CASE REPORT

Germ cell tumor presenting as sellar mass with suprasellar extension and long history of hypopituitarism

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Abstract

OBJECTIVE: Primary central nervous system germ cell tumors are rare neoplasms usually located in the pineal and/or suprasellar region. Pure germinomas do not usually secrete β-human chorionic gonadotropin hormone (β-HCG) or alpha-fetoprotein (AFP) and diagnosis is made a few weeks or months after beginning of symptoms.
CASE: Here we report a case of a pure germinoma in a 20 year-old woman presenting as a sellar mass with suprasellar extension, abnormal serum β-HCG and a long history of polyuria and polydipsia (4 years), that was initially diagnosed as a pituitary macroadenoma.
CONCLUSION: This presentation highlights the importance of thinking in alternative diagnosis to pituitary adenoma when diabetes insipidus is the initial symptom.

INTRODUCTION

Pituitary adenomas account for 6–10% of all symptomatic intracranial tumors. They can be functioning adenomas, usually presenting with signs and symptoms of hormone excess (somatotropinomas, prolactinomas, corticotropinomas and thyrotropinomas) or non-functioning adenomas (Melmed & Kleinberg 2008). Pituitary adenomas with suprasellar extension often present with visual field defects caused by pressure in the optic chiasm (Melmed & Kleinberg 2008). Upward extension of the sellar tumor can also cause compression of the pituitary stalk which in turn compromises the release of dopamine, resulting in an increase in serum prolactin (usually not above 150 ng/dL) (Chahal & Schlechte 2008). Cranial nerve palsy may occur if the cavernous sinus is invaded.

Abbreviations:

β-HCG	- β-human chorionic gonadotropin hormone
AFP	- Alpha-fetoprotein
GCT	- Germ cell tumor
MRI	- Magnetic resonance imaging
TSH	- Thyroid stimulating hormone
FT4	- Free thyroxine
CDI	- Central diabetes insipidus
CSF	- Cerebrospinal fluid

Malignant germ cell tumors (GCT) are rare neoplasms occurring most commonly in the young population, with a peak incidence for the central nervous system in the 10–12 year-old population (Rondinelli *et al.* 2005; Echevarría *et al.* 2008). They comprehend a heterogeneous group with multiple histological subtypes composed of pure germinomas, nongerminomatous GCT (embryonal carcinomas, yolk sac tumors, choriocarcinomas), teratomas and mixed tumors. They usually arise from the pineal and/or suprasellar region resulting in symptoms secondary to increased intracranial pressure and hypothalamic/pituitary axis dysfunction (Rondinelli *et al.* 2005). Diagnosis is usually made in few days or weeks but rare cases with long term evolution before diagnosis (up to three years) have been described (Crawford *et al.* 2007). In these cases, the predominant symptoms were those resultant from hormone deficiency and the age at diagnosis ranged from 9 to 13 years (Crawford *et al.* 2007).

CASE

A 20-year-old female patient presented with bitemporal hemianopsia during routine ophthalmic consultation and a magnetic resonance imaging (MRI) of the sellar region was ordered. The MRI revealed a sellar mass with suprasellar extension compressing the optic chiasm, third ventricle, hypothalamus and cavernous sinuses bilaterally, mainly at the left. The lesion was isointense to the cortex in T1- and T2-weighted images and showed contrast enhancement (Figure 1). She was then referred to our endocrinology unit with the diagnosis of a giant pituitary adenoma. At initial evaluation, she had a history of secondary amenorrhea since she was 12 years old and a four years complaint of polyuria and polydipsia. Nausea, vomiting and hyporexia began six months before the consultation.

Physical examination revealed bitemporal hemianopsia, normal height and weight and no galactorrhea.

