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Clinical Case Seminar **CCS2(1-6)**

Unusual sellar lesions mimicking a pituitary neuroendocrine tumour (PitNET)

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Abstract

Sellar region hosts a wide range of different types of lesions. Most of these lesions present with mass effect symptoms and, often, with symptoms related to hormonal disturbances, mimicking a pituitary neuroendocrine tumour (PitNET). We report two cases of sellar lesions with clinical and radiological features suggestive for PitNET. Histological and immunohistochemical analysis led to a diagnosis respectively for lymphocytic hypophysitis (LH) and meningioma.

Keywords: PitNET, sellar lesions, hypophysitis, meningioma

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Introduction

Pituitary neuroendocrine tumours (PitNETs) are the most common lesions of the sellar and suprasellar region, accounting for 85% of the sellar masses (1). Clinical features of PitNETs include symptoms caused by hyperproduction of hormones as acromegaly, galactorrhoea, and hypogonadism or mass effects symptoms as headache, or visual disturbances(1). PitNETs can also be asymptomatic and detected incidentally on neuroimaging (2). However, other types of lesions (neoplastic, inflammatory, or developmental) may involve the sellar and suprasellar region (3,4). These lesions have characteristic clinical and radiological features that can suggest a preoperative diagnosis. Nevertheless, they can occur with symptoms of hormonal hyper- or hypoproduction and mimicking PitNETs (3,4). Herein, we report two cases of different sellar lesions mimicking PitNETs. The first case is a lymphocytic hypophysitis (LH) in a young woman with oligomenorrhea; the second is a sellar meningioma in a man with hypopituitarism.

Case presentation

Case 1

In 2019, a 22-year-old woman presented a history of oligomenorrhea, polycystic ovary syndrome, and mild hyperandrogenism. Baseline endocrine test undertaken revealed high level of prolactin (89.79 ng/ml, range 1-20) and normal ACTH (13.86 pg/mL range 7-65) FSH (7.52 mUI/mL), LH (6.24 mUI/mL), GH (3.01 ng/ml, range <10). A pituitary magnetic resonance imaging (MRI) scan showed a 1.5 cm lesion without optic chiasm compression, suggestive for pituitary macroadenoma. Cabergolin was administered orally for 3 months resulting in the decreasing of prolactin levels (10.5 ng/ml) and disappearing of oligomenorrhea. In 2021, a pituitary MRI scan confirmed the presence of the unchanged sellar lesion, and biochemical endocrine test revealed a new elevation of prolactin level (72.1 ng/ml) after therapy suspension. In January 2022, the patient underwent transsphenoidal surgery for the removal of the sellar lesion.

Histological examination performed on formalin-fixed paraffin-embedded tissue blocks showed inflammatory infiltration of normal pituitary cells nests, mainly represented by lymphocytes, sometimes arranged in follicles (Fig.1a,b). Reticulin stain section showed the normal architecture of the pituitary gland (Fig. 1c). On immunohistochemical sections, the inflammatory infiltrate was strongly positive per CD20 (Fig. 1d) and CD3, whereas pituitary cells were positive for synaptophysin and prolactin. Ki67 proliferation index was over 50% at the centre of the lymphocytic follicles and less than 1% in the pituitary component. On the light of the histopathological and immunohistochemical findings, the final diagnosis was lymphocytic hypophysitis (LH).

Case 2

A 63-year-old man was admitted to the endocrinology department after an episode of severe fatigue, weight loss, hypoglycaemia, and headache. Baseline endocrine test revealed an anterior panhypopituitarism (TSH 0.02 mIU/ml, range 0.4-4; PRL 3 ng/ml, range 4.79-23.3; FSH 2.9 mIU/ml; LH 1.1 mIU/ml). A pituitary MRI scan showed a 1.3 cm intrasellar lesion with intense and homogeneous enhancement and normal pituitary stalk and optic chiasm, suggestive for pituitary adenoma. The patient underwent transsphenoidal surgery for the removal of the lesion.

Fig.1 a,b: Normal pituitary tissue with lymphocytic infiltrate (HE, original magnification 10x (a) and 20x (b). c: reticulin stain surrounding normal pituitary nests (original magnification 10x). d: lymphocytic infiltrate positive for CD20 (original magnification 20x)

