Article is available online at http://www.webio.hu/por/2003/9/2/0134

CASE REPORT

Rare Sellar Region Tumors

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We present three cases of rare intracranial midline tumor in the sellar region, often mimiking pituitary adenomas clinically. We describe their symptoms, radiological and pathomorphological features. The first case is a pituitary adenoma producing growth hormone with ganglion cell differentiation. In addition, a rare intracranial granular cell tumor of sellar region and germinoma of pituitary fossa are also presented. All tumors were resected and histologically analyzed. Their biological behaviour was favorable with a 10-year follow-up demonstrating no recurrent tumor mass. (Pathology Oncology Research Vol 9, No 2, 134–137)

Keywords: intracranial midline tumor, pituitary adenoma, granular cell tumor, germinoma

Introduction

Our three tumor cases are located in the intracranial midline, these intra- and parasellar tumors are extremely rare. Although their locations are identical, their histology is different. The intracranial midline tumors may manifest at any age. The tumors located in the sella turcica (*Figure 1*) usually cause endocrine disturbances and visual defect. All of them mimic pituitary adenomas both clinically and radiologically.[10,12,17]

First, we present a case of functioning pituitary adenoma with ganglion cell differentiation. By histological and immunohistochemical examination the tumor proved to be neoplastic with neuronal cell differentiation of sparsely granulated growth hormon producing cells.[6]

As the second case, we report a hypophyseal granular cell tumor extended to the infundibulum causing visual disturbance. The infundibular granular cell tumors probably arise either from granular cell tumorlets found in neurohypophysis or from pituicytes of neurohypophysis. [7] The tumor is a benign growth characterised by slow progression and a lack of invasive features.

Finally, a primary intracranial germ cell tumor presenting with symptoms of diabetes insipidus and visual field defects is demonstrated. Germinomas occur primarily at two sites, in the pineal gland and hypothalamic regions but our case was found in the intrasellar region.[11] Generally both extra- and intracranial germinomas are histologically malignant and usually infiltrate the surrounding tissues. Meanwhile, the presented case was incompletely resected and proved to be radiosensitive since follow-up demonstrated no recurrent tumor mass.

Received: Febr 18, 2003; *accepted:* March 15, 2003
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Materials and methods

The surgical samples were fixed in formalin and embedded into paraffin for histological processing. The samples were stained with hematoxylin and eosin (HE) and periodic acid Schiff's (PAS). Immunohistochemistry was performed on all cases using avidin-biotin complex technique and diaminobenzidine as chromogen. The monoclonal antibodies used included ACTH, PrL, GH, TSH, FSH, LH; glial fibrillary acid protein (GFAP), synaptophysin, neuron specific enolase (NSE), vimentin, S-100, KP-1, low molecular weight cytokeratin, placental alcaline phosphatase (PLAP), α-fetoprotein (AFP), human choriogonadotropin (HCG) and MIB1 proliferation marker.

Case 1

Patient History

A 45-year-old female presented with a 1-year history of left temporal visual field defects and thickening of her nose and fingers. Laboratory investigations revealed elevated serum levels of growth hormone (GH). Cranial MRI was performed which demonstrated a sellar mass with suprasel-

lar extension causing chiasmal compression. The patient was operated and the tumor was completely resected. Postoperatively, mean serum GH levels were within normal limits.

Histology

The pituitary adenoma showed saparse intracytoplasmic granulation. In addition, there were large ganglion cells. Morphologically, the neuronal cells demonstrated abnormal architecture with large bi- and trinucleated cells, there were also several smaller foci of neuropils scattered throught the adenoma (*Figure 2A*).

Immunohistochemistry

The adenoma cells showed variable but sparse immunoreactivity for GH and juxtranuclear positivity for cytokeratin. The large ganglion cells showed immunoreactivity for cytokeratin (*Figure 3A*) and neurofilament as well. There was no pituitary hormon secretion in ganglion cells.

