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RESEARCH ARTICLE

AN INTERSELLAR COLLISION TUMOR - GANGLION CELL TUMOR WITH PITUITARY ADENOMA

***,[1]Swati Aggarwal, [1]Karuna Gupta, [1]Arpita Jindal, [2]Sachin Tomar, [2]Ashok Gupta and [1]Ajay Yadav**

[1]Department of Pathology, SMS Medical College, Jaipur, India
[2]Department of Neurosurgery, SMS medical College, Jaipur, India

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ABSTRACT

Ganglion cell tumors in intersellar region are rare. They occur in combination with a pituitary adenoma. The etiopathogenesis of these collision tumors in the sellar region is not clearly defined. Whether these arise from cells of different histogenesis or they are derived from the same cell is still a matter of debate. We report a case of intersellar gangliocytoma with a pituitary adenoma presenting with acromegaly.

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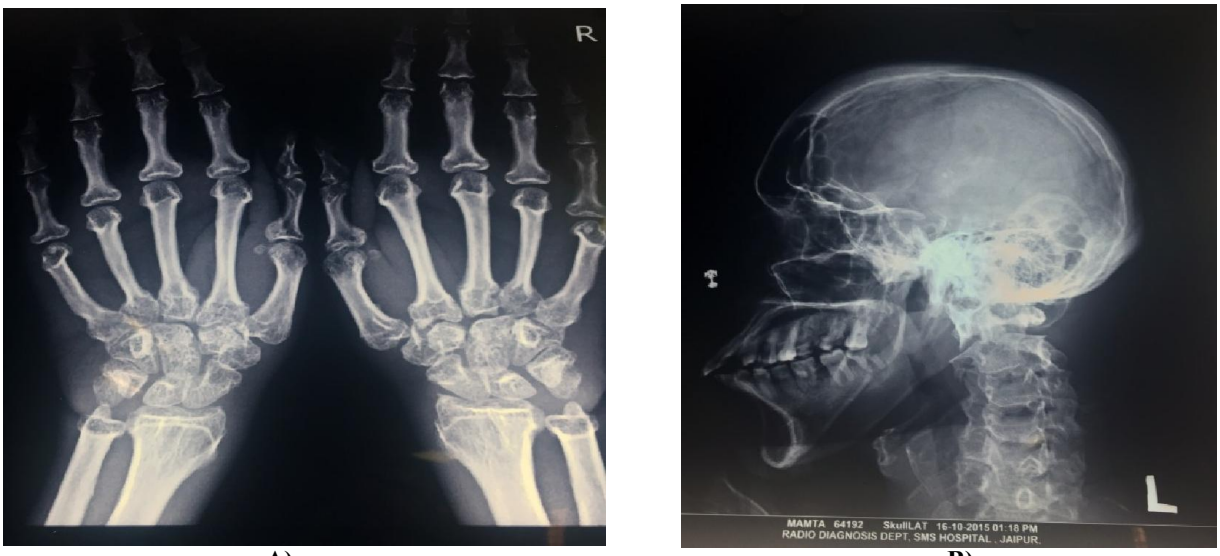
INTRODUCTION

Pituitary adenomas are the most common sellar lesions. The presence of a concomitant tumor along with pituitary adenoma in sellar region is a rare entity. Most of these present clinically and radiologically as pituitary adenomas, thus making a preoperative diagnosis of dual pathology very difficult. Gangliocytomas [World Health Organization (WHO) grade I) are rare benign tumors of the sympathetic nerve fibers arising from neural crest cells, which can grow wherever sympathetic nervous tissue is found (Kovacs *et al*., 1986). The intersellar gangliocytoma arise via neuronal transdifferentiation within growth producing hormone. We present a rare case of gangliocytoma occurring concomitantly with pituitary macroadenoma in the intersellar region

