenomas and gonadotropic adenomas are generally basophilic; somatotrophic adenomas, lactotropic adenomas are acidophilic; null cell adenomas may be stained with synaptophysin.<sup>[4]</sup>

We herein describe a rare case of giant invasive nonfunctioning pituitary adenoma (NFPA) originating from the pituitary gland and exclusively involving the sphenoid sinus, nasopharynx, posterior ethmoidal cells, posterior nasal cavity along with an invasion of bilateral frontal lobes and cavernous sinus.

We primarily focused on the diagnosis with rhinologic examination, immunohistochemical studies and radiologic examinations.

### CASE REPORT

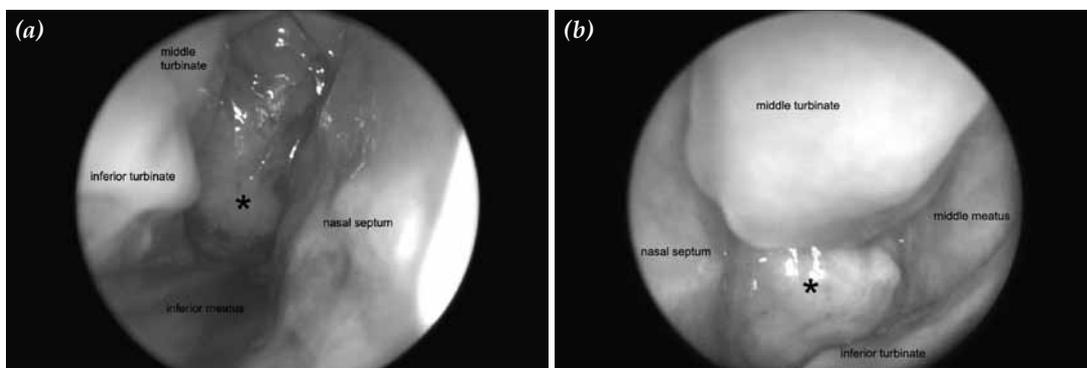
A fifty-seven-year-old male patient was admitted to our clinic with complaints of nasal obstruction for the last six months. No other symptoms were noted. Nasal endoscopic examination was performed on the patient in both nasal cavities. Smooth surfaced, pinkish, pulsatile masses hanging from the speno-ethmoid recess to

both nasal cavities were seen (Figures 1a, b). Eye examination detected bitemporal superior quadrant hemianopsia. No other pathological findings were found in the patient in his systemic examination. Laboratory examinations showed no abnormalities.

Radiologic examinations, including CT and MRI were performed. Axial high-resolution CT images revealed the mass completely filling the sphenoid sinus and posterior ethmoidal cells. Gadolinium-enhanced coronal MRI T1-weighted image demonstrated the mass arising from the sella region and invading bilateral frontal lobes and cavernous sinus, whereas sagittal T1-weighted image showed the mass eroding the floor of the sella turcica and extending to the right posterior nasal cavity. Axial T2-weighted image revealed the mass projecting into the posterior nasal cavity (Figures 2, 3).

In consultation with the neurosurgery clinic, we decided on endonasal biopsy of the tumor because of the possibility of confronting with chordoma, chondrosarcoma, meningioma or pituitary adenoma. Biopsies were taken from both nasal cavities under local anesthesia.

Pathologic findings suggested a diagnosis of null cell pituitary adenoma and revealed histologically that the tumor was composed of monomorphic round cells, arranged diffusely with a characteristic sinusoidal pattern around the capillaries. The tumor cells had round and oval nuclei, conspicuous nucleoli and chromophobic cytoplasm. No mitotic activity was found (Figure 4). The Ki-67 proliferative index using MIB-1 antibody was 1.7%. The Ki-67 proliferative index was less than 3%. And tumor cells had no mitotic activity or pleomorphism (Figure 5).



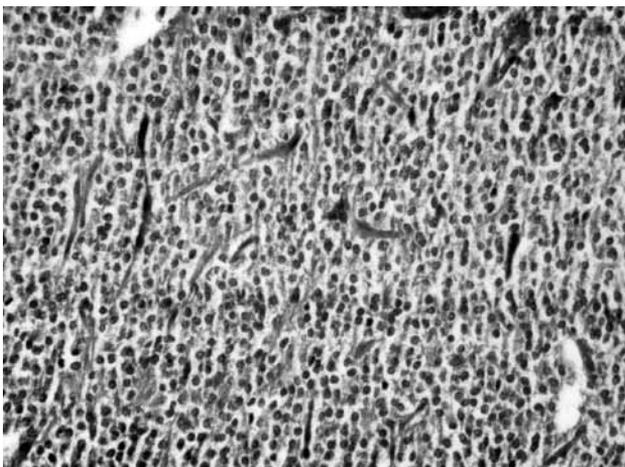
**Figure 1.** Right and left nasal cavities with a views of the zero degree endoscope. (a) Right middle and lower nasal meatus filled by mass. (b) Left middle meatus filled by mass.



