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CASE REPORT

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Cerebellar astrocytoma with extensive lipidization mimicking adipose tissue

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Abstract We report the case of an elderly woman with a history of headache, vomiting and dizziness while walking. On CT scans a mass was identified in the right cerebellar hemisphere exhibiting radiological characteristics of lipomatous tissue. Surgery revealed a compact lesion consisting of whitish-yellow tissue with a fatty aspect and texture. Smears of tissue samples and paraffin sections showed features suggestive of tissue mainly composed of fully differentiated lipocytes. Lipid-specific stainings on fresh frozen material confirmed univacuolar intracytoplasmic fat accumulation. However, immunohistochemistry for glial fibrillary acidic protein and electron microscopy clearly demonstrated the glial lineage of these lipid-laden cells. Therefore, the tumor was diagnosed as a highly lipidized astrocytoma. In our view, this case represents a variant of lipidized gliomas that has not been described previously and that differs phenotypically from the entities documented earlier.

Key words Glioma · Astrocytoma · Lipoma
Lipidization · Cerebellum

Introduction

Tissue mainly composed of lipid-laden cells is unusual in intracranial lesions and can give rise to considerable diagnostic confusion. Basically, lipidized tissue arising in or associated with the central nervous system can occur in three different groups of disorders which comprise hamartomas, primary neoplasias and metastases.

While in intracranial hamartomas fat may be present in fully matured lipocytes [2], primary and secondary brain tumors occasionally exhibit lipidized tumor cells. In primary or secondary neoplastic cells the presence of lipids is usually described in terms of secondary "xanthomatous" changes resulting in multivacuolar "foamy" cytoplasm that can be seen in a variety of primary intracranial neoplasias such as capillary hemangioblastomas, meningiomas, schwannomas and gliomas [16].

In the latter group, lipidization of neoplastic tissue is a rare but well-described and acknowledged fact. Lipid-rich glioma is a morphologically distinct subgroup of astrocytic tumors. Two variants have been established so far, designated as "pleomorphic xanthoastrocytoma" [10, 11] and "heavily lipidized glioblastoma multiforme" [9]. Characteristically, the lipid-laden glial cells in either of the variants exhibited a pleomorphic picture with multivacuolar cytoplasm, considerable cellular and nuclear polymorphism and variable mitotic activity. Consequently, reports on this particular subgroup of glioma emphasize the differential diagnostic problems in relation to more commonly occurring metastases of lipidized malignancies of mesenchymal or epithelial origin.

In the following account we demonstrate one unusual representative of lipidized gliomas which, contrary to cases reported so far, lacks conspicuous polymorphism and atypia.

Case report

A 77-year-old woman presented with a 3-month history of increasing headache, nausea and vomiting. She complained of dizziness while walking. On examination the patient was alert and cooperative. Muscle strength was full. There were no cerebellar signs. Her gait was disturbed but not typically ataxic. CT scans showed a hypodense mass located in the right cerebellar hemisphere exhi-

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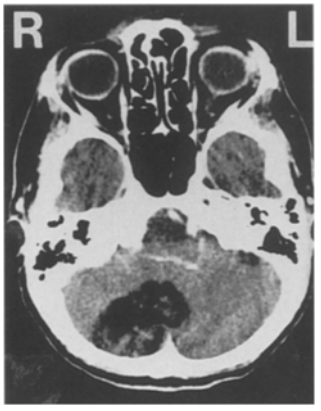

Fig. 1 *Cranial CT scan (horizontal plane)* showing markedly hypodense areas within a lesion in the right cerebellar hemisphere extending to the midline

biting characteristics of lipomatous tissue (Fig. 1). The lesion measured approximately 5 cm in diameter and extended to the midline.

Surgery revealed a compact lesion consisting of whitish-yellow tissue with a fatty aspect and texture. The lesion was partly removed and tissue fragments were fixed in formalin or fresh frozen for further neuropathological investigation.

Postoperatively, the patient recovered almost completely except for a slightly unsteady gait. Headache and nausea have not returned after 9 months of follow up.

