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Case report

NASOPHARYNGEAL CANCER AND TREATMENT RELATED EMPTY SELLA

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Introduction. Empty sella, characterized by herniation of subarachnoid space into the sella turcica, is a frequent radiological finding following therapeutic procedures for disorders involving the pituitary gland or the surrounding structures. We present a case of empty sella secondary to radiotherapy for nasopharyngeal cancer, accompanied by normal pituitary function, that was evaluated in several territorial centers. *Case presentation.* A 37-year-old male patient, with a history of irradiated nasopharyngeal carcinoma at the age of 17, was admitted for occipital headache, diplopia, memory and concentration problems, somnolence, dizziness and recurrent syncope. The pituitary function profile revealed normal levels of FSH (Follicle-Stimulating Hormone), LH (Luteinizing Hormone), PRL (Prolactin), ACTH (Adrenocorticotropic Hormone), with normal testosterone, cortisol and IGF1 (Insulin-like Growth Factor 1) levels. The only pathological findings were related to thyroid function: increased TSH-Thyroid Stimulating Hormone (of 9.55 μIU/mL, normal: 0.4–4 μIU/mL), decreased FT4- Free Thyroxine (of 0.47 ng/dL, normal: 0.61–1.35 ng/mL), with negative anti-thyroid antibodies. Morphological exploration of the hypothalamic-pituitary region by MRI (Magnetic Resonance Imaging) revealed the absence of pituitary parenchyma and pituitary stalk, with empty sella and extension of the subarachnoid fluid into the sphenoid sinus. The diagnosis of empy sella and primary hypothyroidism was established and thyroid replacement therapy was initiated. *Conclusion.* Regular monitoring of pituitary function is essential for patients at high-risk for empty sella. Although pituitary tissue is not visible on imaging, pituitary dysfunction may be absent.

Keywords: empty sella, radiotherapy, nasopharynx.

INTRODUCTION

Empty sella is characterized by the herniation of the subarachnoid space into the sella turcica, which is often associated with variable degrees of flattening of the pituitary gland[1–3].

Primary empty sella, without an apparent cause, is rarely encountered in clinical practice. Most often, empy sella occurs secondary to pathological processes involving the pituitary region or secondary to therapeutic procedures for disorders involving the pituitary gland or the surrounding structures, such as pituitary adenomas undergoing spontaneous regression, infections, trauma, vascular and autoimmune disorders, radiotherapy and surgery[3,4].

Magnetic Resonance Imaging examination of the hypothalamic-pituitary region remains the best diagnostic test in the presence of suggestive symptomatology or medical history. Treatment is rarely necessary and requires correction of the recorded hormone deficiencies[1,4].

CASE PRESENTATION

A 37-year-old male smoker was admitted for occipital headache, diplopia, memory and concentration problems, somnolence, dizziness and two episodes of syncope. His medical history

revealed nasopharyngeal cancer diagnosed at the age of 17, treated by radiation therapy, as well as surgically treated varicocele.

Clinical examination showed height of 192 cm, weight of 105 kg, BMI (Body Mass Index) of 28.4 kg/m^2, normal blood pressure of 110/80 mmHg without postural hypotension, normal heart rate of 78 bpm.

Pituitary function tests excluded the presence of pituitary hormone deficiency. Normal values were also obtained for peripheral hormones: testosterone, serum cortisol, UFC (Urinary Free Cortisol) and IGF1. Thyroid function tests revealed primary hypothyroidism, with high TSH levels of 9.55 µIU/mL (normal: 0.4–4 µIU/mL), low FT4 levels of of 0.47 ng/dL (normal: 0.61–1.35 ng/mL) and negative anti-thyroid antibodies (Table 1).

Biochemical workup showed hypertriglyceridemia (of 296 mg/dL, normal:<150 mg/dL) and isolated ALT (Alanine Amino Transferase) increse of 74 U/L (normal: < 45 U/L). Thyroid ultrasound described low-normal thyroid volume (right lobe measuring 3.1 ml, left lobe measuring 4.2 ml), fine granular echostructure, with a hypoechoic lesion measuring 3 mm located on the anterior side of the right lobe, normal vascularization of parenchyma; there was no laterocervical adenopathy.

Contrast-enhanced pituitary MRI scan revealed the absence of pituitary parenchyma and pituitary stalk, with empty sella and extension of the subarachnoid fluid into the sphenoid sinus (Figure 1). No pathological findings were reported on neurological and ophthalmological exams.

Table 1

The endocrine parameters of a 37-year-old man diagnosed with empty sella and primary hypothyroidism TSH=Thyroid Stimulating Hormone; FT4=Free Thyroxine;FSH=Follicle-Stimulating Hormone; LH=Luteinizing Hormone;UFC= Urinary Free Cortisol; IGF-1= Insulin-like Growth Factor 1; PRL= Prolactin; ACTH= Adrenocorticotropic Hormone

Parameter	**Value**	**Normal**	**Units**
TSH	9.55	0.4–4	µIU/mL
FT4	0.47	0.61–1.76	ng/dL
FSH	6.53	0.7–11.5	U/l
LH	2.26	0.8–7.6	U/l
Testosterone	2.9	1.3–8.53	ng/mL
Cortisol	17.3	6–23	µg/dL
UFC	188	50–190	µg/24 h
IGF1	193.4	117–329	ng/mL
PRL	14.6	2.5–17	ng/mL
ACTH	28.9	7.2–63.3	ng/mL