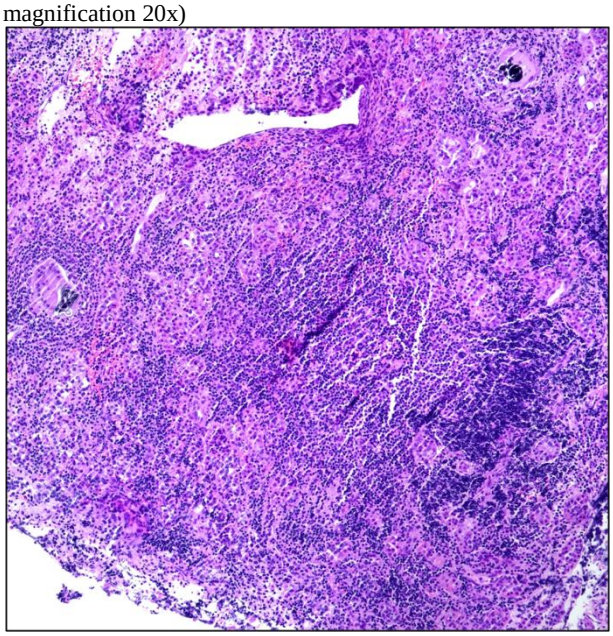

Fig. 1a

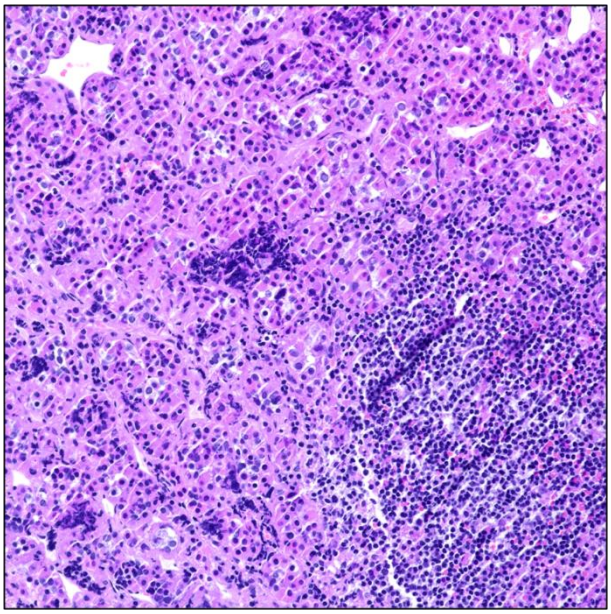

Fig. 1b

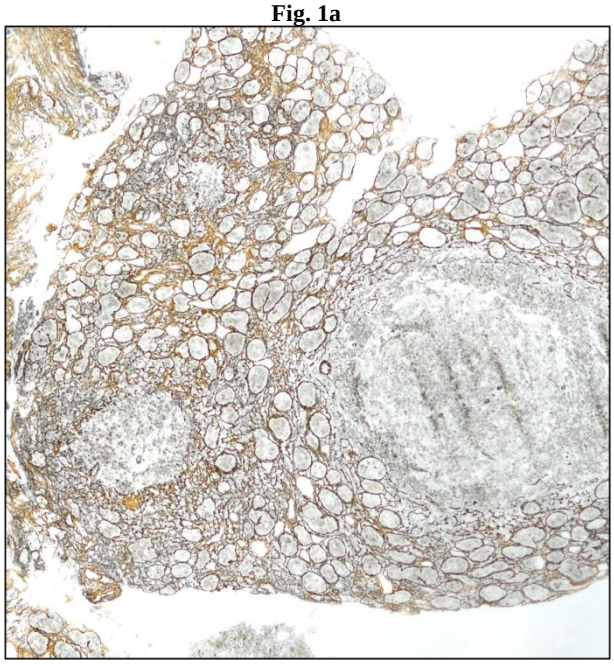

Fig. 1c

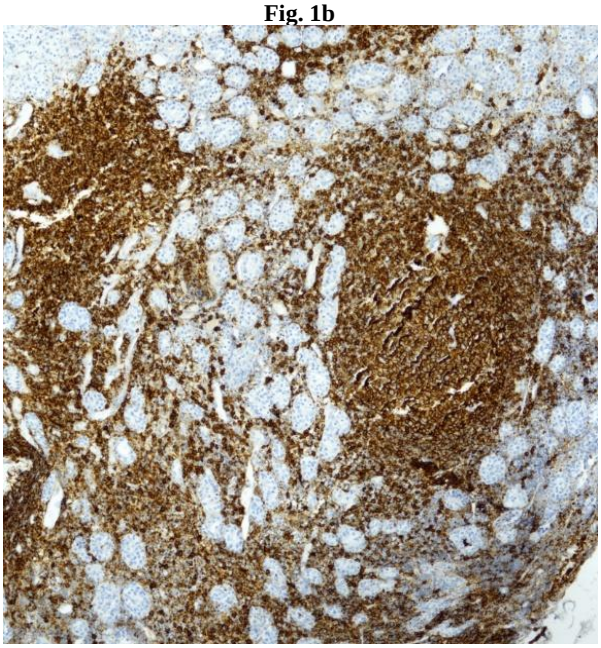

Fig. 1d

Histological examination of the specimen revealed a small fragment of normal pituitary tissue adjacent to a neoplastic proliferation represented by a lobular pattern of epithelioid cells subdivided by thin fibrous septa (Fig. 2a, 2b). Mitotic count and presence of infiltration of nervous tissue could not be evaluated due to the small size of the tissue fragment. On immunohistochemical examination, neoplastic elements were positive for vimentin (Fig. 2c), epithelial membrane antigen (EMA) (Fig. 2d) and progesterone, but always negative for chromogranin and pituitary hormones. On the light of the histopathological and immunohistochemical findings, the final diagnosis was meningioma.