Materials and methods

Cytological smear preparations were stained with toluidine blue or according to Giemsa. For histology, material was obtained either fresh frozen in liquid nitrogen and stored at −70° C or immersed in 4% formaldehyde and embedded in paraffin. Frozen sections (10 µm) were stained with Sudan black and oil-red-O for detection of lipids. Paraffin sections (5 µm) were stained with hematoxylin and eosin (H&E), periodic acid-Schiff reagent (PAS), PAS after diastase treatment (PAS-D) and with the silver impregnation method according to Gomori.

Poly- and monoclonal primary antibodies raised in rabbit and mouse, respectively, were used to detect vimentin (Dako, 1:400), S-100 protein (S100; Dako, 1:3200), glial fibrillary acidic protein (GFAP, polyclonal antibody Z334 raised in rabbit and directed against bovine GFAP; Dako, 1:1000), synaptophysin (Dako, 1:100), 200- and 70-kDa neurofilament (Biogenics, 1:50), Leu-7 (Becton Dickinson, 1:50) and factor VIII (Dako, 1:40). For electron microscopy, material was retrieved from paraffin and processed for electron microscopy according to Van den Bergh-Weerman and Dingemans [21].

Results

Macroscopically, tissue samples had a fatty aspect with a shiny surface and a color ranging from yellow to white. They had a soft-elastic consistency. Fixed material floated on formalin.

Smears and paraffin H&E-stained sections (Fig. 2a, b) showed tissue fragments predominantly composed of cells which contained a single large "optically clear" vacuole. This vacuole replaced the small oval or half-moon-shaped nucleus to the cell periphery and determined largely the isomorphic picture of these cells with a large diameter, distended cell body, rounded or polygonal contours lacking cytoplasmic extensions and, in densely packed areas, appearing in a typical "chicken-wire" pattern (Fig. 2b).

Special stainings on fresh frozen material with Sudan black and oil-red-O confirmed the presence of large single lipid droplets in the cytoplasm (Fig. 2b, inset). Thus, on light microscopy, the predominant tissue component of the tumor exhibited morphological features apparently compatible with differentiated adipose tissue.

There were some areas in which the univacuolar cells were intermingled with variable numbers of smaller cells characterized by having a slightly granular eosinophilic cytoplasm, a centrally located nucleus and an elongated cell shape with some cytoplasmic extensions. Locally, structures suggestive of Rosenthal fibers and calcospherites could be detected. In these areas there was slight anisokaryosis and mild to moderate nuclear polymorphism with hyperchromasia.

There was some intracytoplasmic staining for PAS in some non-vacuolar cells. Staining was negative after diastase treatment. Gomori staining was weakly positive around blood vessels. Mitotic figures could not be identified, and there was no indication of endothelial proliferation. Necrosis was absent.

Virtually all cells, both vacuolar and non-vacuolar, stained strongly for GFAP (Fig. 3a). The positive cells also showed cytoplasmic immunoreactivity for vimentin and, more limited in number and intensity, for S100. Staining for Leu 7 was negative. Immunoreactivity for synaptophysin and neurofilament helped to identify some preexisting neuronal elements of the cerebellar cortex enmeshed within the tumor tissue.

Using electron microscopy we were able to demonstrate broad bundles of closely packed intermediate filaments characteristic of astrocytic differentiation in the cytoplasm of the vacuolated cells, often directly adjacent to the lipid droplets which had no limiting membrane (Fig. 3b). As a result the final diagnosis of a cerebellar astrocytoma with extensive lipidization was established.

Discussion

In the present account we describe a cerebellar tumor characterized by astrocytic differentiation, a lipocytic phenotype and a relatively low grade of anaplasia.

Lipidization is a common observation in a variety of neoplastic tissues, probably secondary to disturbed cellular metabolism as a sign of degeneration. In the present case the tissue fragments showed no degenerative changes and necrosis was not present. The observed lipid-laden cells might, therefore, reflect a form of divergent differentiation.