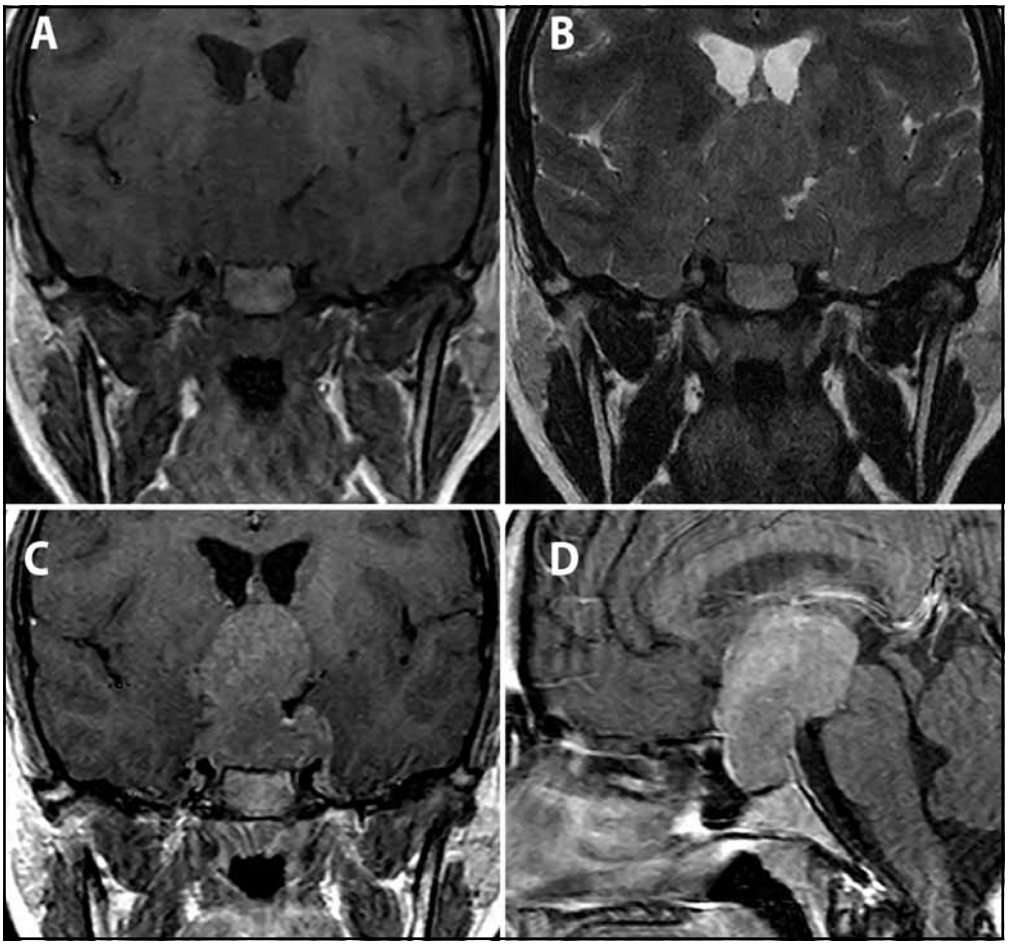

Fig.1. Lesion is isointense to the cortex in coronal T1- and T2-weighted images (**A** and **B**, respectively); tumor after contrast enhancement in coronal and sagittal T1-weighted images (**C** and **D**, respectively). The tumor is compressing the optic chiasm, third ventricle and hypothalamus.

At baseline pituitary function evaluation, patient had hypocortisolism (cortisol: 1.9 mcg/dL), central hypothyroidism (FT4: 0.5 ng/dL, TSH: 0.99 mcUi/mL), serum prolactin level of 118 ng/mL even after dilution to exclude hook effect and a low urinary osmolarity (200 mOsm/Kg) with serum sodium in the upper reference limit (142 mEq/L, normal range 135–142), confirming pan-hypopituitarism, hyperprolactinemia due to stalk compression and diabetes insipidus. Glucocorticoid replacement therapy was started followed by levothyroxine replacement. Since diabetes insipidus is a very rare presentation of pituitary adenomas, we considered other diagnosis. Considering the patient's age, a germ cell tumor was suspected and AFP and β-HCG were requested. Serum AFP was in the normal range but β-HCG level was 18 IU/L (normal range < 5 IU/L), suggesting the diagnosis of a GCT.

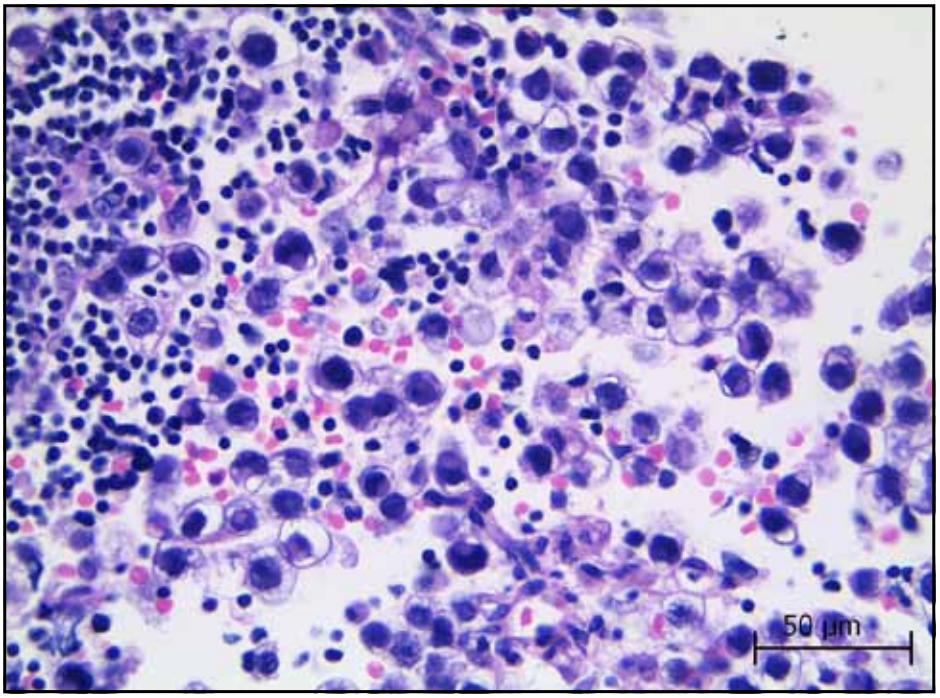

Fig. 2. Tumor germ cells are well defined, have large nuclei and prominent nucleoli. Mature lymphocytes are seen among the germ cells.

