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Case Report

Spindle Cell Oncocytoma of the Adenohypophysis and Pituicytoma: Report of a Rare Case and Review of the Literature

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Abstract

Pituicytoma, Spindle Cell Oncocytoma (SCO) and Granular Cell Tumor (GCT) are scarce tumors in the adenohypophysis. These tumors are composed of fusiform cells, characterized by an excessive amount of mitochondria, resulting in a totally acidophilic granular cytoplasm with no hormonal activity. They all have similar characteristics and therefore might be sometimes confusing and difficult for differential diagnosis. Clinical manifestations of the lesion vary, most commonly including visual loss or disturbances and hypopituitarism as in other nonfunctional pituitary adenomas. So, we present a case with a sellar space-occupying lesion presumptive diagnosis of nonfunctioning pituitary adenoma, the lesion was totally resected via transnasal-transsphenoidal approach and pituicytoma diagnosis was confirmed.

The incidence of oncocytomas, SCOs and GCTs are 0.4% sellar masses. due to the hypervascular feature of the tumors, total resection of the tumor may be impeded leading to high risk of tumor recurrence. Since SCOs and GCTs are rare and a few cases have been reported sometimes its diagnosis can be tricky. SCO tumors had mixed intra- and suprasellar location. The most common clinical complaint in all the cases was visual difficulties. Structural analysis of the three tumors had very similar features. Pituicytomas were made up of spindle-shaped tumor cells and a few short desmosome-like intermediate junctions. Granular cell tumors also consisted of polygonal cells, desmosomes, vacuoles and lysosomes. In the same manner, spindle cell oncocytomas were composed of spindle-shaped or polygonal tumor cells.

Keywords: *Spindle Cell Oncocytoma (SCO); Granular Cell Tumor (GCT); Adenohypophysis; Pituicytoma*

Introduction

Spindle cell oncocytoma (SCO) is a scarce, poorly recognized pituitary tumor, originating from the anterior pituitary gland. The tumor is composed of mitochondrion-rich, fusiform cells, characterized by an excessive amount of mitochondria, resulting in a totally acidophilic, granular cytoplasm with a characteristic immunologic feature and no hormonal activity [1]. It can appear as an indistinguishable tumor from nonfunctioning pituitary adenomas by either clinical features or radiological findings [2], but with a more difficult surgical removal due to the greater blood supply of the tumor [3]. Most tumors arise in adults [4]. Though they are typically large pituitary lesions, the majority of the cases have a benign clinical course, with signs and symptoms of an intrasellar and suprasellar mass [5]. Clinical manifestations of the lesion vary, most commonly including visual loss or disturbances and hypopituitarism as in other nonfunctional pituitary

adenomas [4]. The incidence of oncocytomas in reported series of pituitary tumors vary, including 0.4% sellar masses [6]. Surgery is the best treatment choice in case of appearing symptoms, with reported anticipated outcomes. Although due to the hypervascular feature of the tumor, total resection of the tumor may be impeded leading to high risk of tumor recurrence [2]. We present a case who had a sellar space-occupying lesion presumptive diagnosis of nonfunctioning pituitary adenoma, the lesion was totally resected via transnasal-transsphenoidal approach and pituicytoma diagnosis was confirmed.

Case Presentation

The 42-year old woman was discovered to harbor a sellar space-occupying lesion while being medically prepared for hip joint replacement surgery. Her past medical history had included type 2 diabetes mellitus, dyslipidemia, and arterial hypertension. Neurological examination, including perimetric visual field assessment, was unremarkable.

Endocrinologic laboratory testing, on the other hand, indicated panhypopituitarism without evidence of diabetes insipidus or secondary hyperprolactinemia. Cranial magnetic resonance imaging (MRI) revealed a voluminous yet noninvasive intra- and suprasellar tumor of 2.8 * 2.7 * 2.6 cm (See figure 1).

