

CASE REPORT

Somatotropinoma with neuronal choristoma - a histopathological surprise

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ABSTRACT

A 42-year-old male presented with features of active acromegaly. MRI of hypothalamo-pituitary area revealed pituitary macroadenoma with suprasellar extension. Histopathological examination showed chromophobe pituitary adenoma and - neuronal cells. Immunostaining of tumor tissue was positive for growth hormone, and the neural components showed positivity for neuron-specific enolase (NSE), synaptophysin, cytokeratin and negative glial cell fibrillary acidic protein (GFAP). Our findings support the metaplastic hypothesis of histogenesis of choristomas. [IJEM 2007;11(1&2):53-55]

Key Words: Acromegaly, choristoma, somatotropinoma

INTRODUCTION

The adeno-hypophysis does not normally contain neural tissue. However, occasionally pituitary tumours composed of partly or entirely ganglion cells have been reported. The first case of intrasellar pituitary adenoma containing ganglion cells was described by Kiyono et al(1) Since the first report, these lesions have been named under various headings of ganglioneuroma, gangliocytoma, ganglion cell choristoma, neural choristoma and hypothalamic gangliocytoma. The origin and histogenesis of the ganglion cells in pituitary tumors remains an enigma(2). Various authors believe that this tumor represents either a composite lesion or a collision tumour(3). The histological findings are similar in most of the previously reported cases consisting of chromophobe pituitary adenoma with acromegaly and neurons with or without neuropil(4). Till date only a few cases are described. We report a case and discuss the various hypotheses postulated for development of such lesion.

Case report

A 42 year old male presented with headache, coarsening of facial features and acral enlargement for 2 years. He had no visual disturbances. His height was 168

cms, weight 71 kg and BMI of 25 kg/m. He was normotensive. Biochemical profile was normal. Hormonal profile showed serum 0800 hr cortisol 280 nmol/l (N 400-690 nmol/l), T3 1.58 ng/ml (N, 1.2-2.8), T4 100 ng/ml (N, 60-160) TSH 2.5 mIU/l (N, 0.17-4.05), PRL 19.7ng/ml (N, 5-25), LH 2.1 mIU/ml (N,5-15), FSH 1.56 mIU/ml (N,5-15) testosterone 5.9 nmol/l (N, 9-24) and non-suppressible GH values of 46 ng/ml (N < 1 ng/ml) with 75 gms of oral glucose load. T2- weighted MRI of the hypothalamo-pituitary area revealed a 4.8 x 4.6 x 4.2cm sellar mass with suprasellar extension and unilateral hydrocephalus with a clear cut line of cleavage between the tumor and the frontal lobe (Fig.1). He was subjected to transphenoidal tumor



Fig. 1: T2 weighted coronal MRI of the hypothalamo-pituitary area showing large tumor sellar mass with suprasellar extension and unilateral hydrocephalus. Note is made of a clear-cut line of cleavage between the tumor and frontal lobe.

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excision, which was partial. Histopathological examination of tumor revealed a pituitary adenoma intermingled with numerous foci of apparently neural tissue comprising of large neuron like cells and abundant neuropil (Fig.2A,2B). The neuron like cells and neuropil

