

Spindle Cells Oncocytoma and Rathke's Cyst; A Collision Sellar Tumor–Brief Communication & Case Report

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ABSTRACT

Collision tumors comprising of pituitary adenomas with other sellar neoplasms are rare. Histological examination is necessary since preoperative studies cannot guarantee an accurate diagnosis. A 66-year-old man with headache and progressive visual alterations, MRI showed a sellar tumor that was diagnosed as pituitary adenoma and graduated as HV IIIc. He underwent surgery and two lesions were resected, one on the cavernous sinus and the other one in sellar region. The lesion of the venous sinus corresponds to a cyst covered by a ciliated pseudostratified epithelium that was diagnosed as Rathke's cyst, and the second one was formed by a neoplastic lesion of elongated cells with focal cellular atypia in a sarcomatous pattern, forming fascicles alternating with a pattern formed by medium eosinophilic cells predominantly in elongated cells in a stroma with abundant sinusoids. For immunohistochemistry, the epithelium of the cyst was PTTG-1, cytokeratin 6/8, and chromogranin positive, while the other lesion was positive chromogranin, FSH, LH PTTG-1, TTF-1, while the spindle cells area was positive immunoreaction for PTTG-1, GFAP, S-100, and VIM and weak expression for TTF-1. These histologic and immunohistochemical findings are suggestive of spindle cells oncocytoma and Rathke cyst, is a rare sellar collision tumor. The expression of TTF-1 in the spindle cell oncocytoma with the idea of common histogenesis for pituitary adenoma and SCOs and raise the possibility of more aggressive growth in SCOs as compared to pituitary adenoma.

Keywords

Collision tumor, Pituitary adenoma, Sellar region, Spindle cell oncocytoma, Rathke cleft cysts.

Abbreviations

SCO: Spindle Cell Oncocytoma, AH: Adenohypophysis, WHO: World Health Organization, CNS: Central Nervous System, NNT: Non-Neuroendocrine Tumors, FSC: Folliculostellate cells, RCCs: Rathke's Cleft Cysts, PA: Pituitary Adenoma, PT: Pituitary Tumors, NFA: Nonfunctional Adenomas, ST: Synchronic Tumors, CT: Collision Tumors, EMA: Epithelial Membrane Antigen, TTF-1: Thyroid Transcription Factor-1 and EM: Electron Microscopy.

Introduction

Spindle cell oncocytoma (SCO) of the adenohypophysis (AH) is a rare benign tumor in the sellar region. Accounting for 0.1–0.4% of all sellar tumors [1]. SCO was first identified as a distinct entity by the World Health Organization (WHO) classification of tumors of the central nervous system (CNS) in 2007. A newly proposed as non-neuroendocrine tumors (NNT) [1]. SCO was first reported by Roncaroli et al. [1] in 2002 in five patients [2] and was considered as a tumor of folliculostellate cells (FSC) [3]. The clinical characteristics commonly occurred in middle-aged and elderly males. The average age of the SCO patients is 56.4 years (range, 24–76 years), and it presented with decreased or impaired visual acuity and endocrinal disturbances [4], Etc. Most of the

cases reported have been misdiagnosed as being nonfunctional adenomas [4].

Rathke cleft cysts (RCCs) are benign embryonic remnants of the Rathke's pouch comprising about 1% of all intracranial lesions [5]. Most RCCs are asymptomatic and they may manifest themselves by compressing adjacent structures, causing pressure effects such as headache, visual disturbance, or pituitary hormone deficits, and their management remains controversial [5]. Therefore, like other sellar tumors, SCO and RCC are associated with postoperative complications, such as diabetes insipidus and adverse events can comprise cerebrospinal fluid leak, DI, anterior pituitary deficits, chemical meningitis, sinusitis and bleeding. Complete removal of the tumor is important to prevent tumor recurrence [5]. The origin of both injuries could be the same.

The association between pituitary adenoma (PA) with a second sellar lesion is an uncommon entity and represent two morphologically different tumors that are attached to each other although rare, quite a great variety of lesions have been recognized synchronized with PA [6], as well as, there are called as collision tumors, (CT) or synchronic tumors (ST), or tumor-by- tumor [7]. Assumed the similarities of the clinical and imaging features to those of PT, a preoperative diagnosis of a dual pathological condition of the sellar region is highly difficult. A definitive diagnosis of a collision sellar lesion is usually based on histopathology [5,6].

