Glomus tumor of sella turcica with synaptophysin expression mimicking pituitary adenoma

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Abstract

Glomus tumor can rarely arise in the central nervous system as a sellar turcica mass. We report herein a case of sella glomus tumor in a female patient who presented at the age of 8 years with visual impairment. The tumor recurred at 4 years and 26 years after initial excision and gamma knife therapy. Histologic examination showed a monotonous population of oval cells accompanied by delicate blood vessels, features mimicking pituitary adenoma. The tumor showed histologic progression at the second recurrence. Synaptophysin staining was positive but chromogranin and CD56 were negative. The tumor cells were negative for epithelial markers but expressed actin and SMA. Awareness of the rare occurrence of glomus tumor at this region, careful analysis of morphology and appropriate immunohistochemical work-up are essential to solve this diagnostic challenge. The clinicopathologic features of all previously reported cases are reviewed.

Case report

The female patient presented at the age of 8 years in 1992 with visual impairment. Investigations showed a 2-cm tumour with suprasellar extension and panhypopituitarism. Craniotomy revealed a richly vascularized tumour in the pituitary fossa. Subtotal excision was done and a diagnosis of glomus tumour was made. Post-operative gamma knife therapy was given for residual disease. Four years later, MRI revealed an increase in tumour size, and another course of gamma knife was given. In 2018, 26 years after the initial presentation, she noticed progressive visual impairment of the left eye. MRI showed a 5-cm tumour at the suprasellar region with a large cystic component and strong contrast enhancement. (Fig. 1) Excision was done and the patient was well at 1 year after the surgery and had regained full vision.

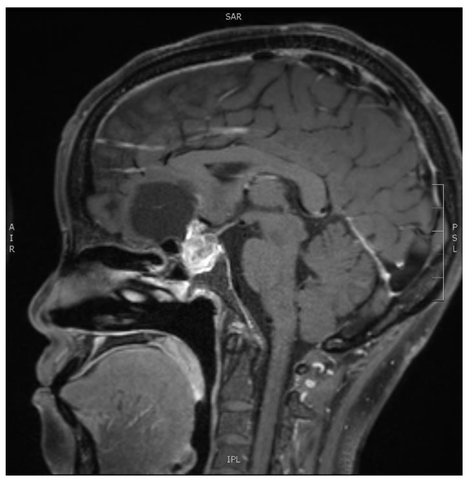

Fig. 1: MRI shows a 5-cm contrast-enhancing suprasellar tumor with a cystic component extending to the frontal lobe.

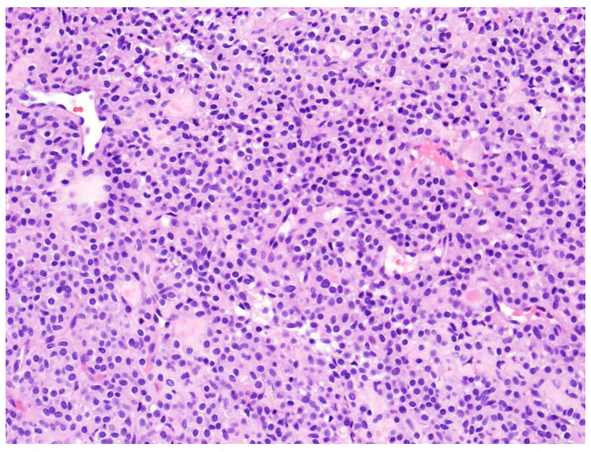

Fig. 2: Packets and nests of monotonous round cells with delicate intervening blood vessels.