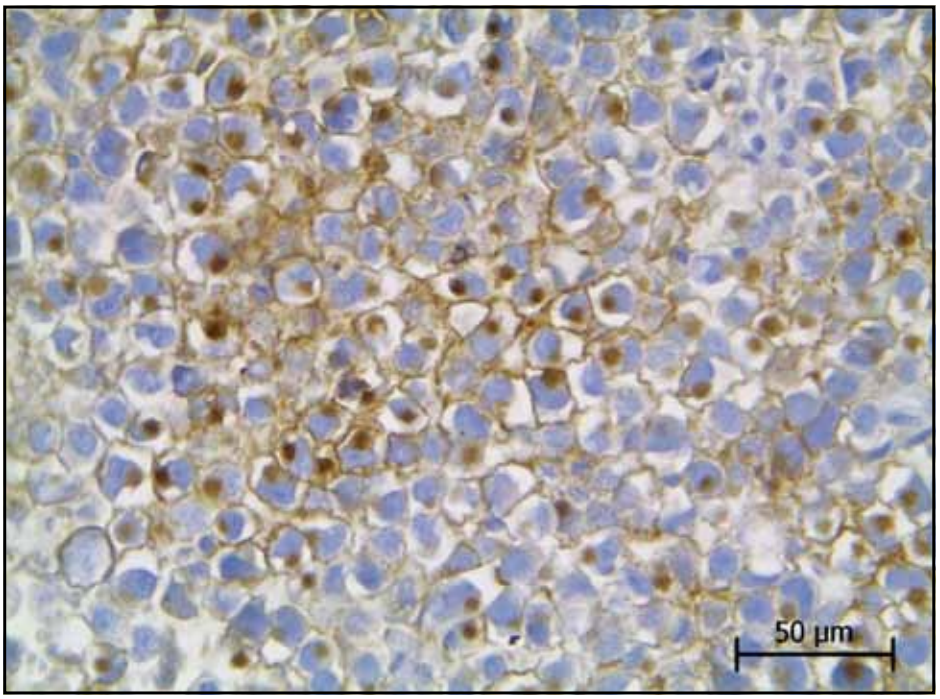

Fig. 3. Germ cells are immunopositive for placental alkaline phosphatase.

Patient underwent frontal craniotomy for third ventricle decompression and to obtain a specimen for tumor histological diagnosis. Histopathology analysis revealed a pure germinoma, consisting of large germ cells mixed with mature lymphocytes (Figure 2). Germ cells were immunopositive to placental alkaline phosphatase (Figure 3). Radiotherapy was then indicated.

DISCUSSION

In the case described, the patient presented with a sellar mass with suprasellar extension associated with a long history of pan-hypopituitarism suggesting the diagnosis of a non-functioning pituitary macroadenoma. However, the presence of central diabetes insipidus raised the suspicion of an alternative diagnosis (Wildemberg *et al.* 2008). Central diabetes insipidus (CDI) results from deficiency of arginine vasopressin peptide. It is caused by destruction or degeneration of the neurons that originate in the supraoptic and paraventricular nuclei of the hypothalamus. It can be caused by infiltrative diseases or tumors, although pituitary adenomas very rarely cause CDI (Silva *et al.* 2008; Kaltsas *et al.* 2008).

All patients with suspected GCT require measurement of AFP and β-HCG in serum and/or cerebrospinal fluid (CSF). Many groups consider a tumor as having positive markers if the serum and/or CSF AFP is ≥ 10 ng/dL (or higher than the laboratory normal values) and when the β-HCG is ≥ 50 IU/L (or higher than the laboratory normal values) (Echevarría *et al.* 2008). Nongerminomatous GCT often present tumor marker elevation, while pure germinomas and teratomas usually present with negative markers (Balmaceda & Finlay 2004), which makes the differential diagnosis with other causes of sellar masses a challenge task. However, some rare cases have been described (Sawamura *et al.* 1998) and this case represents another example.

In conclusion, clinicians should always have in mind that the presence of signs and symptoms of diabetes insipidus associated with a sellar mass ought to raise the suspicion of alternative diagnosis to pituitary adenomas. When GCT is a possible diagnosis, tumor markers should be measured in blood or CSF.

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