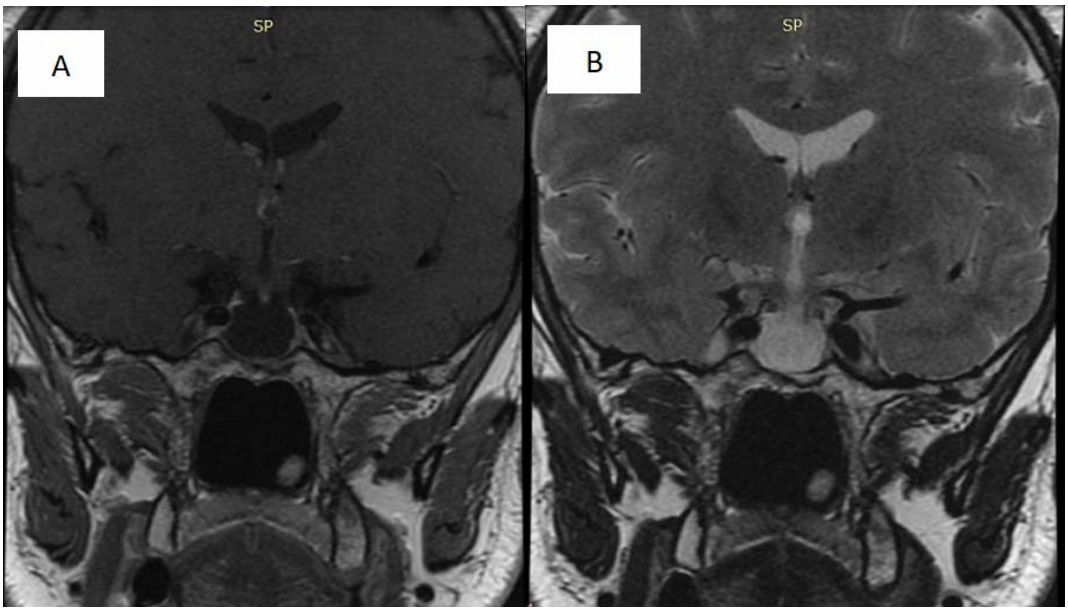

Figure 1. T1 (A) and T2 (B) contrast-enhanced pituitary MRI scan of a 37-year-old man with empty sella: absence of pituitary parenchyma and pituitary stalk, extension of the subarachnoid fluid into the sphenoid sinus. Coronal plane.

The diagnosis of empy sella and primary hypothyroidism was established and thyroid replacement therapy with 50 μg thyroxine daily was initiated. Periodic follow-up by a multidisciplinary team is required.

DISCUSSION

This case highlights the link between the late effect of radiotherapy for nasopharyngeal cancer and the presence of empty sella. Radiotherapy has an important role in treating head and neck cancer. It represents the main curative option in advanced tumors[5]. In nasopharyngeal carcinoma, radiation therapy may induce late complications due to partial irradiation of healthy neighboring organs. Concomitant chemotherapy increases the risk of endocrine disorders due to involvement of the thyroid gland or hypothalamic-pituitary axis[6]. Radiation-induced empty sella or pituitary atrophy/small pituitary and endocrine dysfunction, including pituitary and gonadal dysfunction, can manifest decades after initial irradiation[7].

Empty sella is also found in patients with brain tumors that are not situated in the pituitary fossa. While cases of empty sella resulting from primary pituitary tumors and their surgical treatment are frequently reported, the incidence and its relationship to other brain tumors has rarely been described[8–10]. In this case the clinical symptomatology raised suspicion of a pituitary adenoma. The absence of morphological changes on MRI, normal pituitary function and medical history allowed the exclusion of an empty sella secondary to spontaneous pituitary tumor necrosis.

There are multiple reports in literature of primary empty sella and empty sella caused by surgery, radiation or chemotherapy for pituitary fossa pathologies, but there are few reports on empty sella secondary to brain tumors[10].

The basic diagnostic evaluation for empty sella includes measuring morning cortisol levels as well as FT4, estradiol or testosterone, IGF-1 and prolactin. If pathological changes are detected, further exploration may be required, such as additional hormone stimulation tests[11]. In our case there were no reported pathological findings in any of the aforementioned parameters.

According to one study, the prevalence of endocrine dysfunction in secondary empty sella is higher (62%) compared to 46% reported for primary empty sella[12].

Empty sella should be distinguished from other pituitary abnormalities or cystic lesions, such as arachnoid and epidermoid cysts and congenital pituitary anomalies. Suprasellar arachnoid cysts may in fact herniate into the sella, which may appear enlarged or eroded[13].

Empty sella syndrome requires a multidisciplinary team including endocrinology, neurology and ophthalmology specialists in order to reach a correct diagnosis and ensure adequate management[12]. Indications for surgical treatment are: spontaneous cerebrospinal fluid rhinorrhea, because of the risk for meningitis, visual disturbances and severely increased intracranial pressure[14]. In this case, no specific therapy was required except for the correction of primary hypothyroidism. Opposite to secondary empty sella primary types (associated or nor with secretor or non-functioning pituitary adenoma) usually do not require specific therapy, only imaging and endocrine follow-up in addition to specific therapy for neoplasia[15–18].

CONCLUSION

Regular monitoring of pituitary function is essential for patients at high-risk for empty sella. Although pituitary tissue is not visible on imaging, pituitary dysfunction may be absent. Close follow-up by a multidisciplinary team is usually required.

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