Acta Neuropathol (1991) 81: 471 – 473

Acta Neuropathologica

Lipomatous differentiation in a medulloblastoma*

L. Chimelli[1], M. D. Hahn[1], and H. Budka[2]

[1] Department of Pathology, Universidade Federal Fluminense, Hospital Universitario Antonio Pedro, Rua Marqués de Parana, CEP 24030, Niteroi, Rio de Janeiro, Brazil
[2] Neurologisches Institut, Universität Wien, Schwarzspanierstrasse 17, A-1090 Wien, Austria

Received March 22, 1990/Revised, accepted October 23, 1990

Summary. A surgically resected medulloblastoma of the left cerebellum in a 42-year-old man contained numerous mature fat cells; many of these adipocytes expressed glial fibrillary acidic protein (GFAP), S-100 protein, and vimentin as seen by immunocytochemistry. The cellular parts of the tumor showed varying immunoreactivities for GFAP, S-100 protein, neuron-specific enolase, and synaptophysin. It is concluded that this tumor exhibits a unique spectrum of differentiation along multiple lines, including transformation of neuroectodermal cells to fat cells. The significance of this new type of differentiation in primitive neural tumors remains to be elucidated.

Key words: Medulloblastoma – Differentiation – Metaplasia – Fat cells

Neuronal and/or glial differentiation have been found in medulloblastomas [2, 4, 6–12, 14]. In rare instances, myogenous [5, 13] and cartilagenous [1] differentiation have also been reported. Here we describe a unique medulloblastoma which showed multiple lines of differentiation including prominent lipomatous changes.

Case report

A 42-year-old Brazilian man with an 8-month history of headaches presented with blurred vision bilaterally. He was lucid, orientated, and fell to the right when closing eyes. There was reduced visual acuity mainly on the left; fundi showed papilledema. Computerized tomography (CT) revealed an enhancing lesion in the left cerebellar hemisphere. Posterior fossa craniotomy found a well-circumscribed tumor located superficially in the superior left cerebellar hemisphere which could be easily dissected from the surrounding tissue. The subsequent course was uneventful; postoperative CT revealed no evidence of tumor. No further treatment was given. Follow up examinations at 6 and 20 months later revealed only slightly reduced visual acuity on the left.

Materials and methods

Pinkish and soft tissue fragments received from surgery measured approximately 3 × 2 × 1.5 cm. A few smears were made from fresh tissue and stained with toluidine blue (TB). The bulk of the material was fixed in 10% formalin, embedded in paraffin, and stained with hematoxylin-eosin (H&E), periodic acid-Schiff (PAS), Sudan black B, Gomori, hematoxylin-van Gieson, and Giemsa stains. Immunocytochemistry used polyclonal or monoclonal antibodies against glial fibrillary acid protein (GFAP), S-100 protein (S-100), vimentin (VIM), neuron-specific enolase (NSE), neurofilament proteins (NFP), and synaptophysin (SYN). Several 1-mm cubes were fixed in 2.5% glutaraldehyde in cacodylate buffer, postfixed in osmium tetroxide and dehydrated through graded alcohols for Epon embedding. One-micrometer semithin sections were stained with TB.

Results

The tumor was composed of densely packed small cells with darkly stained oval or round nuclei and rather ill-defined sparse cytoplasm (Fig. 1). Mitoses were inconspicuous. No Homer Wright-type rosettes were seen. Tumor cells were either arranged in a finely fibrillary eosinophilic background, or intermingled with univacuolar fat cells which composed large areas within the tumor (Figs. 1, 4). Semithin sections confirmed the presence of fat globules (Fig. 2). There was a spectrum of fat loading of tumor cells with univacuolar globules of various size, from small vacuoles up to large mature adipocytes with vacuolated nuclei ("Lochkerne"), indistinguishable from components of adult fat tissue (Fig. 4). Many adipocytes strongly expressed GFAP (Figs. 5, 6), S-100 and VIM (Fig. 3), and weakly expressed NSE. The cell-dense parts of the tumor showed varying immunoreactivities for GFAP (Fig. 5), S-100, NSE, and

* Dedicated to the memory of the late Prof. Lucien J. Rubinstein who gave his invaluable advice to the senior author in many difficult diagnostic problems

Offprint requests to: H. Budka (address see above)