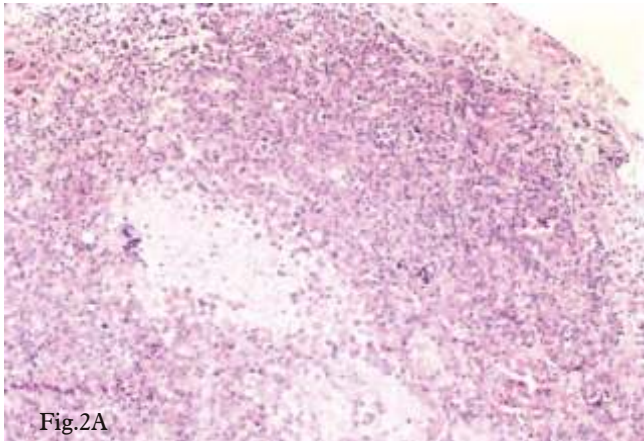


Fig.2A

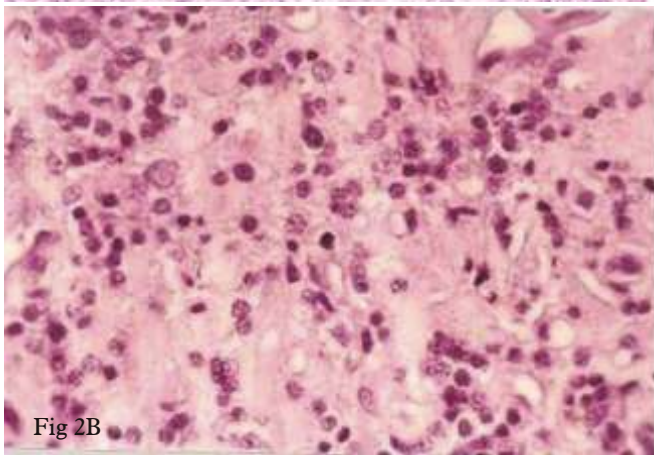
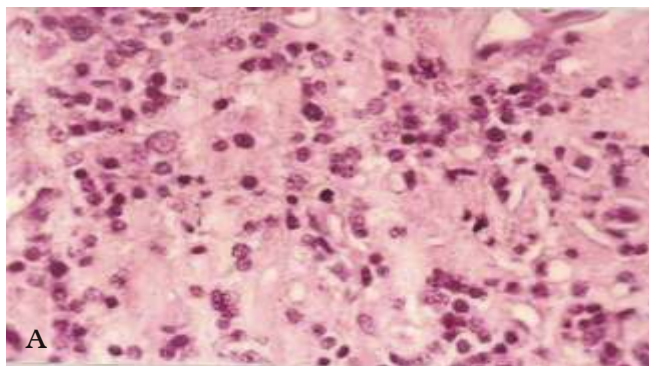


Fig 2B

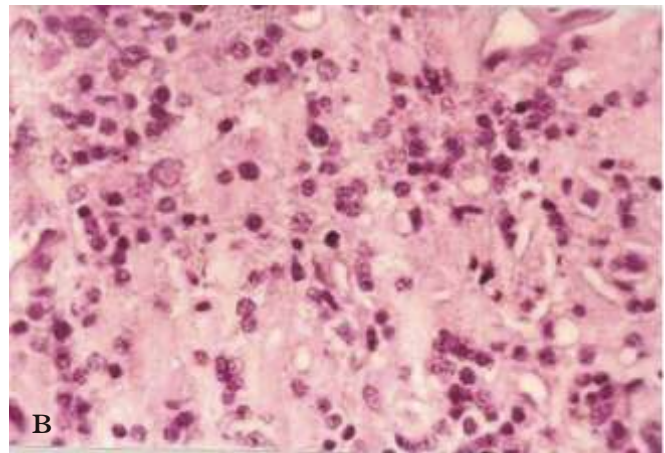
Fig.2A: Photomicrograph showing central area composed of gangliocytes in a background neuropil surrounded by sheets of tumour cells of pituitary adenoma (X 160)

Fig 2B: Photomicrograph showing small to intermediate tumour cells with mild nuclear atypia and moderate amount of eosinophilic cytoplasm lying adjacent to larger tumour cells with mild to moderate nuclear atypia, prominent nucleoli and moderate to abundant cytoplasm(X 360).

showed strong positivity of NSE; synaptophysin and positivity for GFAP respectively (Fig3A, 3B) The



A



B

Fig.3A, 3B Immunostaining with synaptophysin and neuron specific enolase showing intense positivity within cytoplasm of larger cells with gangliocytic differentiation (X 440)

adenomatous component was positive for GH but negative for ACTH and PRL. (Fig. 4,5). On follow up there was partial improvement of symptoms and MRI at 3 months showed a reduction in tumor size. The patient continued to have nonsuppressible growth hormone on oral glucose