Case report

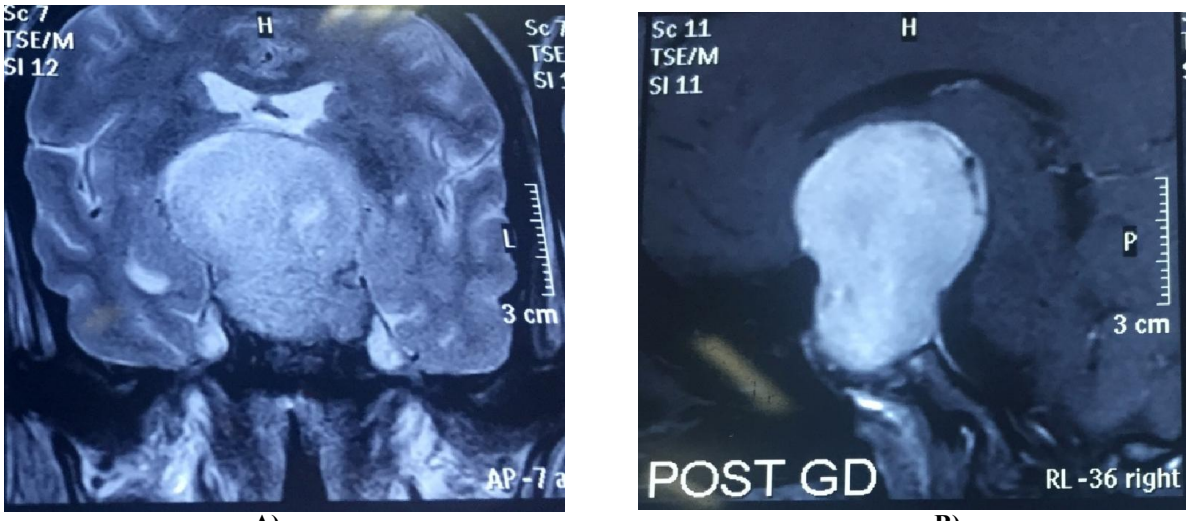
A 38year old female presented to Sawai man singh Hospital, Jaipur with complaints of blurred vision and change in facial features that had been present for the past one year. The patient had no obvious symptoms of nausea, headaches, no notable diuresis and no limb activity disorder or body convulsions. On examination patient was drowsy. The patient was able to fix and follow objects. Vision was 6/60 in both the eyes. Pupils were 3mm in size and reactive. On examination of facial and skeletal features a diagnosis of acromegaly was made. (Fig 1) There were no signs of meningeal irritation. Preoperative laboratory examination found raised growth hormone of >200.0ng/ml (<8ng/ml), slightly raised prolactin (27.52ng/ml), normal cortisol levels [8.31mcg/dl (5.0 -25.0mcg/dl)], and slightly reduced TSH levels (0.23µIU/ml) CT scan and MRI brain revealed a large SOL in the sellar region extending into the suprasellar region. (Fig 2 and 3) A transsphenoidal resection of the tumor was carried out. Tumor was soft, white and suckable. The intraoperative squash cytology revealed variable sized ganglion cells. (Fig 4) On histopathological examination two types of tumor component were found closely related to each other. One component shows irregular distribution and clustering of variably sized ganglion cells in a delicate fibrillar matrix. Adjacent component is composed of round medium sized cells in a diffuse growth pattern and around blood vessels (Fig 5) .A diagnosis of a collision tumor - gangliocytoma with pituitary adenoma was made. Postoperative examination found a decrease in growth hormone levels (>40ng/ml), and prolactin levels (18.80ng/ml), with a normal cortisol (15.02mcg/dl) and TSH (0.60µIU/ml)