The aim of this word is reported a rare case of a 66 years-old male with a collision tumor; a spindle cell oncocytoma and Rathke cyst. This is the first collision tumor observed with this rare histological combination.

Case Report

A 66-year-old man started with frontal headache with loss of visual acuity, predominance of the left eye, chiasmatic syndrome, and bitemporal hemianopsia. A TAC was performed and shows a sellar lesion and a left frontal cystic lesion, the diagnosis of non-functional PA, graded as Hardy-Vezina IIIC (Figures 1). On examination, he had hypothyroidism and hypercortisolism, during surgery he performed hyponatremia.

Two specimens are sent for histopathological study. The first corresponded to a cystic lesion measuring 10x10mm, whitish with a thin wall, histologically this lesion was covered by a stratified cylindrical high epithelium (Figure 2a and 2b). For HIQ, it was positive for low molecular weight cytokeratin (Figure 2c), PTTG-1 (Figure 2d).

The second sample corresponded to several fragments of tissue that measured 20x10mm, white, rubbery, soft. Histologically, a neoplasm formed by two different patterns, one forming swirls and eosinophilic cells intermingled with numerous vessels and dilated sinusoids (Figure 3a) there were no mitosis figures, no necrosis, no cellular pleomorphism. HIQ examination this pattern was positive immunoreaction for vimentin (Figure 3b), pit-1, PTTG-1 (Figure 3c), TTF-1 (Figure 3d), s-100 (Figure 3e) showed strong immunoreaction in RSC, FSH, LH, and was negative for cytokeratin, adenohipophys hormones (GH, Prolactin, ACTH), NSE, syn, chromogranin, tubulin, GATA and the ki67 labeling index was 2%. And the second histologically pattern observed was a spindle cells forming irregular's fascicles (Figure 3f), in this area the immunohistochemistry analysis was vimentin, GFAP (Figure 3g), S-100 (Figure 3h), GTTG-1 (Figure 3i), TTF-1 (Figure 3j),

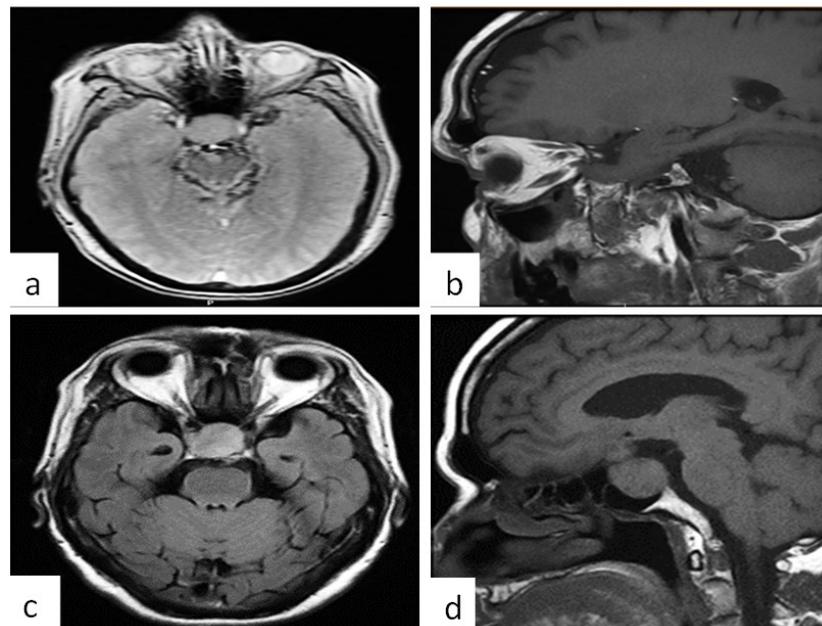


Figure 1: MRI images (a) The mass showing a contrast-enhanced mass compressing the pituitary stalk and optic chiasma in T1-weighted enhanced imaging appeared isointense on T1-weighted images (T1WI), and there was signal heterogeneity on T2-weighted images (T2WI); (b) and (c) the central homogeneous enhancement was remarkable following gadolinium-diethylenediamine pent acetic acid (Gd-DTPA) administration, showing a contrast-enhanced mass compressing the pituitary stalk and optic chiasma in T1-weighted enhanced imaging in (d).

