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CASE REPORT

Ependymoma with Extensive Lipidization Mimicking Adipose Tissue: A Report of Five Cases

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Lipomatous ependymoma is a recently described entity and only 3 cases of this variant have been reported in the literature. We report 5 cases of this rare variant of ependymoma. Patients' age ranged from 4 years to 45 years and, interestingly, all of them were males. Two tumors were supratentorial in location, 2 in the fourth ventricle and 1 was intramedullary. Microscopically all of them showed the classical histology of ependymoma along with lipomatous differentiation. The lipomatous component was composed of cells with a large clear vacuole pushing the nucleus to the periphery and giving a signet ring cell appearance. This component demonstrated positivity for GFAP and S-100 protein thereby confirming its glial lineage. Three of the 5 tumors were high grade (WHO-grade III), had a high MIB-1 labelling index (MIB-1 LI) and showed recurrence on follow-up. However, 2 were low grade (WHO grade II) and patients are free of disease till the last follow up. (Pathology Oncology Research Vol 6, No 2, 136–140, 2000)

Keywords: Ependymoma, adipocyte, metaplasia, lipomatous change, signet ring cell, intracranial tumor

Introduction

Ependymomas constitute 2–4% of all glial tumors. The variants of ependymoma according to the WHO classification[10] are cellular, papillary and clear cell types. Recently Ruchoux et al[12] have reported three cases of otherwise classical ependymomas with lipomatous differentiation. We report 5 cases of this new variant of ependymoma because of its rarity and discuss hypotheses for the lipomatous change seen in this tumor.

Materials and Methods

During a period of 19 years (1980–1998) 8865 cases of intracranial tumors were diagnosed in the Department of Pathology, All India Institute of Medical Sciences. Of these 2910 were astrocytic tumors (32.8%) and 193 (2.1%) were ependymomas. Hematoxylin and eosin (H&E) stained sections of these tumors were reviewed to look for lipomatous change. In all, 5 cases were encountered where this change was observed.

In these 5 cases of ependymoma with lipomatous change, immunohistochemical staining was done by the streptavidin-biotin conjugate immunoperoxidase technique (LSAG, M/s) using antibody to: glial fibrillary acidic protein (GFAP dilution 1:500, M/s); neuron specific enolase (NSE dilution 1: 100 M/s); S-100 protein (dilution 1:100 M/s); synaptophysin (1:20 M/s); epithelial membrane antigen (EMA dilution 1:20 M/s); cytokeratin (pancytokeratin dilution 1:20 M/s' – all from Dakopatts, Denmark; MIB-1 (dilution 1: 100 M/s Immunotech, USA)

In 3 of the 5 cases, there was recurrence of tumor. Hence the above parameters were studied both in the original and recurrent tumor.

Results

In the present series, lipomatous ependymomas comprised 2.5% of all ependymomas (5/193) and 0.05% of all intracranial tumors (5/8865). The age ranged from 4 to 45 years (mean 23.8 years) and all occurred in male patients.

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Case 1

An 18-year-old male presented in August 1994 with headache of 4 months duration. There was history of vomiting, diplopia and generalized tonic clonic seizures since 8 days. Examination revealed right-sided hemiparesis, right temporal field defect and visual acuity of 5/6 in the right eye. There was bilateral papilloedema and right sixth nerve palsy.

Computer tomography (CT) scan of the head revealed a large hyperdense mass lesion with an enhancing nodule in the left parietal lobe. There was also gross midline shift. Radiological diagnosis of an astrocytoma was made. Through a left parietal craniotomy, decompression of the cystic lesion was done. Postoperative radiation was given in a dose of 4000 rads spanning a period of 6 weeks. In July 1996, he again presented with signs and symptoms of raised intracranial tension and visual deterioration. Contrast enhanced computerized tomography (CECT) of head revealed a non-homogenous enhancing lesion in the left parieto-occipital region which extended to the falx. Through a left parieto-occipital approach, subtotal decompression of the tumor was done. Chemotherapy was planned but he was lost to follow up.