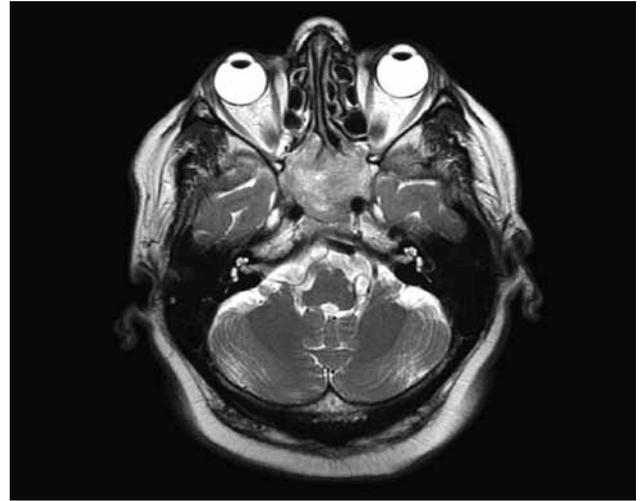
**Figure 2.** Gadolinium-enhanced sagittal T1-weighted image shows the mass which eroding the floor of the sella turcica, extending to the right posterior nasal cavity.

Hormonal examination showed normal levels of serum thyroid stimulating hormone (TSH), and gonadotropins such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH), prolactin (PRL), growth hormone (GH) and adrenocorticotropic hormone (ACTH). So this tumor was a null cell giant pituitary adenoma without atypical features.

As a complementary surgical treatment, the patient was referred to the Neurosurgery Department for the excision of the remaining intracranial portion of the tumor. However, he declined



**Figure 4.** Monomorphic round adenoma cells with round and oval nuclei, conspicuous nucleolus and chromophobic cytoplasm (H-E x 200).



**Figure 3.** Axial T2-weighted image reveals the mass projecting into the posterior nose.

an intracranial operation and is being followed up with no other complaints.

#### DISCUSSION

Pituitary tumors can also be classified by size and invasive characteristics. Microadenomas are <10 mm whereas macroadenomas are >10 mm. Intrapituitary adenomas are within the substance of the pituitary gland; intrasellar adenomas are confined to the sella; diffuse adenomas fill the sella and cause focal sellar bone erosions. Invasive adenomas erode sellar and sphenoid bone walls, and spread into surrounding soft tissues like the cavernous sinuses, optic chiasm, third ventricle and brain.<sup>[4]</sup>

Nonfunctioning pituitary adenomas account for approximately 30% of pituitary tumors.<sup>[1]</sup> These



**Figure 5.** Nuclear staining for Ki-67 proliferating index was 1.7% (H-E x 200).

tumors do not cause clinical hormone hypersecretion. Despite the lack of clinical hormone hypersecretion immunocytochemical staining of hormones reveals evidence for hormone expression in up to 79% of these tumors. This situation can be explained by non-effective hormone synthesis.<sup>[1,6]</sup>

Nonfunctioning pituitary adenomas can be classified into two main groups: null cell adenomas and silent adenomas. Null cell adenomas are divided into non-oncocyctic and oncocyctic adenomas. Oncocytomas contain large numbers of mitochondria, show focal immunostaining for anterior pituitary gland hormones, and produce hormones *in vitro*. Silent adenomas consist of three morphological subtypes: silent corticotrope, silent somatotrope and gonadotrope NFPA.<sup>[6]</sup>

Enlargement of a tumor into the suprasellar area results in optic chiasmal compression which may cause visual field deficits. The initial visual field deficits are frequently bitemporal superior quadrant defects. Occasionally these tumors extend into the cavernous sinus.