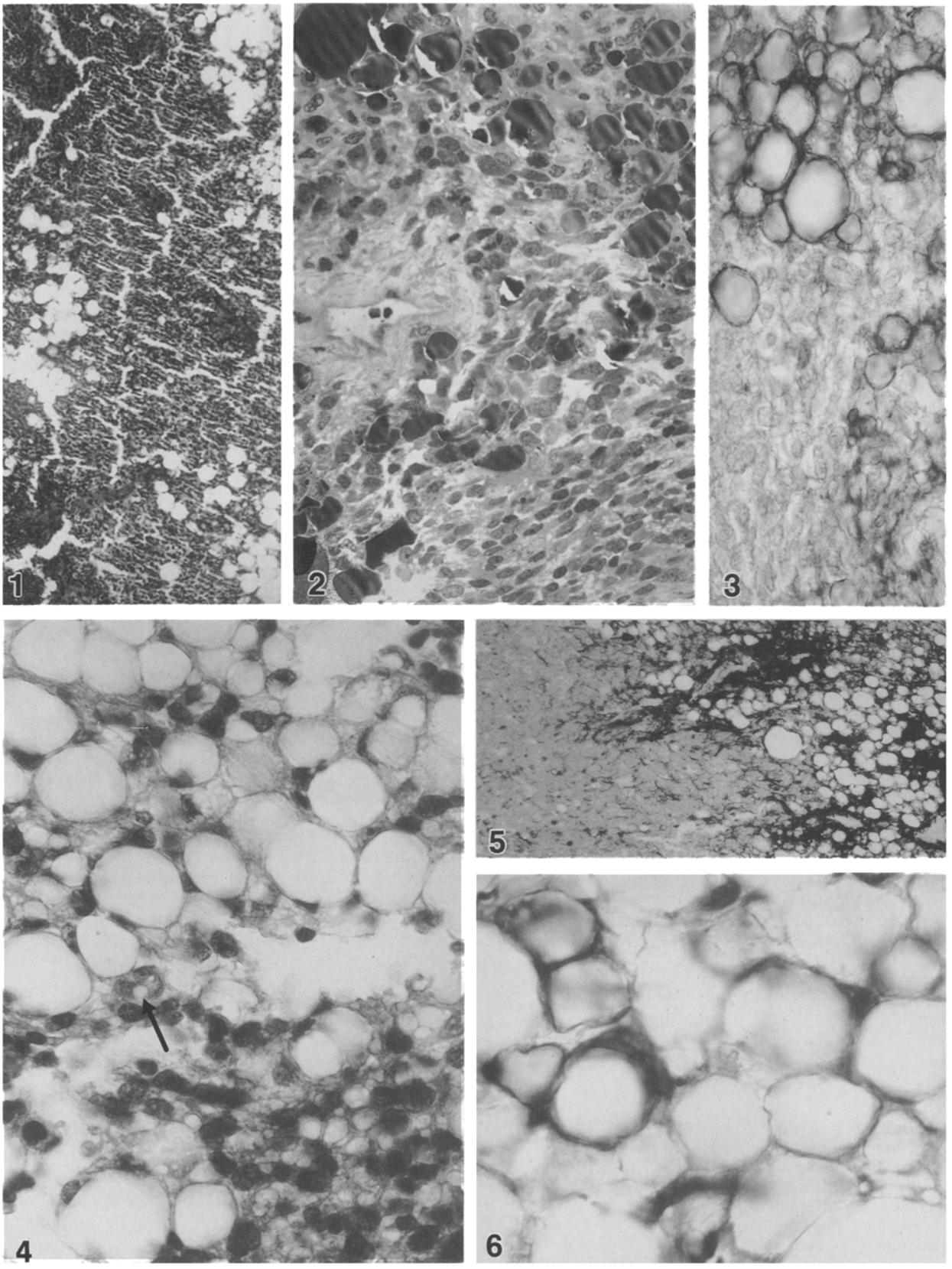

Fig. 1. Highly cellular tumor with interspersed areas of fat cells. H&E, × 100

Fig. 2. Semithin section of Epon-embedded specimen with numerous fat globules of varying size. Toluidine blue, × 400

Fig. 3. Vimentin is strongly expressed by adipocytes but barely by compact tumor parts. Avidin-biotin-peroxidase complex technique for vimentin, × 630

Fig. 4. Spectrum of small tumor cells with small fat globules (at *lower right*) to typical large adipocytes with vacuolated nucleus ("Lochkern"; *arrow*). H&E, × 630

Figs. 5, 6. Strong expression of glial fibrillary acidic protein (GFAP) by fat cells (**5,** *right*; **6**), whereas the compact tumor areas express GFAP variably (**5**, *left*). Peroxidase-antiperoxidase technique for GFAP. **5** × 100; **6** × 1,000

focally for SYN, whereas VIM was usually absent or sparse (Fig. 3). NFP were not detected. Other stains were noncontributory.

Discussion

This unusual tumor had a morphology compatible with medulloblastoma, with immunocytochemical evidence of differentiation along neuronal and glial lines. Its particular features, however, were lipomatous changes which have been observed by L. J. Rubinstein in several cases of medulloblastomas (personal communication) but, to our knowledge, have not been described in the literature.

Mesenchymal features are occasionally encountered in medulloblastomas, including so-called medullomyoblastoma [5, 13]. Anwer and co-workers [1] described a medulloblastoma with evidence of both glial and neuroblastic differentiation and foci of mature and immature cartilage. They postulated that the production of cartilage could have resulted from the metaplastic transformation of pre-existing mesenchymal elements within the tumor, or from multipotential neural crest-derived ectomesenchymal cells. Alternatively, the cartilage could have been produced directly by the neuroectodermal tumor cells themselves. These possibilities also apply to lipomatous changes in our case. The strong immunoreactivity for neural markers of fat cells suggested that they were neuroectodermal cells transformed into fat cells.

Fat tissue has been observed exceptionally in relation with medulloblastoma. A lipomatous hamartoma infiltrated secondarily by an adjacent cerebellar medulloblastoma was reported by Budka [3]. In our case, fat cells were an integral part of the tumor and included transitional forms of tumor cells; thus this tumor does not represent just a lipoma adjacent to a glioma.

We conclude that this tumor exhibits a unique spectrum of differentiation along multiple lines, including transformation of neuroectodermal cells to fat cells. The significance of this new type of differentiation in medulloblastoma remains to be elucidated. However, the fact that the patient is doing well 20 months after the operation without any postoperative treatment may foster speculation that this variant of tumor might have biological properties different from the classical medulloblastoma.

Acknowledgement. The authors gratefully acknowledge the late Prof. Lucien J. Rubinstein's help in confirmation of the diagnosis of this tumor.

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