****Corresponding author: Swati Aggarwal,***
Department of Pathology, SMS Medical College, Jaipur, India.



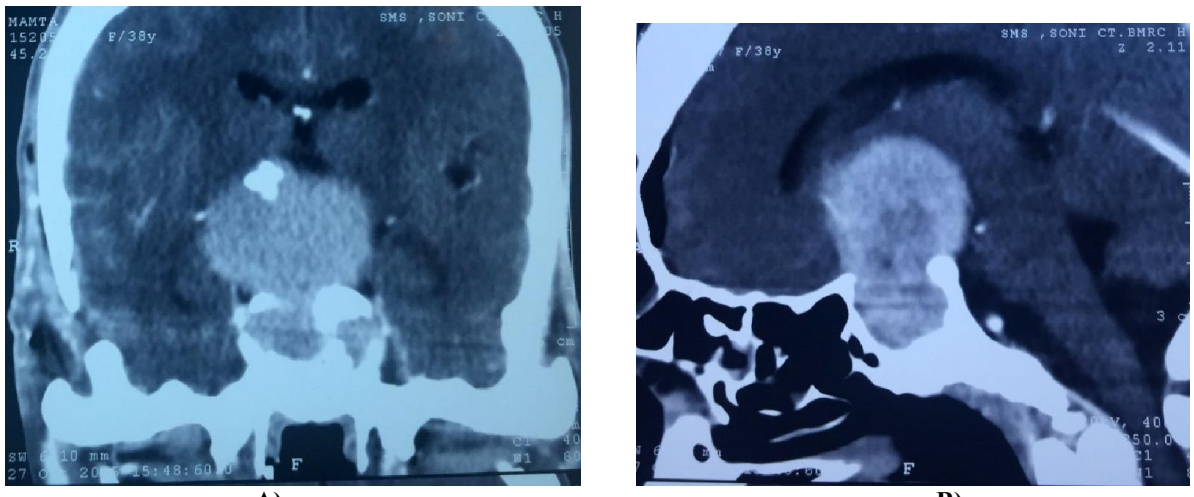
A) B)

Fig. 1. A) AP radiography of the hand- Shows ungual tufting, widening of bases of distal phalanges, and metacarpal osteophytes on radial aspect
B) Lateral radiography of skull reveals enlarged sella with double flooring, pneumosinus dilantans and prognathism



A) B)

Fig. 2. A) coronal Section MRI BRAIN -revealed a large SOL in the sellar region extending to the suprasellar cistern upto the floor of 3rd ventricle and elevating it. A) Post contrast Sagittal section MRI Brain Depicted a large SOL in the sellar region showing intense homogenous enhancement with gadolinium contrast



A) B)

Fig.3. A) coronal CT scan B) Sagittal CT scan – depicts a heterogeneously enhancing mass in the sellar region extending superiorly into the suprasellar region with widening of the sella

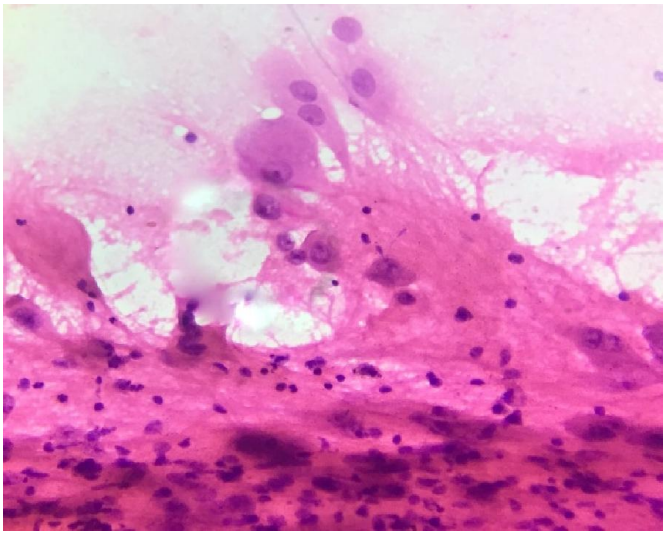
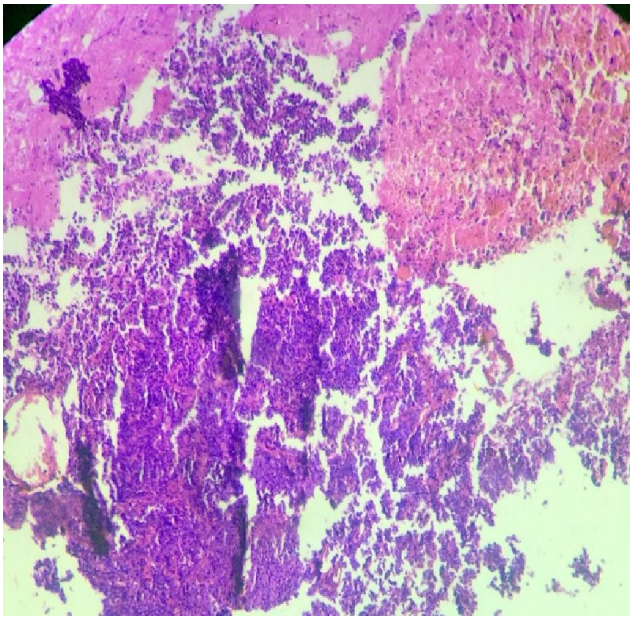
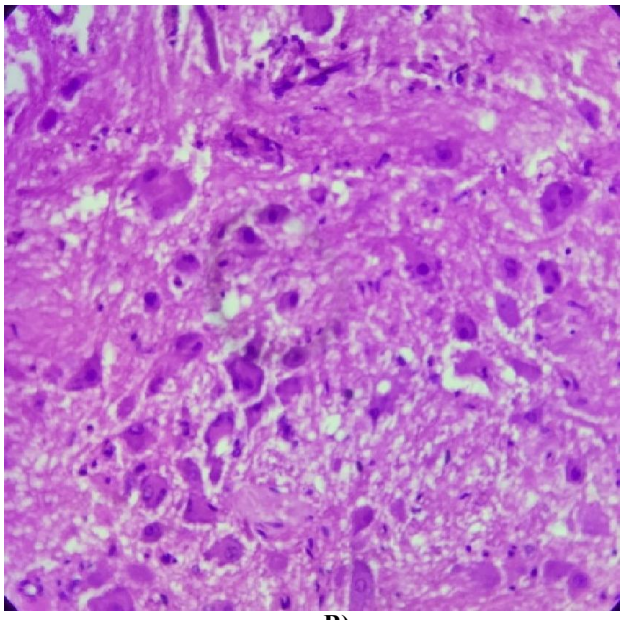