Enlargement of a nonfunctioning adenoma can cause progressive loss of pituitary function over months or years. Gonadotropic hormone function is usually lost first, while adrenocorticotrophic hormone is lost last. Loss of antidiuretic hormone function is almost never a presenting symptom.<sup>[7]</sup>

Although progressive bitemporal visual field loss and progressive hypopituitarism are the typical presenting clinical manifestations, they may rarely be obvious symptoms. Occasionally, there may be cranial hemorrhage or infarction, in which case patients may complain of headache, visual loss and present acute hormonal insufficiency or loss of consciousness.<sup>[8]</sup>

If the enlarged adenoma is asymmetrical, the lateral radiograph may give the impression of a double sellar floor. The sella becomes more rounded. Also the dorsum sella may be thin, pushed back and anterior clinoids may be undercut.

The CT and MRI shows the exact anatomical configuration of the adenoma.<sup>[9]</sup> In our case, the CT and MRI clearly depicted the presence of a large, soft mass in the sphenoid sinus and its extensive invasion to the peripheric tissues.

In particular, MRI was found useful in delineating precise anatomic relationships between the sphenoid sinus, tumor and the pituitary fossa. It was useful both in defining anatomic relationships

among the sphenoid sinus, tumor and the sella turcica, and in differentiating from nontumorous mucosal lesions.

Radiologic differential diagnosis of a pituitary adenoma is a very extensive spectrum. Tuberculum sella meningiomas do not show enlargement of the sella, internal carotid artery aneuysm can be diagnosed as a flow void seen on an MRI, malignant tumor metastasis to the sella is frequently associated with extraocular muscle palsies or diabetes insipidus. Rathke's pouch cleft cyst presents as sellar or suprasellar cystic masses. Tuberculoma, giant cell hypophysitis and sarcoidosis may mimic NFPA.

A review of the literature indicates very few cases of pituitary adenomas of ectopic origin. In this case the mass was completely within the pituitary gland; it reached the widest diameter in this region and demolished all the sellar walls. Therefore, the tumor was thought to originate from the sellar region.

Pituitary tumors, which primarily infiltrate the sphenoid sinus and nasopharynx, are therefore uncommon disorders. They frequently produce such unique symptoms as nasal obstruction, recurrent epistaxis, or intermittent mucoid nasal discharge. In addition to these nasal symptoms, the majority of tumors also develop visual field defects, decreased visual acuity, and oculomotor or trochlear nerve palsy, which are attributable to simultaneous suprasellar and parasellar extensions of the tumor. In this case, in spite of massive tumor tissue, the patient's only complaint was nasal obstruction. Patient had no other complaints and no other pathological examination results apart from the sellar mass extending to the sphenoid sinus and beyond nasopharynx and oropharynx.

It was recently demonstrated by Scheithauser et al.<sup>[10]</sup> on the basis of immunocytochemical and ultrastructural analysis of 365 pituitary adenomas that there was a correlation between the frequency and the nature of invasiveness and the functional type of the adenoma. Prolactin producing adenomas and mixed GH- and PRL-producing adenomas are prone to grow in any direction, but the preferential pathway is infrasellar. They often invade the sphenoid bone and extend further into the nasopharynx.<sup>[10]</sup> In the present report, however, despite its nonfunctioning nature, the current adenoma appears to show a radiographic evidence of paranasal and posterior nasal cavity invasiveness.

Recently cDNA (Complementary deoxyribonucleic acid) microarray analysis has revealed that the folate receptor (FR- $\alpha$ ) is significantly overexpressed in clinically non-functional adenomas. Folate receptor- $\alpha$  is a high affinity folate transporter. Folate receptor- $\alpha$  is significantly overexpressed by NFPA. Overexpression of FR- $\alpha$  provides growth advantage to tumor cells and this may be detected by Western Blot technique.<sup>[11]</sup>

The usual treatment of a NFPA is microscopic or endoscopic transsphenoidal removal of the tumor.<sup>[2]</sup> Sellar and suprasellar tumors can be removed through a transsphenoidal approach by either a sublabial, transseptal or direct endonasal route using the endoscope or microscope. Relative contraindications to transsphenoidal surgery include a dumbbell tumor, especially if the neck is narrow and the upper part of dumbbell tumor is large. Occasionally, craniotomy will be needed in patients for whom transsphenoidal surgery is contraindicated.

Radiation therapy can be used in patients with NFPA. It controls tumor growth in 80-98% of patients with NFPA. If the patient is medically unstable, radiation therapy may be the sole option. The patient who postoperatively has a significant amount of residual tumor or who shows regrowth may be a candidate for fractionated radiation therapy.<sup>[12,13]</sup>

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