Case 2

This 17-year-old male presented in October 1991, with history of vomiting and gait disturbances since 6 months. CECT of head showed a hyperdense lesion in the posterior fossa suggestive of medulloblastoma. Through a suboccipital craniotomy near subtotal excision of the tumor was done. Postoperatively he received radiotherapy. In November 1993, recurrence of the tumor was detected and near total excision was again done.

Case 3

A 4-year-old boy presented in August 1981 with progressive left hemiparesis intermittent vomiting, left focal seizures and headache of 1 year duration. CT scan of head revealed a cystic and solid tumor in the right frontal lobe which extended to the lateral ventricle. Radiological diagnosis of an ependymoma was made. Through a right frontal approach, subtotal excision of the tumor was done. The tumor was solid and cystic and was projecting into the right lateral ventricle and third ventricle. Post-operatively he received a course of radiotherapy. In 1985, he presented with complaints of headache, vomiting and right focal seizures for 2 months. There was bilateral papilloedema and left seventh nerve palsy.

Gross decompression of a large solid and cystic tumor was done. Tumor was extending into the right temporal lobe and medially to the septum pellucidum.

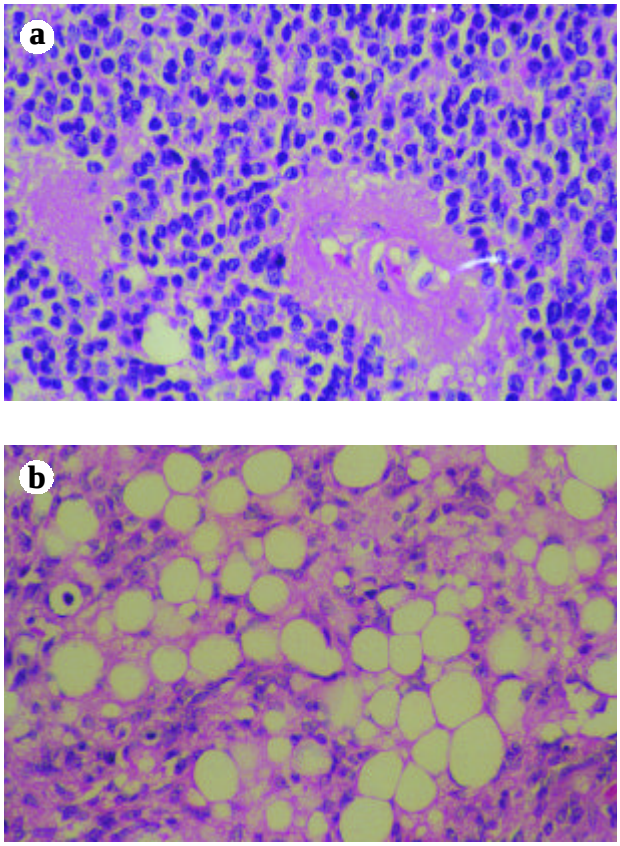

Figure 1. Photomicrographs of Case 1 showing sheets of small round cells with perivascular nuclear free zone (a, HE x40). Another area shows diffuse lipomatous change. Adipocyte like cells show a single intracytoplasmic vacuole pushing the nucleus to the periphery (b, HE x200).

Case 4

A 35-year-old man presented with complaint of headache for 2 years. CT scan of the head revealed a heterogenously enhancing mass in the fourth ventricle suggestive of an ependymoma, and there was obstructive hydrocephalus. Through a suboccipital craniotomy, subtotal excision of tumor was done. Post-operatively he was treated with radiotherapy.

Case 5

This 45-year-old man presented with difficulty in walking and numbness of the right lower limb for 3 years. There was involvement of urinary bladder and bowel for last 9 months. CT scan of the spine showed an intramedullary tumor in T2-3 segment of spinal cord. There was a syrinx both above and below the tumor. Subtotal excision of the tumor was performed.

Cases 4 and 5 are recurrence-free on follow-up at 1 and 3 years, respectively.