Biochemically it has been demonstrated that gliomas can contain up to three times more lipids compared to normal brain tissue [12]. However, vacuolar lipid accu-

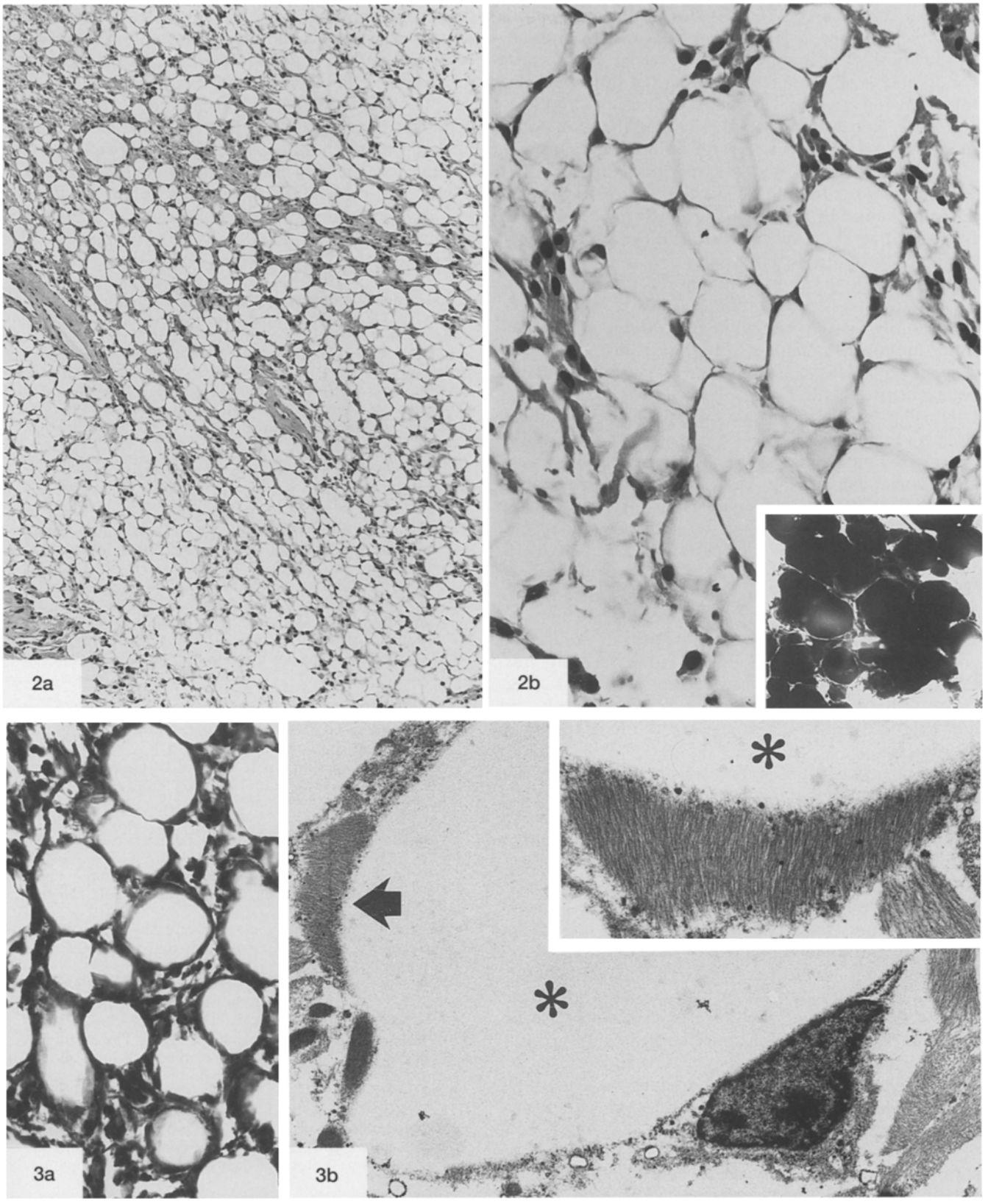

Fig. 2a, b Histological characteristics of the tumor. **a** Representative paraffin section (H&E) with conspicuous vacuolated cells intermingled with smaller, isomorphic cells. **b** Same section at higher magnification. Note the small nuclei at the cell periphery and the "chicken-wire" pattern of the tissue. *Inset* shows frozen section, stained with Sudan black, exhibiting large univacuolar fat droplets. **a** ×90; **b** × 350, *inset* ×175

