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# Mixed Gangliocytoma – Pituitary Adenomas: Rare Sellar Tumors

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**Conflict of interest:** Nil



## Abstract

Gangliocytomas are rare benign neuronal tumors, those originating in the sellar region are extremely rare, represent < 1 % of sellar tumors.

The coexistence of Mixed gangliocytoma–pituitary adenoma is a rare condition, with an incidence of 0.14–0.52%. This report describes two cases: one involving a somatotroph adenoma and the other a mixed somatotroph–lactotroph adenoma

First case being 54-year-old female with blurred vision, second is 43-year-old female with generalized swelling. Imaging revealed a sellar/suprasellar mass in both cases, leading to tumor resection.

Histological analysis identified a biphasic tumor with mature ganglion and neuroendocrine cells. Immunohistochemistry (IHC) for the first case showed GH, Pit-1, SSTR-2, synaptophysin, NeuN and NF positivity, with MIB-1 index of 1–3%. The second case exhibited strong GH, prolactin, Pit-1 SSTR-2, synaptophysin, NeuN and NF positivity, with MIB-1 index of 2–4%.

This condition is rare, requires detailed histological and immunohistochemical analysis for accurate diagnosis.

**Keywords**: Pituitary adenoma, Gangliocytoma, Dual lineage, somatotroph adenoma mammosomatotroph adenoma, mixed somatotroph – lactotroph adenoma.

## Introduction

Gangliocytomas are extremely rare benign tumors representing < 1% of Sellar tumors.[1,2,3,4] Gangliocytomas existing with pituitary adenomas account for 0.14% - 0.52% of Sellar tumors and are recognized as mixed gangliocytoma – pituitary adenomas.[1,2,5,6]

The most common functioning mixed gangliocytoma – pituitary adenoma are growth hormone secreting adenomas associated with acromegaly.[3,7] Endocrinopathies if absent, as in non-functioning adenomas may lead to delayed diagnosis as in our case, the lack of clinical signs of acromegaly delayed the diagnosis. The following reports describe two rare cases of mixed gangliocytoma adenomas.

## Case History

Two cases reported with the complaint of blurred vision and generalized body swelling respectively.

Neurologically patients were conscious, obeying verbal commands. MRI showed sellar/ suprasellar mass. Endoscopic transsphenoidal resection of tumor and drainage of sellar cyst with autologous fat duroplasty was done. Intraoperatively tumor was greyish white in colour, soft, suckable, moderately vascular. Post operative course was uneventful, on discharge patients were stable.

**First case of a 54yr/ F**: Histopathological examination (H&E) shows cells with moderate to marked nuclear atypia including some bizarre forms with eosinophilic, granular & clear cytoplasm arranged in small sheets. There is a focus showing large ?? ganglion like cells /?? Granular cells (posterior pituitary) in a fascicular background. Mitotic activity is not significant. Differential diagnosis was pituitary adenoma, mixed gangliocytoma- adenoma tumor & pituicytoma. IHC showed GH scattered strong positive, Pit-1 positive, SSTR-2 diffuse strong positive, Synaptophysin, NeuN and neurofilament positive while T-pit, SF-1, GFAP, TTF-1, Oct-4, ACTH, TSH, PRL, FSH, and LH was negative. MIB-1 was 1– 3 %. Final diagnosis of mixed gangliocytoma somatotroph adenoma was made.

**Second case of a 43yr/F:** H& E showed cells with round to oval nuclei arranged in sheets and nests. A focus shows large ganglionic cells of various shapes and sizes in a neuropil - like matrix. Mitotic activity is not significant. D/D was pituitary adenoma, mixed gangliocytoma-adenoma tumor & pituicytoma. IHC shows GH strong diffuse positive, prolactin, Pit 1, SSTR-2, synaptophysin, NeuN and neurofilament were also positive. T-Pit, SF-1, Oct-3/4, TTF-1, GFAP, ACTH, TSH, FSH, and LH were negative. MIB-1 was 2–4% in the highest proliferating areas, slightly higher than normal range. Diagnosis of mixed gangliocytoma somatotroph adenoma was made.