Case 2

Patient History

A 63 year old male presented to the clinic with a history of deteriorating visual acuity in the right eye. Neurologically, meningeal signs were abscent, cranial nerve review showed constricted visual fields bilaterally and a large central scotoma on the right side. Visual acuity was also reduced bilaterally. Extra-ocular movements were intact to both command and tracking, eye movements were conjugated with no nystagmus. Muscle trophy, tone and strengh were normal as were superficial and deep sensory modalities.

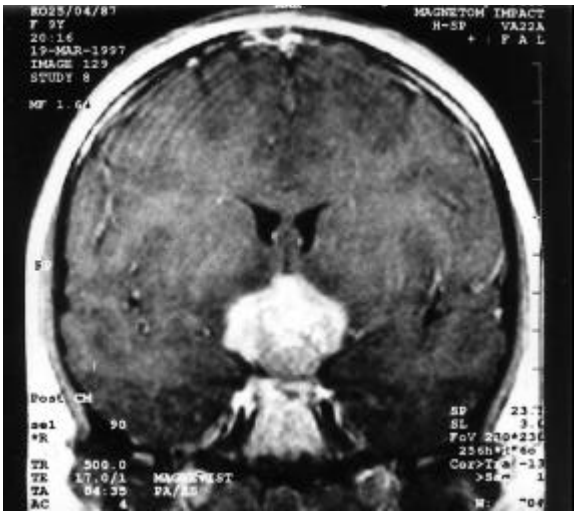

Figure 1. Diagnostic MRI (frontal section) demonstrating a midline mass in intra- and suprasellar region

Pathological reflexes could not be evoked. Cranial MRI was performed which demonstrated an intra- and parasellar mass occupying lesion (17 by 19 mm) which was enhanced by contrast. The patient was operated and the tumor resected via a right fronto-temporal approach. The well circumscribed tumor enveloped the infundibulum, compressing the right optic nerve and dislocating the right internal carotid artery laterally. The procedure was well tolerated without any intraoperative or postoperative complications. Control MRI proved total tumor resection, by 5 years-follow up the patient is well with mild improvement of his visual acuity.

Histology

The tumor was composed of round and polygonal cells with eccentric nuclei and abundant granular eosinophilic cytoplasm. The tumor cells were sharply demarcated and their cytoplasm was PAS positive. The architecture was predominantly nodular but focally fascicular (*Figure 2B*).

Immunohistochemistry

Positive reactions was detected by KP-1, S-100 protein *(Figure 3B)* and NSE antibodies. Immunohistochemical stains for GFAP and vimentin were negative. There was no elevated intranuclear labeling for MIB1 proliferation marker.

Case 3

Patient History

A 10-year-old girl presented with a history of polydipsia, polyuria and recent onset of visual disturbance. The patient was slightly obese with a normal physical and mental development. The results of physical and neurological examinations were normal with the exception of moderate ataxia, visual disturbance on left eye with papillar edema. Cranial MRI demonstrated an intra- and suprasellar mass (3 by 4 cm). The lesion, irregular and sharply demarcated with an inhomogeneous structure involved the pituitary stalk and gland, and extended backward to the upper edge of the pons and interpeduncular space, compressing the 3rd ventricle. The child was operated from a right fronto-temporal approach with partial tumor resection and decompression of the optic nerve. There were no intraoperative complications. Hormonal replacement and postoperative radiation were administered. At present the child is well, her vision improved although the visual field is restricted.