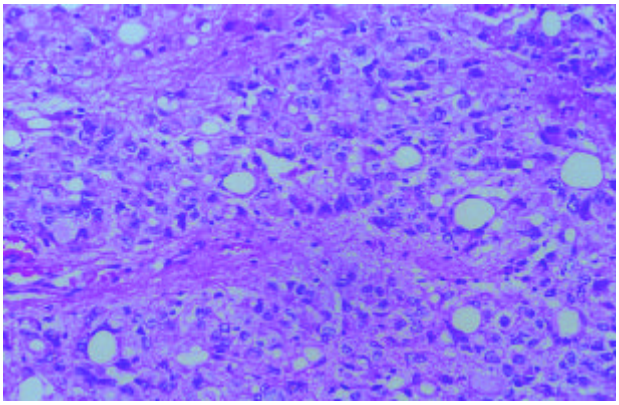

Figure 2. Photomicrographs of Case 5 showing sheets of cells with moderate to abundant cytoplasm and focal lipomatous change (HE x100).

Pathologic examination

Examination of H&E stained sections of these 5 cases revealed a cellular tumor consisting of small round to oval cells with scant amounts of cytoplasm (*Figure 1a*). Nuclei were hyperchromatic and an occasional nucleolus was identified. True ependymal canals were seen in only 1 case but perivascular pseudorosettes were identified in all. In 3 cases the mitotic rate was 2–3 per 10/hpf with areas of necrosis being present in 2 of these 3 cases. In the others neither mitosis nor necrosis was identified. Endothelial proliferation was absent. No evidence of astrocytic differentiation was seen. In addition, there were large areas where the tumor cells had a signet ring appearance with large vacuoles in the cytoplasm, pushing the crescentic nucleus to the periphery along the cell membrane (*Figure 1b*).

There was a gradual transition from ependymal areas to these lipomatous areas. The extent of lipomatous change varied being minimal in 1 case (*Figure 2*), moderate in 2 cases and very extensive in 2 cases. In the 2 tumors where necrosis was present, this change was encountered both around and distant from the necrotic areas. This lipomatous change was also observed in the recurrent tumors but to lesser extent.

Immunohistochemical staining for GFAP showed focal positivity in the classical ependymal areas as well as rim positivity in the signet ring cells (*Figure 3a*). Both areas stained positively for S-100 protein (*Figure 3b*) but were negative for EMA, CK and synaptophysin. Even the periphery of vacuoles showed no positivity for EMA. The MIB-1 LI varied from 0% to 20% (*Table 1*). In the non-recurrent cases, MIB-1 LI was zero. In the recurrent cases, the original MIB-1 LI ranged from 9–20% and on recurrence MIB-1 LI varied from 7.5–17%.

Discussion

Tissue mainly composed of lipid-laden cells is unusual in intracranial lesions and has been described in three different groups of disorders, namely – hamartomas, primary neoplasms and metastases.[17] Intracranial hamartomas are rare and composed of fully mature adipocytes.[1,14] In primary neoplasms the presence of fat as a secondary xanthomatous change has been described mainly in capillary hemangioblastomas, meningiomas, schwannomas, medulloblastomas and neurocytomas.[3,4,5,6,13,15,16]

Kepes et al[8] in 1979 described a distinct type of astrocytoma with favourable prognosis designated as pleomorphic xanthoastrocytoma in which xanthomatous change was in the form of multiple cytoplasmic vacuoles resulting in a foamy appearance of the cells. However, no mature adipose-like cells were seen. Later they also described glioblastoma multiforme with lipidized tumor cells[9] where the cytoplasm was foamy rather than vacuolated.

Lipomatous differentiation in medulloblastoma was first described by Chimelli[3] in 1991 followed by other reports.[4,6,16] This variant of medulloblastoma occurs in adults and has relatively good prognosis. Similar lipomatous change has been described in cerebellar and central