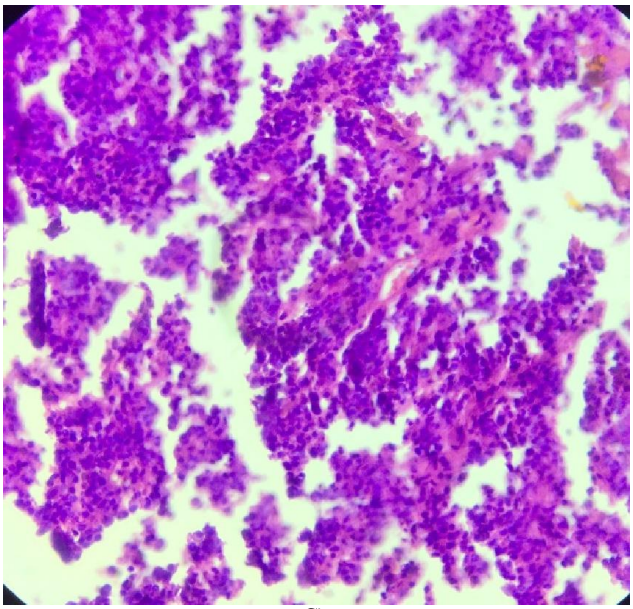
Fig.4. Intraoperative squash smear - shows numerous variable sized ganglion cells



A)



B)



C)

Fig. 5. Photomicrographs of the tumor specimen. A: Two types of tumor component found closely related to each other. H&E stain, 40X. B: Variably sized ganglion cells in a delicate fibrillar matrix. H&E stain, 100X. C: Diffuse pituitary adenoma H&E stain, 100X

DISCUSSION

Most common tumors arising from intersellar region are pituitary adenomas, craniopharyngiomas and glial and neuronal neoplasms. However, occurrence of these tumors together is very rare. Pituitary adenoma is a common benign tumor of the sellar region, which typically originates from the anterior pituitary. Gangliocytoma is a rare benign tumor of neuroblastic origin. It consists of mature ganglion cells and non-neoplastic glial elements and can occur in any part of the central nervous system. However, gangliocytoma occurring in the sella turcica is extremely rare and originates from the posterior pituitary. Most of these tumors are related to functioning or nonfunctioning pituitary adenomas or pituitary cell hyperplasia. Most of the previous studies report gangliocytomas most commonly occurring in association with a GH-secreting adenoma, with the clinical manifestation of acromegaly (Asa *et al*., 1984a) (Azapira *et al*., 2013) (Crowley *et al*., 2012) (Kurosaki *et al.,* 2002); less often, they are associated with ACTH-producing adenomas, and present with Cushing's disease (Saeger *et al*., 1994). However, independent of such relationship, they can cause a variety of clinical symptoms that reflect mass effect or their own endocrine activity. Occasionally, pure ganglion cell tumours are themselves hormonally active.