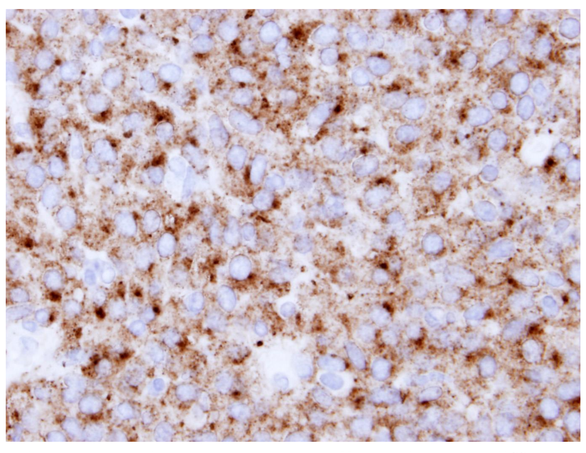

Fig. 5: The tumor cells show diffuse granular cytoplasmic immunostaining for synaptophysin.

The initial specimen (1992) was not available for review. Histologic examination of the recurrent tumor showed cellular tumor fragments, consisting of monotonous round cells with delicate intervening blood vessels (Fig. 2), arranged in sheet and packet, possessing central ovoid nuclei, pale chromatin, indistinct nucleoli and moderate amount of eosinophilic cytoplasm. The intervening blood vessels had narrow or ectatic lumens, and the endothelium often directly abut tumor cells without intervening pericytes. The stroma showed focal fibrosis and hemosiderin deposition. **One fragment showed increased cellularity, featuring tumor cells with increased N/C ratio and nuclear pleomorphism, and occasional mitotic activity (Ki67 index increased from 1% to 15%) (Fig. 3 & 4).** On immunostaining, the tumor cells were negative for cytokeratins, pituitary hormones, S100, GFAP & CD34. Synaptophysin was positive but not chromogranin & CD56 (Fig. 5). The tumor cells were diffusely positive for muscle-specific actin, SMA & calponin. Actin staining confirmed absence of pericytes between endothelium and tumor cells in some blood vessels. BRAF V600E staining was negative. **The overall features were consistent with recurrent glomus tumor with focal histologic progression.**

Discussion

Glomus tumor of the central nervous system is exceedingly rare, with only 3 cases (2 glomangiomas and 1 glomus tumor) reported in the English language literature at the time of this study (Table 1). The current case, except for the unusual localization of sellar turcica, shows the typical morphology and immunophenotype of glomus tumor. However, the packeting of bland-looking cells accompanied by a rich vascularity and expression of synaptophysin can easily lead to an erroneous diagnosis of pituitary adenoma, a much more common tumor at this anatomic location.

Microscopically, the eosinophilic cytoplasm of the **glomus tumor cells lack the usually granular quality of cytoplasm in pituitary adenoma**. The finding of vessels with spindly **endothelial cells abutting directly on the surrounding tumor cells without an intervening layer of pericytes is a characteristic feature of glomus tumor**, a growth pattern recapitulating the perivascular origin of the neoplastic cells in the normal glomus body. **Glomus tumors of soft tissues usually do not express synaptophysin, but focal to diffuse synaptophysin expression has been well documented in glomus tumors arising in visceral organs** such as stomach, esophagus, duodenum, bronchus, kidney, liver and nose. In all these cases, **other neuroendocrine markers such as CD56 and chromogranin are negative**, as in the current case. Other tumors of the sellar region such as craniopharyngioma, germ cell tumor, pituicytoma, meningioma, hematolymphoid tumor and metastatic tumor should pose no problems in the differential diagnosis.

Literature review shows that the age of presentation ranged from 8 to 72 years (median 44.5 years), affecting 2 males and 2 females.(Table 1) The most common presentation was visual impairment (3), followed by headache (1) and cranial nerves palsy (1). All patients developed local recurrences with long term follow-up, and the mean duration from tumor excision to the first recurrence was 5 years. This is most probably due to the strategic site and high vascularity of the tumors precluding complete excision.

In this study, histologic progression with increased cellularity, nuclear pleomorphism and mitotic activity were found focally, most consistent with glomus tumor with uncertain malignant potential. *BRAF* V600E mutation has been found in a subset of malignant glomus tumor, and this case is negative for BRAF V600E on immunostaining. Histologic progression has also been reported in one previously reported sellar tumor and that patient died of disease at 12 years with no metastasis.