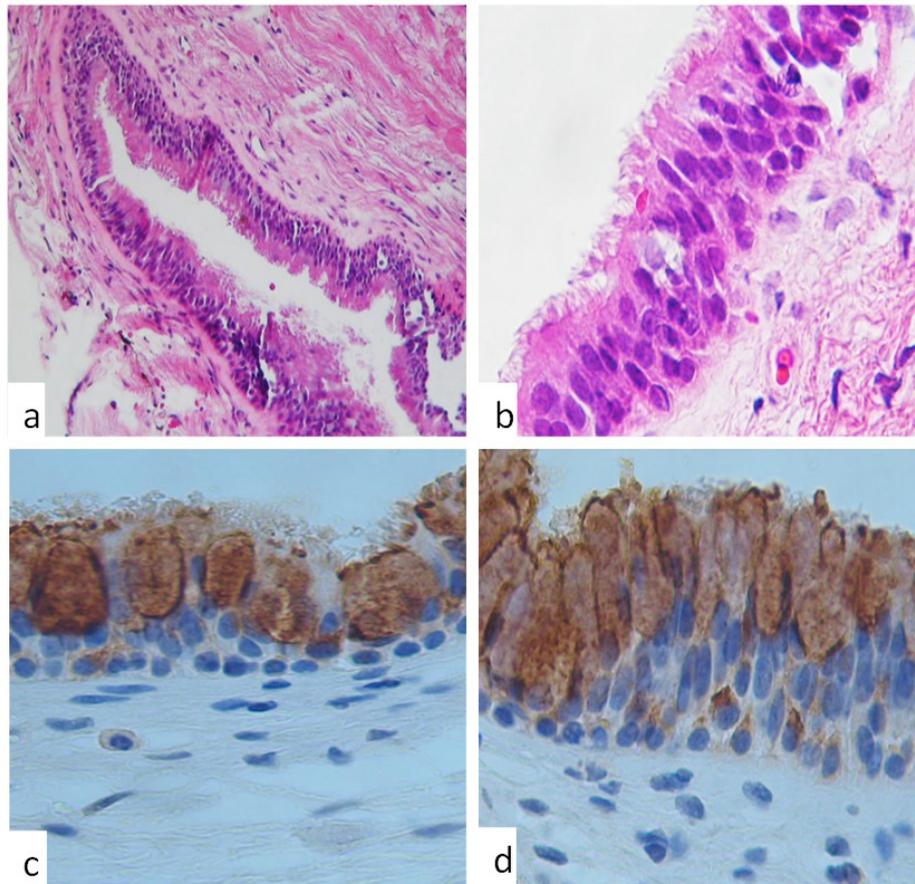


Figure 2: Histologically images for the first surgical specimen, formed by a cyst lesion (a) and (b) covered by a stratified cylindrical high epithelium (H&Ex400), and for HIQ examination (c), it was positive for low molecular weight cytokeratin and for (d) PTTG-1 positive expression (x400).