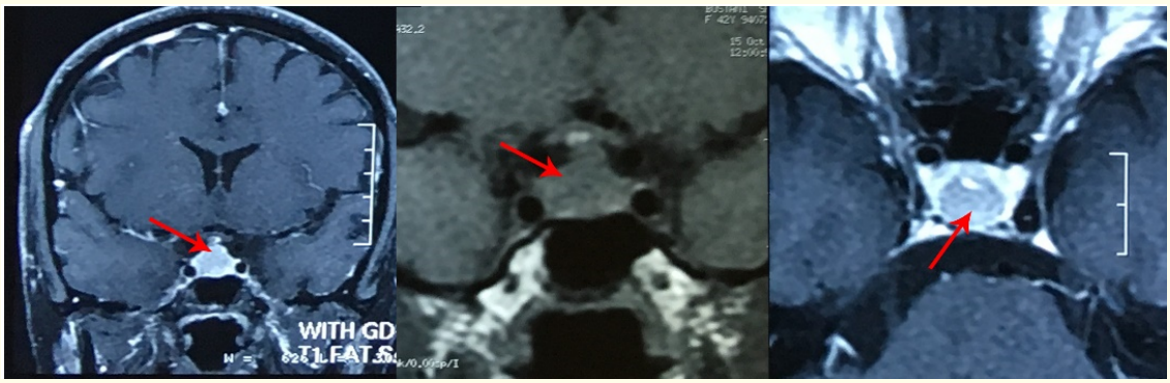

Figure 1: *Pituitary fossa tumor with expanding the fossa and also suprasellar extension. Mild flattening of optic chiasm is observed and no cavernous sinus invasion represented.*

The Ki-67 marker analysis showed 6 - 7% proliferative activity in spindle cells (See figure 2). Vimentin and Epithelial Membrane Antigen (EMA) markers were positive in spindle cells. Progesterone receptor was patchy weakly positive in spindle cells. Glial fibrillary acidic protein (GFAP), S-100, synaptophysin and chromogranin-A immunohistopathological analysis were all negative.

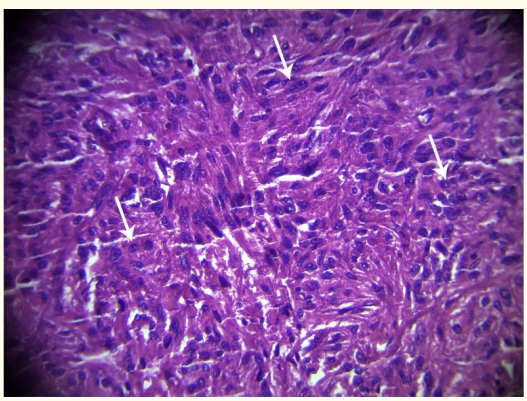

Figure 2: *Histologic and cytologic features of spindle cell oncocytoma. Fascicles of compact spindle cells with eosinophilic cytoplasm. Occasional scattered pleomorphic cells are noted (200 × original magnification).*

On a presumptive diagnosis of nonfunctioning pituitary adenoma, the lesion was totally resected via transnasal-transsphenoidal approach. The patient made an uneventful recovery and has been discharged on hormonal substitution therapy (See figure 3).

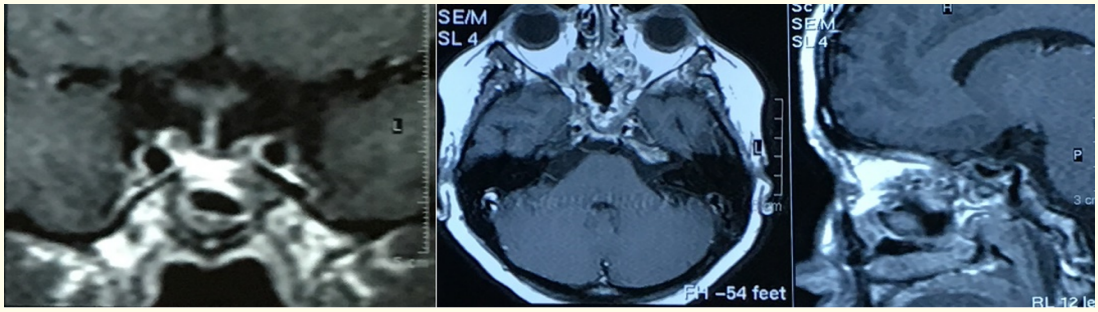

Figure 3: *Post-operative MRI revealed total resection of the tumor via ETSS approach.*

Discussion

Pituicytoma, Spindle Cell Oncocytoma (SCO) and Granular Cell Tumor (GCT) are all rare tumors of the adenohypophysis. They all have similar characteristics and therefore might be sometimes confusing and difficult for differential diagnosis. Here, we intend to present some cases in order to clarify their resemblance and differences.

In literature, there are several case reports focusing on the description of different aspects of cases with the diagnosis of pituicytoma or spindle cell oncocytomas. These aspects include clinical signs and symptoms, genetic studies, discoveries on imaging or laboratory tests, microscopic findings, treatment and follow-up of the cases [7-12].