Histology

Histologically the tumor was a typical germinoma. The tumor was composed of monomorphous large cells resembling primitive germ cells. Large vesicular nuclei,

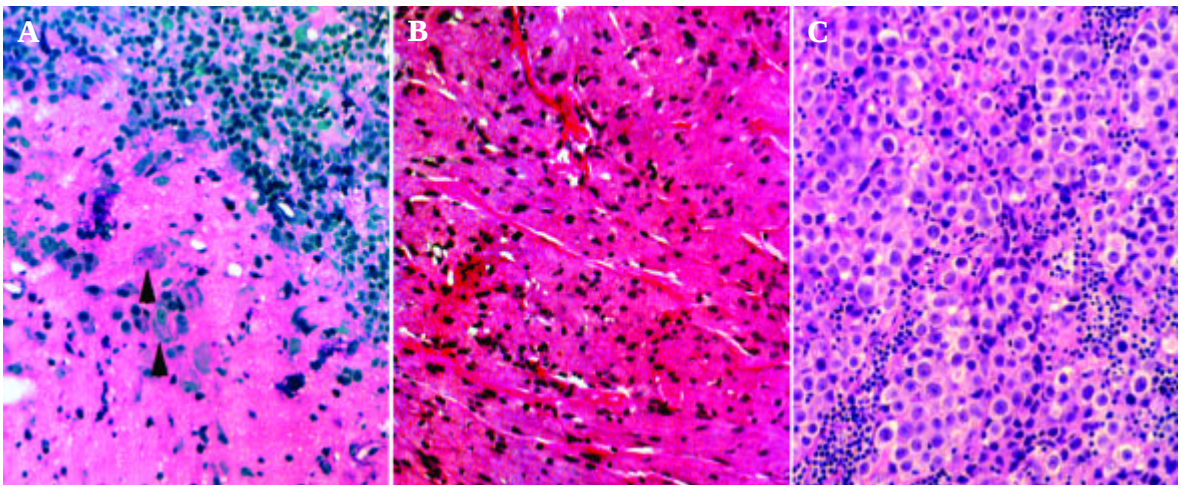

Figure 2. Histological feature of sparsely granulated growth hormon cell adenomas with neuronal differentiation. Ganglion cells are shown by arrowhead (A) H&E, x250, granular cell tumor with intracytoplasmic PAS positive granulations (B) PAS, x250 and primary intracranial germinoma with clear cytoplasm and non-neoplastic lymphocytic infiltration (C) HE, x250.

prominent nucleoli with eosinophilic cytoplasm was set in a lobular pattern separated by a delicate fibrovascular stroma and infiltrated by mature lymphocytes (*Figure 2C*).

Immunohistochemistry

Immunohistochemistry was positive for PLAP *(Figure 3C)* but not for AFP, HCG or cytokeratin. Proliferation activity was elevated, mitotic figures were identified 3-4/10 HPF (high power field) and MIB1 labeling index was also elevated (18-22/HPF).

Discussion

A variety of intracranial neoplasms arising from the midline region pilocytic astrocytoma, third ventricle ependymoma and choroid plexus tumors, ganglioglioma, gangliocytoma, neurocytoma, craniopharyngioma, pinealoma, rhabdoid and germ cell tumors are typically present in childhood and young adults. However, third ventricle chordoid glioma, hypophysis tumors, meningeoma, papillary craniopharyngioma and metastases more frequently occur in adults. Presented are three extremely rare intracranial midline tumors of the intrasellar region; their locations are