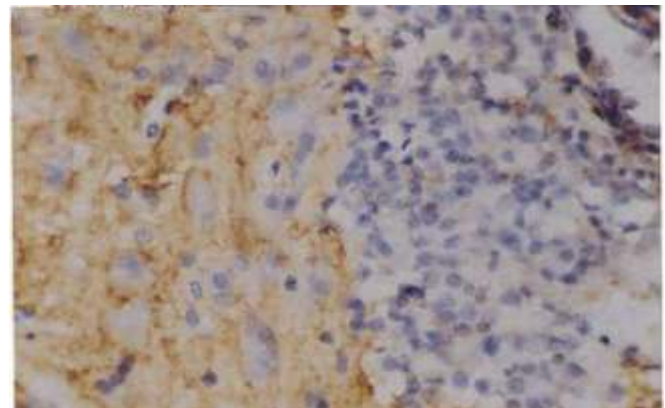


Fig.4: Immunostaining with GFAP showing intense positivity within neuropil. Adjoining adenoma cells are conspicuously absent (X 440)

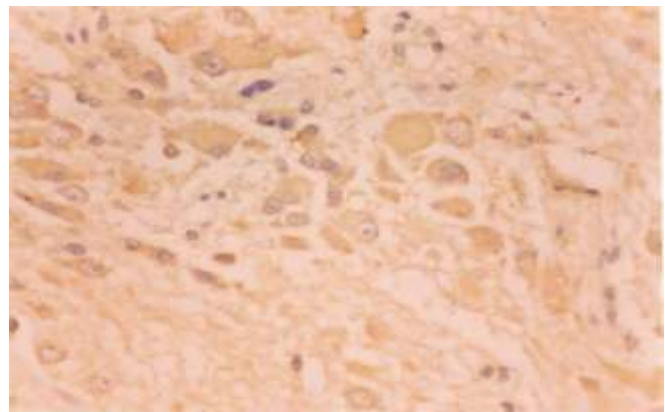


Fig.5 Immunostaining with growth hormone showing intense positivity within cytoplasm adenoma cells. Adjoining larger gangliocytes are also seen (X 360)

load. He underwent redo-surgery with near total removal of tumor. Histopathology revealed previous findings. In addition, immunostaining with cytokeratin showed positivity. At one year of follow-up the patient is doing well.

DISCUSSION

Neuronal choristoma in the region of sella turcica is an unusual entity and its histogenesis is an enigma. To our knowledge only 57 cases have been reported in the literature till date(1-6). Morphological findings are stereotypic, consisting of chromophobe adenoma and neurons with or without neuropil. The proportion of the two components varies considerably in individual cases(7). The ganglion cells usually resemble hypothalamic neurons. Intermediate cells showing features of both adenomatous and neuronal cells have also been described. Initially it was believed to be choristoma and proliferation of heterotopic intrasellar hypothalamic neurons conglomerating as gangliocytoma, which through their secretions induce the adenomatous proliferation of pituitary cells. This theory is substantiated by positivity of these neurons to hypothalamic releasing hormones eg ; growth hormone releasing hormone (GHRH). Presence of adenoma rather than hyperplasia and no correlation between the type of adenoma and the type of releasing hormone from the ganglion cells are against this hypothesis(7-10).

The second hypothesis proposes that both the neuronal and adenoma component originate from embryonal rests showing features intermediate between adeno-hypophyseal cells and neuronal cells. This is supported by close embryonic origin of adeno-hypophyses and infundibulum, positivity for pituitary hormone and neuronal markers by intermediate cells and intrasellar neurons(11-12). In our patient many ganglion cells were positive for neuronal markers but negative for GH and PRL.