In 2013, Mete., *et al.* worked on 7 cases of SCO, 4 cases of pituicytoma, 3 cases of GCT and 5 non-tumorous pituitary cases. They evaluated their genetic, immune-histochemical and ultrastructural features. None of the cases showed BRAFV600E mutation or BRAF-KIAA fusion [13].

All the tumor cases had positive TTF-1 and negative chromogranin. TTF-1 was negative in all non-tumorous cases. Other measured objects such as vimentin, BCL-2, CD56, CD68, EMA, GFAP, S100protein and galectin-3 were positive in variable and non-commentary numbers of cases.

In the ultrastructural analysis, the three tumors had very similar features. Pituicytomas were made up of spindle-shaped tumor cells containing cytoplasmic intermediate filaments, a variable amount of mitochondria, lysosomes and a few short desmosome-like intermediate junctions.

Granular cell tumors also consisted of polygonal cells with cytoplasmic intermediate filaments, desmosomes, vacuoles and lysosomes. In the same manner spindle cell oncocytomas were composed of spindle-shaped or polygonal tumor cells, desmosomes, intermediate filaments, and lots of mitochondria [13].

In 2015 Cambiaso., *et al*. presented a very uncommon case with the coincidence of pituicytoma and Cushing's disease(CD); a 7-year-old girl with classic signs and symptoms of CD such as weight gain, mus5cular weakness, moon face, hypertrichosis and elevated levels of cortisol and corticotropin [14].

In MRI she had an enlarged pituitary gland with two lesions. After the biopsy the tumor was confirmed to be pituicytoma (spindle-shaped cell with positivity for vimentin and S100 protein). They suggest that there might be an association between the raised levels of corticotropin and cortisol and the pituicytoma in his case, for example, pituicytoma and tumors with corticotropin secretion could come from the same origin cells [14].

Another interesting issue discussed is the relation between Adenohypophysis spindle cell oncocytoma (ASCO)'s recurrence and the Ki-67 index (associated with cellular proliferation). A 30-year-old Chinese man with a diagnosed ASCO underwent surgery in order to remove it but hid symptoms recurred for several times and he had to take 3 surgeries.

The noteworthy finding was the elevating level of Ki-67 index during this process. (from 6% at the time of first surgery to 19% at the second and 45% at the third surgery) [15]. Since SCO is rare and a few cases have been reported sometimes its diagnosis can be tricky. One of its rarest reported manifestations was severe hyponatremia in a 60-year-old man with a syncopal episode preceded by nausea, vomiting, and malaise. In some of the cases, the hypervascularity of the tumor can harden the surgical removal [3].

There are some animal studies on this subject. Satoh., et al. carcinogenesis in rats and after 2 years of research they presented two cases of pituicytoma. In both cases, the tumoral cells had eosinophilic cytoplasm and nuclei of different size and were arranged in the spindle-shaped patterns. In the female rat, polymorphism of the tumoral cells was notable, while in the male rat there were areas of mitotic activity in several regions of the tumor [16].

Among all the papers featuring these 3 tumors, one of the most comprehensive studies was Covington., *et al.*'s meta-analysis. They collected data from 145 cases (81 GCTs, 48 pituicytomas, and 16 SCOs) and compared the tumor location, imaging and clinical findings, sex and age of the patients. Pituicytoma cases were purely intrasellar lesions that and were completely separate from the pituitary gland.

GCT cases were entirely suprasellar masses. SCO tumors had mixed intra- and suprasellar location. The most common clinical complaint in all the cases was visual difficulties. The male: female ratio for pituicytoma, SCO GCT was 18:17, 5:8 and 22:24 respectively. The average age of diagnosis for pituicytoma, SCO and GCT were 50.3, 59.4 and 49.2 respectively [17].

Conclusion

SCO of pituitary and pituicytoma are rare tumors. Clinical behaviors of these tumors are very similar. Both tumors have a tendency to recur locally if not completely resected. The incomplete resection of the tumor was a significant risk factor for recurrence in both SCO and pituicytoma.

Both tumors have a tendency to be hypervascular, which may hamper total resection. EMA and mitochondria positivity is characteristic of SCO and they are considered to be important immunomarkers to distinguish these tumors.

Author Contributions

GS and AP designed the study; GS and NA acquired data; FB and MM did pathological examinations; LJ and AP and HH wrote the manuscript; AP and TE revised the manuscript; GS and AP drafted the article; all authors critically revised and approved the final version of the article.

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