As PRL was positive, we tried to differentiate between the morphological variants - mammosomatotroph adenoma (MSA) and mixed somatotroph – lactotroph adenoma (MSLA). It is necessary to distinguish whether the IHC staining for GH and prolactin was in the same or different cells. IHC for GH & PRL showed it to be the same cell population & Pit-1 positivity was seen both somatotroph and lactotroph cells. However, only the cells expressing PRL are positive for ERα but we could not analyse it. So, ERα and ultrastructural examination was advised but no follow up was received.

Serum hormonal levels were not available /not done in both the cases.

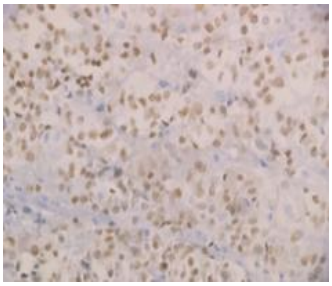

Figure 1: Pit-1 (IHC)

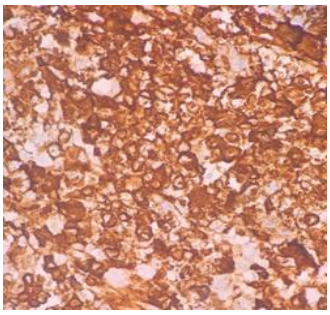

Figure 2: GH (IHC)

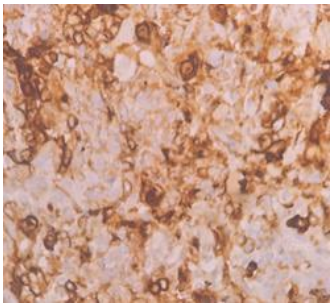

Figure 3: Prolectin (IHC)

## Discussion

These pituitary tumors have also been called pituitary adenoma – neuronal choristoma (PANCH), pituitary adenoma with neuronal choristoma and pituitary adenoma with gangliocytic component.[3,8]

The identification of a dual sellar pathology is considered challenging since majority cases are present clinically and radiologically as pituitary adenomas. The definitive diagnosis is determined by the histological and/or immunohistochemistry studies.

The origin of the pituitary gangliocytomas remains controversial, with several proposed hypotheses. First, the pituitary adenoma formation occurs as a result of endocrine or paracrine stimulation of adenohypophysial cells by the pituitary hormone-releasing hypothalamic hormones, produced by ganglion cells. Second, the ganglionic component originates from the neural differentiation of a preexisting pituitary adenoma in a process suggestive of transdifferentiation. Third, a common origin for both neuronal and adenomatous components from uncommitted stem cells from the adenohypophysis, which is capable of multidirectional differentiation.[1,9,10]

Transcription factors important to cell specific differentiation include: Pit1 leads to the differentiation of somatotrophs, lactotrophs and thyrotrophs. Tpit drives the differentiation of corticotrophs. SF1 regulates gonadotroph cell differentiation.[3]

In our study, first case showed GH scattered strong positive, Pit-1 positive, SSTR-2 diffuse strong positive, Synaptophysin, NeuN and neurofilament positive.

Reviewing the literature, M. Beatriz S. Lopes et al (2017), stated that IHC was positive for GH, Pit-1, Synaptophysin, Neu N & NFP, similar to our diagnosis of mixed gangliocytoma somatotroph adenoma.[3]

Second case showed GH strong diffuse positive, Pit-1, prolactin, SSTR-2, synaptophysin, NeuN and neurofilament were also positive.

Tavares et al (2020) stated that IHC was positive for GH, prolactin, synaptophysin and neurofilament on the fibrillary stroma similar to our diagnosis of mixed gangliocytoma somatotroph adenoma.[1]

To rule out the presence of neurohypophysis or pituitary stalk in the area of neuropil-like matrix, immunostaining for pituicytes using TTF-1 was performed in both the cases with no reactivity in any area of the tumors.[3]

The differential diagnosis of Mixed gangliocytoma – pituitary adenoma should be kept in mind while evaluating tumors of Sellar / suprasellar region. Other diagnosis apart from commonly found pituitary adenoma & craniopharyngioma are pituitary nodular hyperplasia, metastatic neuroendocrine tumor, pituicytoma, ependymoma and pituitary blastoma. Their diagnosis is only possible after immunohistochemistry evaluation as many of the cases may be clinically as well as biochemically silent.

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