Fig.2 a,b: Neoplastic proliferation of meningothelial cells with lobular architecture (HE, original magnification 20x (a) and 40x (b)). c,d: meningothelial cells are positive for vimentin (c, original magnification 20x) and EMA (original magnification 40x

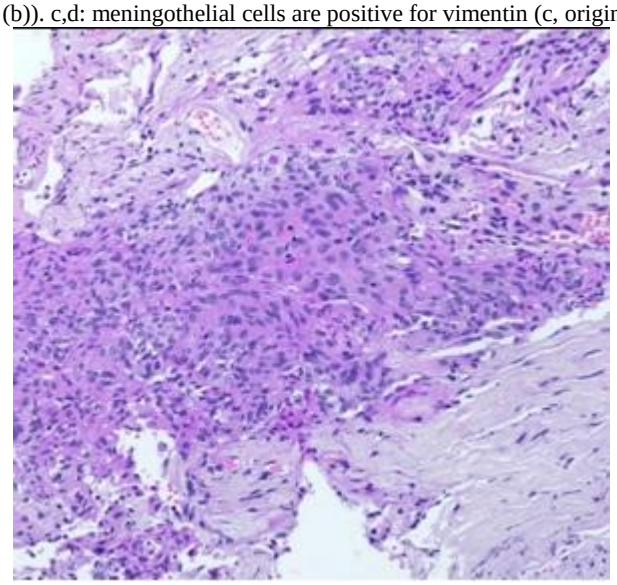

Fig. 2a

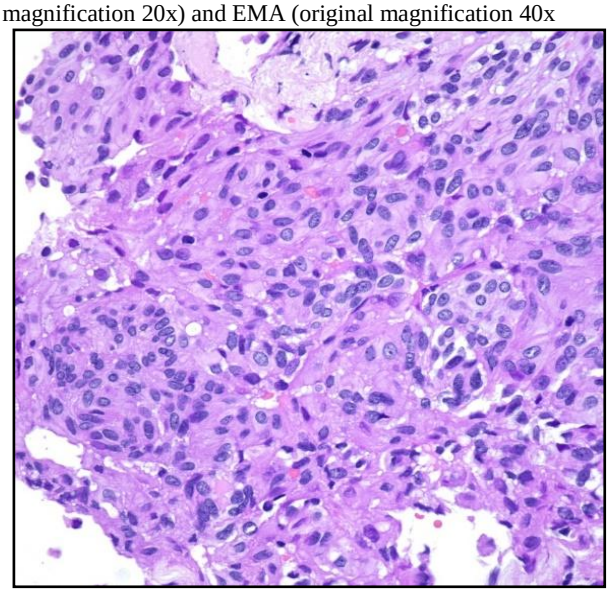

Fig. 2b

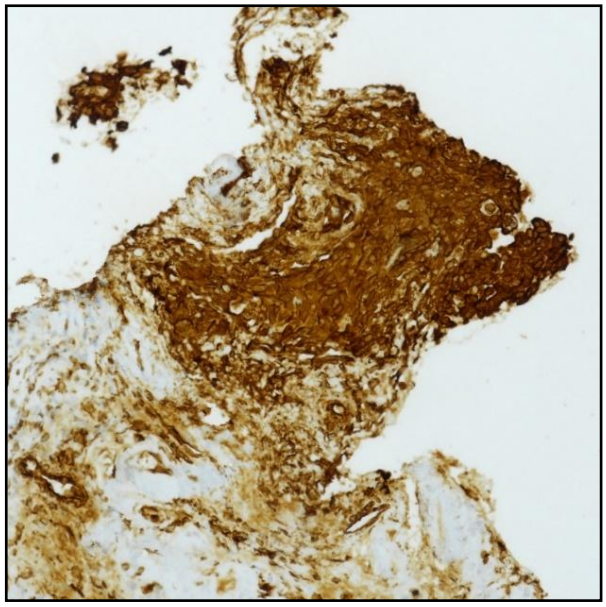

Fig. 2c

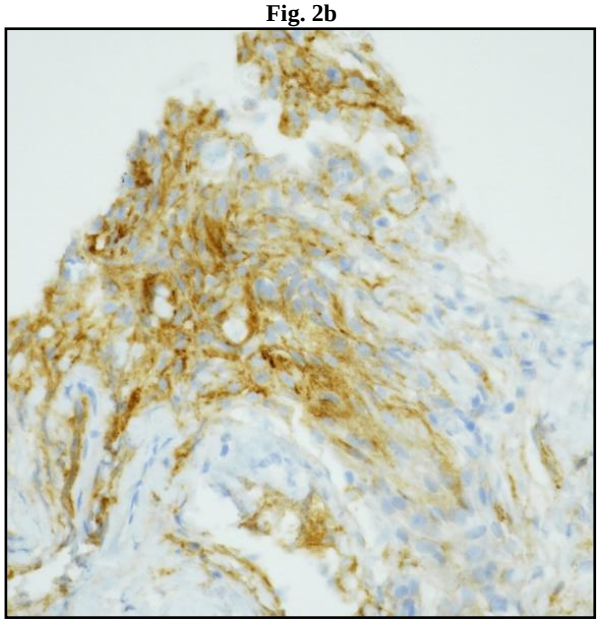

Fig. 2d

Discussion

The sella turcica is a saddle-shaped depression in the sphenoid bone located in the central part of the skull base that contains the pituitary gland. The most common lesion occurring in the sellar and suprasellar region is PitNET accounting for 85% (1) of the sellar masses and for 15% of all central nervous system tumours (2). However, sellar and suprasellar region can be the location of a large variety of neoplastic, inflammatory, developmental, or vascular lesions (3,4). The most common of these lesions are Rathke's cleft cyst (28-33%), craniopharyngioma (12-16%), LH (5%), and meningioma (3-8%) (5,6). Clinical features of sellar lesions include endocrine, visual, and neurological symptoms (3-6). It is important, in a case of a sellar lesion, to perform a complete diagnostic evaluation comprehensive of endocrinologic, ophthalmologic, neurologic

assessments and neuroimaging studies. In most cases, these lesions show characteristic clinical and imaging features that will lead to a preoperative diagnosis but in some cases, a histological and immunohistochemical evaluation is necessary to reach a definitive diagnosis (4).

Our first case concerned a young woman with symptoms referred to a hyperproduction of prolactin. The MRI scan and biochemical findings suggested the possibility of the diagnosis of PRL-secreting adenoma. Nevertheless, histopathological and immunohistochemical examinations revealed the presence of an inflammatory lymphocytic infiltrate in the pituitary gland, hence the diagnosis of LH.