The third hypothesis postulates that these neuron like cells originate from the sparsely granulated adenoma as a result of metaplasia(13). This is supported by demonstration of neuronal processes on ultra structural examination of sparsely granulated GH-cell adenomas and spontaneous transformation of normal adeno-hypophyseal cells into cells with neuronal processes in vitro studies(14). Therefore, the composite lesion may represent lineage infidelity in an endocrine tissue. The possibility of collision tumor of pituitary adenoma and hypothalamic gangliocytoma is unlikely in our case as radiologically there was no evidence of hypothalamic invasion and the dumb-bell shaped extension towards the frontal lobe demonstrated a clear cut line of cleavage during surgery.

In conclusion we describe a rare case of pituitary lesion which is a pathologically distinct entity composed of

adenomatous and ganglion cells that does not have any characteristic radiological features but should not be a surprise to clinicians.

REFERENCES

1. Kiyono H: Die histopathologie der hypophyse. *Virchows Arch A pathol Anat Histopathol* 1926:259:388-465.
2. Towfighi J, Salam MM, Mc Lendon RE, Powers S, Page RB: Ganglion cell containing tumors of the pituitary gland. *Arch Path Lab Med* 1996: 120: 369-77.
3. Horvath E, Kovacs K, Scheithauer BW, Lloyd RV, Smyth HS: Pituitary adenoma with neuronal choristoma (PANCH): Composite lesion or lineage infidelity? *Ultrastruct Pathol* 1994: 18: 565-74.
4. Tajika Y, Kubo O, Takeshita M, Jajika T, Shimizu T, Kitamura K: An intracranial collision tumor composed of intrasellar gangliocytoma and pituitary adenoma. *No Shinkei Geka* 1989: 12: 1181-6.
5. Geddes JF, Jansen GH, Robinson SFD, Gomori E, Holton JL, Monson JP, Besser GM, Revsz T: Gangliocytoma of the pituitary: A heterogenous group of lesion with differing histogenesis. *Am J Surg Pathol* 2000:(4): 607-13.
6. Li JY, Racadot O, Kujas M, Kudari M, Peillon F, Racadot J: Immunohistochemistry of four mixed pituitary adenomas and intrasellar gangliocytoma associated with different clinical syndromes, acromegaly, amenorrhoea-galactorrhoea, cushings disease and isolated tumoral syndrome. *Acta Neuropathol* 1989: 77: 320-8.
7. Puchner MJA, Ludecke DK, Saeger W, Riedel M, Asa SL: Gangliocytoma of the sellar region-A review. *Exp Clin Endocrinol diabetes* 1995: 103: 129-49.
8. Rhodes RH, Dusseau 11, Boyd AS, Knigge KM: Intrasellar neural adeno-hypophyseal choristoma: a morphological immunohistochemical study. *J Neuropathol Exp Neuro* 1982: 41: 267-88.
9. Asa SL, Scheithauer BW, Bilbao JM, Horvath E, Ryan N, Randal RV, Laws ER, Singer W, Linfoot JA, Thorner MQ, Vale W: A case of hypothalamic acromegaly: a clinicopathology study for six patients with hypothalamic gangliocytoma producing growth hormone releasing factor. *J Clin Endocrinol Metab* 1984: 58: 796-803.
10. Asa SL, Bilbao JM, Kovacs K, Linfoot JA: Hypothalamic neuronal hamartoma associated with pituitary growth hormone cell adenoma and acromegaly. *Acta Neuropathol* 1980: 52: 231-4.
11. Takor TT, Pearse AGE: Neuroectodermal origin of avian hypothalamo- hypophyseal complex: the role of the ventral neural ridge. *J Embryol Exp Morph* 1975: 34: 311-25.
12. Bugnon C, Bloch B, Lenys D, Fellmann D: Infundibular neurons of human hypothalamus simultaneously reactive with antisera against endorphins. ACTH, MSH and α -LPH. *Cell Tissue Res* 1979: 199: 177-96.
13. Stefanescu L, Ryan N, Kovacs K: Immunocytochemical localization of synaptophysin in human hypophysis and pituitary adenoma. *Arch Pathol Lab Med* 1989:112:801-4.
14. Martinez-campos, Dannies PS: A possible differentiation of anterior pituitary cells in collagen gel into neurons. *Cell Tissue Res* 1986: 244: 21-6.