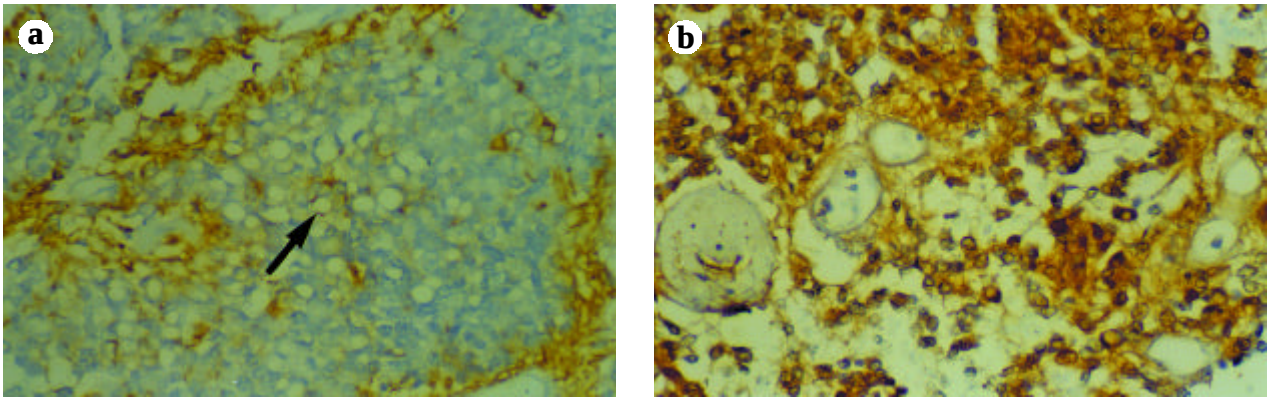

Figure 3. Photomicrographs showing a) ring positivity for GFAP (arrow) and b) diffuse positivity for S-100 (x 200).

Table 1 **Clinical features of lipidized ependymomas**

No	*Age/ Sex*	*Site*	*Duration of symptoms*	*Original tumor MIB-1 LI*	*Recurrent tumor MIB-1 LI*	*Recurrence*
1.	18 / M	Lt. Parietal lobe	4 mths	20%	7.5%	2 years
2.	17 / M	Post fossa	6 mths	9%	17%	2 years
3.	4 / M	Rt. Frontal	12 mths	Not done	Not done	4 years
4.	35 / M	Post fossa	6 mths	0	No recurrence	Nil
5.	45 / M	T2-3 segment	9 mths	0	No recurrence	Nil

Abbreviations: Mths – Months, Lt. – Left, T – Thoracic, Post – Posterior, Rt. – Right

neurocytomas[5,15] cerebellar and spinal astrocytomas[11,17] mixed neuronal-glial tumor of the brain[2] and recently in ependymomas.[12]

Ruchoux et al[12] in 1998 described 3 cases of otherwise classical ependymoma with lipomatous differentiation. The lipomatous component was composed of mature adipose-like cells with the nucleus pushed to the periphery by a large single cytoplasmic vacuole. This adipose-like component demonstrated ring-like cytoplasmic positivity for GFAP and S-100 protein, thereby exhibiting a glial lineage. The ependymal nature was further confirmed by electron microscopy in one case.

All the 5 cases in the present series demonstrated the classical histologic appearance of ependymoma with lipomatous differentiation. The lipomatous component was also positive for GFAP and S-100 protein. A histologic stain for fat and electron microscopy could not be carried out as all cases were studied from archival material. Three of them showed areas of necrosis and mitosis, i.e., features of a high grade malignancy and were diagnosed as anaplastic ependymomas. The lipomatous change was seen both near and far from the areas of necrosis.

Lipomatous differentiation, although rare in ependymomas, should be differentiated from xanthomatous and clear cell change. In the xanthomatous variant of ependymomas, the cytoplasm is more foamy with multiple tiny vacuoles, whereas in lipomatous change a single vacuole pushes the nucleus to the periphery of the cell membrane, mimicking a mature adipocyte. Hirato et al[7] described an ependymoma with extensive vacuolization of cytoplasm, giving an appearance of an adipocyte. Immunohistochemical staining for EMA showed positivity of the vacuolar periphery and electron microscopy demonstrated microvilli and intracytoplasmic lumina. However, EMA was negative in all our cases ruling out the possibility of this variant of ependymoma.

Lipomatous change in neuroectodermal tumors may be the result of divergent differentiation[3] or disturbed cellular metabolism[12,17] rather than as a result of metaplasia. This latter hypothesis is further supported by the fact that the signet ring cells demonstrate positivity for GFAP.