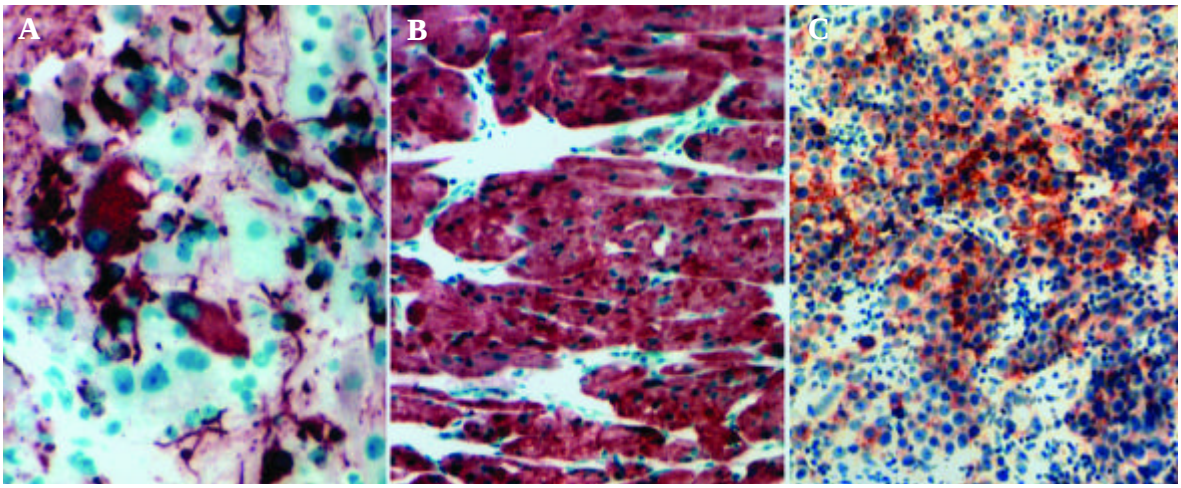

Figure 3. Immunohistochemical feature of these midline tumors. The sparsely granulated growth hormon cell adenomas with neuronal differentiation, ganglion cells showed intracytoplasmic cytokeratin positivity (A) x400, granular cell tumor with strong S-100 immunoreactivity (B) x250 and primary intracranial germinoma with placental alcaline-phosphatase immunoreactivity (C) x250.

identical thus accounting for their similar clinical symptoms, however, their histology is widely different. Ganglion cell-containing neoplasms of pituitary adenoma have been infrequently described. Histogenesis of neoplastic ganglion cells in pituitary adenomas have been debated.[2,9,10] It is suggested that their origin is either from embryonal pituitary cell rests or from a common hypothalamic origin.[14,18] Recently, eight ganglion cell-containing pituitary lesions were published, representing a heterogeneous group of tumors with differing histogenesis.[6] It was suggested that the sparsely granulated growth hormon producing adenoma cells can differentiate to the neuronal lineage.

Intracranial granular cell tumors mostly occur in adults and usually infiltrate the posterior pituitary and pituitary stalk impinging on the optic chiasma or the floor of the 3rd ventricle producing endocrine disturbances and hydrocephalus.[4] Meningeal locations have been sited as well. Small nodules of granular cells in the posterior pituitary usually present as incidental asymptomatic autopsy findings.[17] They are usually solitary but can be multiple. Extracranial granular cell tumors occur at a variety of sites including the oral cavity, salivary glands, larynx, gastrointestinal tract, urinary bladder, breast and subcutaneous tissues. The histogenesis of these tumors is controversial which is evident from the various terms in the literature including choristoma tumorlet, myoblastoma and pituicytoma. Immunohistochemical and ultrastructural findings suggested that neurohypophyseal granular cell tumors are derived from the pituicytes[5,7] which are modified astrocytes normally occuring in the posterior pituitary, therefore it may also be considered to be a form of glioma.[3,15]

Germinomas are malignant intracranial germ cell tumors with a peak incidence in children and adolescents. Germinomas usually infiltrate the ventricular system and the spinal meninges. They have been well defined clinically with endocrine complications[11] and morphologically by histology, immunohistochemistry and by their ultrastuctural features.[12] The familial nature of these tumors can be supported by their association with different genetic disorders, for instance Klinefelter's- and Down's syndrome and neurofibromatosis type-1.[13,19] According to current scientific literature intracranial germinomas are less well characterized cytogenetically than their malignant extragonadal germ cell counterparts. Frequent genetic findings of primary intracranial germ cell tumors involving chromosomes 1, 4, 5/19, 12, 15 and 17 have been published but the p53 gene mutation has been detected at low frequency.[1,8,16] In spite of malignant histology of germinomas, they have a favourable biological behaviour.

For conclusion, sellar region tumors are characterized by similar clinical symptoms and radiological pictures. Most frequently these are pituitary adenomas but our presented cases represent histologically different uncommon tumors with a favourable clinical prognosis.

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