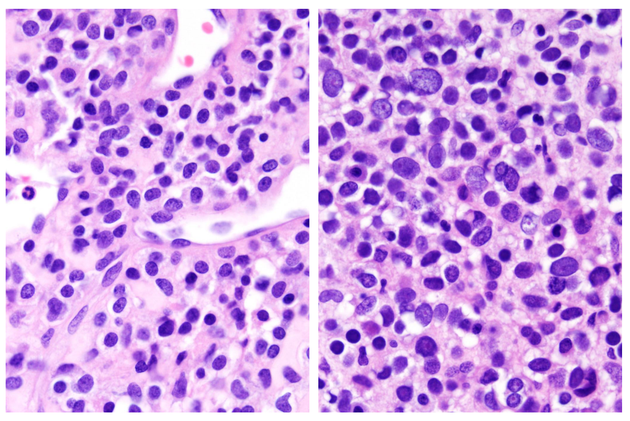

Fig. 3: Histologic progression of glomus tumor with increased cellularity, raised N/C ratio & nuclear pleomorphism.

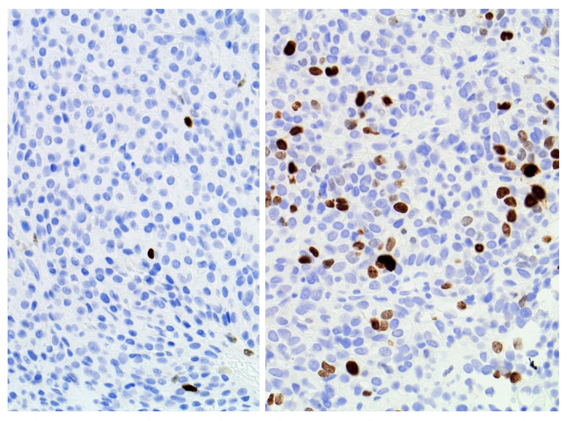

Fig. 4. The Ki67 index is 1% in the glomus tumor (left), but has increased to 15% in the area with histologic progression (right).

Conclusion

Sellar glomus tumor is a rare tumor which can be potentially mistaken for pituitary adenoma. Awareness of this rare occurrence, careful analysis of morphologic features and appropriate immunohistochemical work-up would be essential to solve this diagnostic challenge.

Declaration

The study was published as Tsang JCH, Ng CS, Fung CF, Chan JKC, Cheuk W (2020) Glomus tumor of sella turcica with synaptophysin expression mimicking pituitary adenoma. Int J Surg Pathol 28(4):401–405.

Table 1. Clinicopathologic Features of Sellar Glomus Tumors in the literature

Authors	Gender/Age	Presentation	Histological diagnosis & immunophenotype	Treatment	Clinical Outcome
Asa SL	M/42	Headache	**Glomangioma** (+): actin, desmin, myoglobin (-): GFAP, GH, ACTH, TSH, FSH, LH	Resection, postoperative radiotherapy	Recurrences at 3 years and 4 years
Hanggi D	F/47	Diplopia, palsy of III, IV and VI cranial nerves	**Glomus tumor with histologic progression at the second recurrence** (+): SMA, vimentin, laminin, CD99, Ki67: 10% in histologic progression (-): synaptophysin, chromogranin, S100, placental ALP, CK, GFAP, desmin, CD117	Resection, postoperative radiotherapy, Gamma knife	Recurrences at 8 years and 10 years; died of disease at 12 years
Ebinu JO	M/72	Bitemporal hemianopsia,	**Glomangioma** (+): SMA, vimentin (-): CK, EMA, chromogranin, GFAP, desmin, TTF1, S100, CD68, ER, PR, tyrosine hydroxylase	Resection	No follow-up data
Current case	F/8	Visual impairment	**Glomus tumor with histologic progression at recurrence** (+): actin, SMA, synaptophysin, Ki67: 15% in histologic progression (-): MNF116, CAM5.2, GFAP, S100, CD34, chromogranin, CD56, GH, PRL, ACTH, BRAF V600E	Resection, gamma knife	Recurrences at 4 years and 26 years