In lipomatous medulloblastomas prognosis has been reported to be better than in ordinary medulloblastomas.[3] The biological behaviour of the lipomatous variant of ependymoma, however, remains to be established. None of the 3 cases published by Ruchoux et al[12] demonstrated areas of necrosis or endothelial proliferation and all had a low MIB-1 LI. On the contrary 3 of the 5 cases under discussion showed areas of necrosis, high mitotic rate and high MIB-1 LI. Moreover, 3/5 cases recurred. In 2, the recurrences occurred within 2 years (cases 1 and 2) while in the third (case 3) the recurrence occurred within 4 years. In contrast, the 2 cases without necrosis / mitoses also had a low MIB-1 LI. The follow-up was less than a year in both cases; however, no recurrence or metastasis was noted. Therefore, we propose that the behaviour of this variant of ependymoma is possibly similar to that of ependymomas of similar grades. However, this needs further confirmation on a larger number of cases.

References

1. *Budka H*: Intracranial lipomatous hamartomas (intracranial "lipomas"). Acta Neuropathol 28:205–222, 1974.
2. *Cenacchi G, Cerasoli S, Giangaspero F*: Cerebral mixed neuronal glial neoplasm with lipidization. An immunohistochemical and ultrastructural study (Abstract 85). J Neuropathol Exp Neurol 55:626, 1996.
3. *Chimelli L, Hahn MD, Budka H:* Lipomatous differentiation in a medulloblastoma. Acta Neuropathol 81:471-473, 1991.
4. *Davis DG, Wilson D, Schmitz M, et al:* Lipidized medulloblastoma in adults. Human Pathol 24:900-995, 1993.
5. *Ellison DW, Zygmunt SC, Weller RO:* Neurocytoma/Lipoma (neurolipocytoma) of the cerebellum. Neuropathol Appl Neurobiol 19:95-98, 1993.
6. *Giangaspero F, Cenacchi G, Roncarfil F, et al.* Medullocytoma (lipidized medulloblastoma). A cerebellar neoplasm of adults with favourable prognosis. Am J Surg Pathol 20:656-64, 1996.
7. *Hirato H, Nakazato Y, Iizima M:* An unusual variant of ependymoma with extensive tumor cell vacuolization. Acta Neuropathol 93:310-316, 1997.
8. *Kepes JJ, Rubinstein LJ, Eng LF*: Pleomorphic xanthastrocytoma: a distinctive meningocerebral glioma of young subjects with relatively favourable prognosis. Cancer 44:1839-1852, 1979.

9.[2]*Kepes JJ, Rubinstein LJ:* Malignant gliomas with heavily lipidised (foamy) tumor cells: a report of three cases with immunoperoxidase study. Cancer 47:2451-2459, 1981.
10.[2]*Kleihues P, Burger PC, Soheithauer BW:* Histological typing of tumors of central nervous system. Ed. 2nd, Springer-Verlag. Berlin Heidelberg New York; 1993.
11.[2]*Roda JM, Gutierrez–Molina M:* Multiple intraspinal low grade astrocytomas mixed with lipoma (astrolipoma) Case report. J Neurosurgery 82:891-894, 1995.
12.[2]*Ruchoux MM, Kepes JJ, Dhellemmes P, et al*: Lipomatous differentiation in ependymomas. A report of three cases and comparison with similar changes reported in other central nervous system neoplasms of neuroectodermal origin. Am J Surg Pathol 22:338-346, 1998.
13.[2]*Russel DS, Rubinstein LJ:* Pathology of tumors of the nervous system. Vol. 2nd Ed. 6th Ed, Arnold, London; 1998.
14.[2]*Sharma MC, Gaikwad S, Mahapatra AK, et al:* Hypothalamic hamartoma: Report of a case with unusual histological features. Am J Surg Pathol 22:1538-1541, 1998.
15.[2]*Shuster D, Herrick M, Horoupian D:* Two unusual cases of central neurocytoma: a concomitantly occurring under fourth ventricular PNET, b-mixed with lipoma. Brain Pathol 4:433, 1994.
16.[2]*Soylemezoglu F, Soffer D, Onol B, et al:* Lipomatous medulloblastoma in adults. A distinct clinicopathological entity. Am J Surg Pathol 20:413-418, 1996.
17.[2]*Walter A, Dingermans KP, Weinstein HC, Troost D:* Cerebellar astrocytoma with extensive lipidization mimicking adipose tissue. Acta Neuropathol 88: 485-489, 1994.