Hypophysitis is a rare condition characterised by acute or chronic inflammation of the pituitary gland (7). It can be classified according to location (involving anterior pituitary, posterior pituitary, or infundibulum), etiology (primary or secondary to systemic diseas), or histology (lymphocytic, granulomatous, Ig4-related, xanthomatous, or necrotizing) (7).Clinically, hypophysitis presents with symptoms related to pituitary deficiencies and/or symptoms related to mass effect of an enlarged pituitary gland. MRI findings of hypophysitis are a thickened, pituitary stalk, that can be associated with gland enlargement (7,8). LH is the most common variant. The majority of LH occur in women and the majority of the cases are associated with pregnancy, post-partum period, or autoimmune diseases (7,8). Histologically, LH is characterized by focal or diffuse infiltration of predominantly lymphocytes with fewer plasma cells, eosinophils, and fibroblasts (7,8).

Our second case concerned a man with anterior panhypopituitarism, and an MRI finding was suggestive for pituitary adenoma. In this case, histological examination revealed an epithelioid lesion adjacent to normal pituitary nests. Immunohistochemical stains suggested the meningothelial nature of the tumour.

Meningiomas are commonly slow-growing, extra-axial lesions, accounting for 20% of intracranial neoplasms, and 3-8% of sellar and suprasellar lesions (4,9). Meningiomas are usually benign, but some can show aggressiveness signs, therefore, they are classified in three grades based on the mitotic count, the presence or absence of brain infiltration, the presence of particular subtypes, and other minor criteria (9). Sellar meningiomas may present with headache, visual disturbances, hypopituitarism, or a combination of these conditions. On MRI, meningiomas are often bright, homogenously enhancing lesions that arise from the skull base (10). Histologically, meningiomas are composed by epithelioid cells admixed with a fibroblastic component; whorls and psammoma bodies are common (9,10).

Conclusions

The present cases highlight the importance to make a proper diagnosis of sellar and suprasellar

lesions, since their heterogeneity leads to different prognosis and treatment. A multidisciplinary approach is often needed for a better understanding and evaluation of these lesions.

Conflicts of interest: The authors declare no conflict of interest.

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