In the present case, the histopathological examination of surgical specimens from the patient revealed pituitary adenoma closely intermingled with neoplastic ganglion cells. The adenomatous contribution appeared to be a GH-secreting adenoma based on the preoperative lab finding of increased GH. The neuronal contribution was diagnosed as a purely gangliocytic lesion composed exclusively of groups of neoplastic mature ganglion cells. The two components were close together and in some places intermingled with each other. The close relationship of both neoplastic components suggests that they share a common origin. Distinction of pituitary adenoma from hyperplasia is difficult. In our case a diagnosis of pituitary adenoma was made based of the presence of distorted and disrupted acinar pattern of cells and perivascular arrangement of cells. Gangliocytomas should be differentiated from hamartoma (Kamel *et al*., 1989). A hamartoma is an ectopic nervous tissue of the pituitary, and forms nodules composed of ganglion cells, astrocytes and branch cells. Differentiation from the normal neurohypophysis is also important. It is the normal tissue changing, in which spindle-shaped glial cells are sparse, and there are no metatypical cells, no hemorrhage and necrosis, and no Rosenthal fibers and eosinophilic bodies (Chen *et al*., 2014).

The etiopathogenesis of these mixed pituitary lesions remains controversial. Various theories have been put forward to explain this relationship. The theory of an incidental concurrence of pituitary adenoma in a pre existing neuronal choriostoma was supported by the hypothesis of abnormal migration of hypothalamic neurons within the adenohypophysial parenchyma during the early phase of embryogenesis (Harding *et al*., 1997). Another hypothesis supported by Vidal *et al*., 2001 describes that somatotrophs exhibit plasticity and under certain conditions can undergo transdifferentiation. This is described as neuronal metaplasia of pituitary adenoma cells. However it is difficult to understand transformation of a neoplastic pituitary cell to a well-differentiated mature neuron with the dominating embryological concepts (Kontogeorgos *et al*., 2006). The third etiopathogenetic theory suggests that the primary gangliocytoma producing pituitary hormone releasing hypothalamic hormones stimulate the adenomatous transformation of the adjacent normal pituitary gland. It has been suggested that the intrasellar gangliocytoma might promote the growth of a pituitary adenoma through chronic overstimulation resulting from excess GHRH production (Kurosaki *et al*., 2002).

The recent reasonable speculations confirmed the common origin of neuronal and adenomatous elements. The stem/progenitor cells possess the ability of multidirectional differentiation and are the most likely cells of tumour origin. This suggestion was confirmed by morphological findings, which demonstrated significant intermixing of adenomatous and gangliocytic elements. Histopathological and immunohistochemical findings documented the presence of cells that exhibit intermediate features between ganglion and GH or PRL adenoma cells (Asa *et al*., 1984a) (Baysefer *et al*., 1997) (Deng *et al*., 2014). A close relationship between neurons and adenomatous GH cells was also confirmed by electron microscopy (Asa *et al*., 1984 b). Whether such composite lesions are collision tumours that arise from cells of different histogenesis or the two components are derived from the same cell is still a matter of debate. Our case documents close morphological correlation between ganglion cells and adenomatous cellular elements. In these cases the term "pituitary adenoma with gangliocytic component "best emphasizes the clinical importance of the adenomatous parts of the lesion (Balci *et al.,* 2015). These mixed tumors do not have the ability to metastasize. The recurrence rates are very low except for one case which recurred 17 years after radiation therapy (Rhodes *et al*., 1982). The recurrence is mainly because of subtotal resection of tumor. Thus, a transsphenoidal resection of tumor is curative and also improves any clinical symptoms.

Conclusion

''Collision tumors '' in case of patients operated upon for a pituitary adenoma is extremely rare. Histopathological examination is essential to confirm the diagnosis. Various interesting theories have been suggested to explain the relationship between a pituitary adenoma and a second sellar lesion. However there is still no proven pathogenetic mechanism. Further research in molecular genetics and various new technologies will shed more light on the mechanisms of pituitary adenomatogenesis/ tumorigenesis and their potential interaction.

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