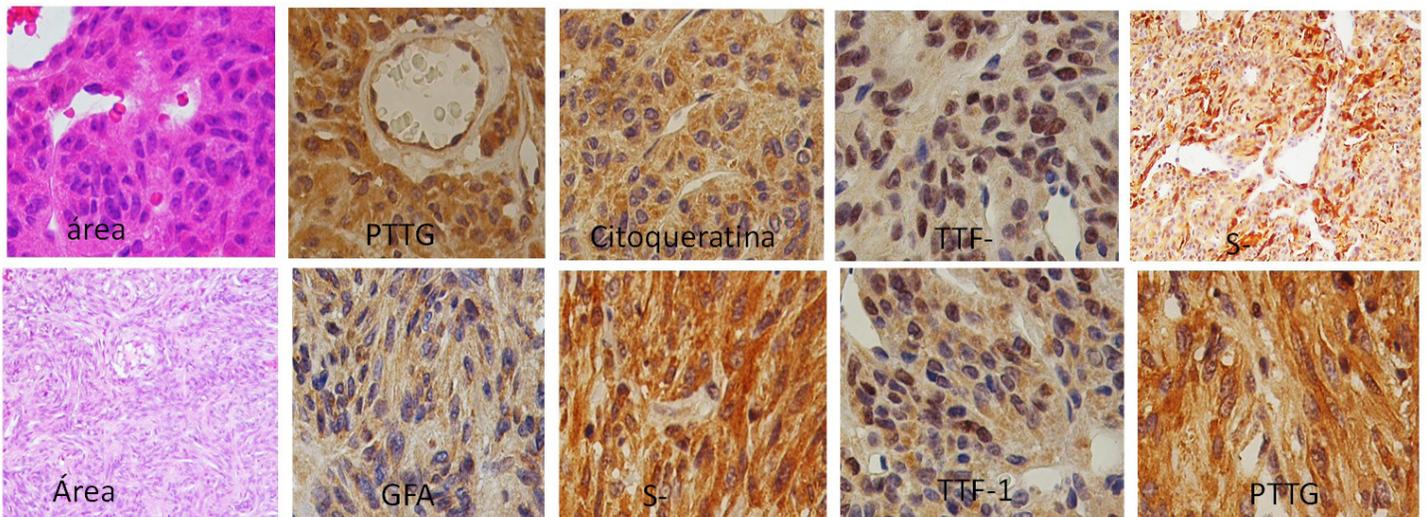


Figure 3: Histologically, observed a neoplasm formed by two different patterns, one with eosinophilic cells intermingled with numerous vessels and dilated sinusoids in (a) (H&Ex400). HIQ examination this pattern was positive immunoreaction for vim (b), PTTG-1 (c), TTF-1(d), s-100 (e). The second pattern observed spindle cells forming irregular is fascicles in (f) (H&Ex200), the immunohistochemistry analysis showed GFAP (g), S-100 (h), PTTG-1 in (i), TTF-1 expression in (j), and s-100 (k) positive immunoreaction (IH stain x400).

s-100 (Figure 3), and adenohipophysial hormones, synaptophysin, chromogranin and Pit-1 were negative. Spindle cell oncocytoma and Rathke's cleft cyst were diagnosed.

Discussion

We present a rare case of a hypophysial tumor, in a 66-year-old man with visual disturbance and data of hypofunction of ACTH, clinically and radiologically behaved as a pituitary adenoma, with adequate age range for any pituitary tumor. Histologically, presents two tumors in the same anatomical site, one corresponding to a Rathke's cyst and the second due to a biphasic tumor that presented two patterns; one of a oncocytic non-producing pituitary adenoma (FSH+, LH+, Pit-1+, PTTG-1+ and TTF-1 - and the second one formed by spindle cells (FSH-, LH-, Pit-1-, PTTG-1+ and TTF-1 +, GFAP+ AND S100+), based on the immunohistochemical results the diagnosis of SCO was made.

Histologically, SCO cells are principally composed of a bundle and fascicles of eosinophilic of spindle cells exhibiting abundant eosinophilic cytoplasm of oncocytes or granular appearance, lymphocytic infiltration, and mitotic features are observed. They are immunopositivity reaction for vimentin, EMA, GFAP, S-100 and galectin-3, TTF-1, but immunonegative reaction for pituitary hormones, cytokeratin, chromogranin, IDH1-R132H mutation, Syn and BRAF alterations (BRAF (V600E) mutation and BRAF-KIAA fusion [3]. Electron microscopy (EM) revealed that SCO cells contain plentiful swollen mitochondria and that packages of intermediate filaments are captured in the lysosomes and profiles of the rough endoplasmic reticulum [2,3] and the differential diagnosis including with all spindle-like shape cells tumors; schwannoma, meningiomas, pituicytoma, and granular tumor of the neurohypophysis.

Pituicytoma consists of elongated, bipolar spindle cells in interlacing fascicles or storiform array, with capricious immunopositivity for vimentin, S-100 protein, and Bcl-2, and GFAP were focally detectable [3] and immunonegative for synaptophysin, chromogranin. Ultrastructural analysis remarkable for absence of secretory granules, cells are composed of elongated cells containing in the Golgi area aggregates of intermediate filaments in a concentric pathway (fibrous body) and secretory granules, and it is considered as a low-grade glioma WHO Grade I of the neurohypophysis is an enormously rare tumor arising from the pituicytes of the neurohypophyses or the infundibulum. Pituicytes have 5 ultrastructural variants: light, dark, granular, ependymal, and oncocytic type. TTF-1 is an excellent marker of pituicytes, specialized glia of the neurohypophysis [3]. Recent data suggest that, while pituicytes and pituicytoma, SCO and GCT are positive for TTF-1, FSC are negative for TTF-1. However, the expression of TTF-1 in in those tumors suggesting a mutual histogenesis [3]. s-100 staining positive expression, is observe in the FSC oncocytic areas that formed nodules and were becoming more spindle cells until forming fascicles which were GFAP+, PTTG-1+, TTF-1+ and Pit-1, chromogranin- and pituitary hormones. The expression of Pit-1, FSH, LH in the oncocytic areas and negative in the spindle cells areas could explain a de-differentiation of the tumor.