Fig. 3a, b Immunohistochemical and ultrastructural evidence for the glial nature of the lipid-laden cells. **a** Paraffin section stained with GFAP. **b** Electron microscopic detail of a lipid-laden cell. Note astrocytic intermediate filaments (*arrow*) in vicinity of lipid droplet (*star*). *Inset* shows the same bundle of filaments at higher magnification. **a** ×350; **b** ×9200; *inset* (× 27000).

mulation in astrocytomas is very rarely detectable at the light microscopical level on morphological grounds.

Obviously, the features of the present case are not compatible with earlier descriptions of lipid-rich gliomas, which were subdivided into two distinct entities.

Firstly, Kepes and colleagues coined the term "pleomorphic xanthoastrocytoma" for lipidized gliomas with conspicuous atypical and polymorphical features but without necrosis [8, 10]. Characteristically, tumor cells are surrounded by an extensive meshwork of reticulin fibers. Several cerebral localizations have been described including a lipid-rich subtype in the pineal gland [18], but so far no infratentorial variant of a xanthoastrocytoma has been reported [8,16].

Secondly, in the rare lipidized variant of glioblastoma multiforme anaplastic features must be accompanied by necrosis to establish the diagnosis. Kepes and colleagues were the first to report two cases of what they called a "malignant glioma with heavily lipidized (foamy) tumor cells" [9], later designated as "glioblastoma with lipidized cells" [8]. Brain tumors with identical features had earlier been considered intracranial localizations of mesenchymal malignancies [14]. Now the application of GFAP immunohistochemistry can help to elucidate the glial origin of such lesions [6, 15, 19].

The lesion in question represents an astrocytoma which shares some features of a cerebellar pilocytic astrocytoma, in particular its subtentorial localization and mild nuclear polymorphism. However, only scattered Rosenthal fibers were found in the described tumor. What is more, the non-lipidized tumor cells did not exhibit the slender elongated form of pilocytic astrocytes.

The presence of lipid-laden cells is the predominant feature of "intracranial lipomatous hamartoma." The majority of these lesions are interpreted as congenital malformation and are as such more often encountered in infancy but old age does not rule out this diagnosis [2]. The cerebellar localization, although unusual, has been described previously [17]. However, an intracranial lipomatous hamartoma is thought to arise from orthotopic primitive meningeal or mesenchymal tissue, which basically retains the potency of lipocytic differentiation. The lipid-laden cells which are found in excess in these lesions should, therefore, be designated as true lipocytes [2]. As has been shown, the lesion in the present case originated from astrocytic cells and lipidization appeared to be a secondary phenomenon. Therefore, this lesion should be designated a neoplasm rather than a hamartoma.

Differential diagnostic considerations become more complicated in view of several reports of lipomatous hamartomas associated with true neoplastic lesions such as "gliosarcoma" [13], spongioblastoma [7], subependymoma [2], medulloepithelioma [20] and desmoplastic medulloblastoma of the cerebellum [2].

Cells with a lipocytic phenotype were found in association with neurocytoma [5] and an unusual cerebellar tumor comprising elements of a medulloblastoma, astrocytoma, and oligodendroglioma [1]. In this context it is interesting that in the meantime three cases of adult medulloblastoma have been published [3, 4] in which considerable parts of the tumor showed clusters of univacuolar lipid-laden cells which could be identified as primitive neuroectodermal tumor cells. In view of this, it seems worthwhile to review earlier cases of lipoma-like intracranial lesions, as immunohistochemical and ultrastructural techniques may be necessary to elucidate the true nature of intracranial lipidized lesions.

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