In another hand, SCO are considered to arise from folliculostellate cells, which are sustentacular cells of the adenohipophysial, they are positive to s-100, GFAP, [4] and they express TTF-1. Based on the immunohistochemical and ultrastructural similarities common by SCO and FSCs. FSCs are star-like non-hormone-secreting cells in the anterior pituitary, which provide organizational support for hormone-secreting cells, accounting for 5-6% of the pituitary cell population [7]. FSCs have been observed and hypothesized to be adult stem cell-like pituitary cells, which have a purpose for divergent differentiation [8]. FSCs are endocrine cells of both the non-tumorous and the PA are accomplished of transforming into FSC while fluctuating from endocrine to non-endocrine phenotype [8]. The Transformation of those endocrine cells into FSC may signify retro differentiation into their Rathke's pouch derived precursors as suggested by occasional presence of ciliated and/or mucin producing cells in the lining of microcysts [8]. TTF-1 expression in no tumorous pituicytes, pituicytoma, SCO and GCT designates a common pituicytes lineage [3]. The expression of TTF-1 and GTTG-1 that generally expressed in the fetal procedures. For what has been hypothesized that SCO and GCT are subtypes of pituicytoma and has been proposed the new terms 'oncocytic pituicytoma' and 'granular cell pituicytoma' to refine the classification of these neoplasm according with WHO classification in 2016 [3].

These tumors are classified as a different group of low-grade neoplasms or astrocytoma of the sellar region that express of TTF-1, and include pituicytoma, granular cell tumor of the sellar region (S-100, NSE, CD56, EMA, and inhibin), spindle cell oncocytoma (vimentin, S-100 protein+, EMA+, GFAP-, AMA+, galectin-3+, inhibin+, chromogranin+, and pituitary hormones-, AE1/AE3-), SMA+, Bcl-2+), and sellar ependymomas (CK+, GFAP+), which expressing pituitary tumors of the posterior lobe as representing a morphological spectrum of a single nosologically entity [1]. Furthermore, have been suggested a common histogenesis.

On the other hand, PTTG-1, also, it is known as securin, is a crucial component of the spindle checkpoint that controls faithful chromatid separation. It has also been identified as a proto-oncogene, is upregulated in various tumors such as pituitary tumors, PTTG-1 plays a vital role in tumorigenesis [9]. It also contributes to angiogenesis by Trans activating the fibroblast growth factor 2 (FGF-2) and vascular endothelial growth factor (VEGF) via the Src homology 3 (SH3)-interacting domain [9]. Little is known about PTTG-1 however, it has been associated with invasion, metastasis, and serve to identify pituitary tumors in cases of metastasis [10]. Is less easily explained but invites speculation [9].

The origin of RCC is derived from remnants of Rathke pouch, while PA is formed by proliferation of the anterior wall of Rathke pouch. Although they have a possibility to share a common embryological origin, the coexistence of PA and RCC is extremely rare. The main differential diagnoses are CP, cystic pituitary adenoma, arachnoid cyst, epidermoid cyst and teratoma, according the main epithelial covering. Our observations may have implications for

the classification of these rare sellar neoplasms, all the while acknowledging the morphological diversity of pituicytes vs FSC-related neoplasms. Recent studies suggest that adult pituitary stem cells may play a role in pituitary tumorigenesis. Cells staining these stem cell markers have been isolated and brought to differentiate into each lineage of the anterior pituitary [11].

The incidence of two distinct tumor types occupying the same anatomical location is rarely observed and may be accounted for by two separate mechanisms, tumor to tumor metastasis and "collision" or synchronous tumors" where two together tumors invade one another [2]. However, is debated with importance on pathogenetic theories of dual sellar lesions. While there is no direct evidence to confirm the pathogenetic relationship of collision sellar lesions, the few cases reported in literature makes the theory of an incidental incidence rather uncertain. Recommended hypotheses about a common embryonic origin or a potential interaction between PA and the immune system disturbances.

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