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Hemosiderin pigmentation of tumour cells in cerebellar pilocytic astrocytoma associated with post-traumatic hemorrhage in adults

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Abstract

The pilocytic astrocytoma is only rarely associated with gross intratumoral hemorrhage despite rich vasculature and blood vessel changes, accompanied often by perivascular depots of hemosiderin.
We report an unusual case of pigmented cerebellar pilocytic astrocytoma presenting with posttraumatic hemorrhage in a 38-year-old man with no history related to the tumor. CT and MRI examination after head injury demonstrated unexpectedly the cystic lesion of 2 cm in diameter in the region of the right cerebellar hemisphere and vermis. The lesion was associated with hematoma and it was surgically removed 3 weeks after trauma.
Histopathological examination revealed pilocytic astrocytoma tissue with broad hemorrhagic changes and with an unusual pattern of massive pigmentation of the cytoplasm of pilocytic astrocytes, consistent with hemosiderosis. Positive stains for iron and ferritin and ultrastructural study confirmed deposition of hemosiderin granules in the tumour cells. There was no evidence of melanin or melanosomes. This finding of hemosiderin accumulation in the cytoplasm of neoplastic astroglia seems to be analogous to post-hemorrhagic pigmentation of the normal Bergmann glia and subpial astrocytes.
In the literature, the examples of neuroepithelial tumors with hemosiderin pigmentation of tumor cells have been rarely documented. To our knowledge, this is the first reported case of pigmented pilocytic astrocytoma exhibiting extensive intracellular hemosiderin deposition.

Key words: *pilocytic astrocytoma, hemosiderin pigment, intratumoral gross hemorrhage*

Introduction

Pigmentation of neuroepithelial tumors is mostly ascribed to melanin or neuromelanin accumulation [17]. Several cases of the melanotic variants of such neoplasms as medulloblastoma [1], schwannoma and ganglioglioma [7] or ganglioglioma with PXA component [10] have been described. On the other hand, the examples of neuroepithelial tumours with the hemosiderin pigmentation of the tumour cells are only rarely documented. Recently, one case of pigmented central neurocytoma exhibiting intracellular deposition of hemosiderin granules following intratumoral hemorrhage has been reported [11].

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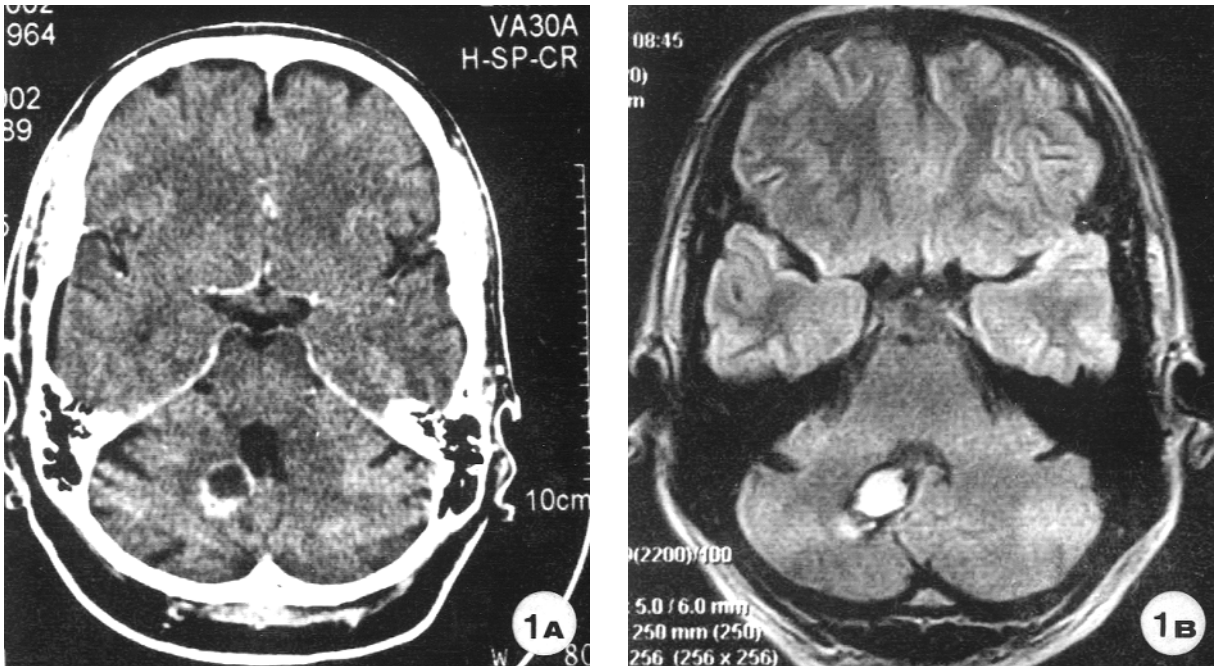


Fig. 1. CT (A) and MRI (B) appearance of the cerebellar lesion

Among the cases of pigmented tumours, the purely astrocytic neoplasms seem to be exceptionally rare. To our knowledge, only one case of pigmented pilocytic astrocytoma containing neuromelanin has been described [20]. We know of no previous report where pigmentation of the astrocytic neoplasm was related to hemosiderin accumulation. From a diagnostic point of view, any case of tumour cells pigmentation requires special attention for establishing the proper nature of the pigment.

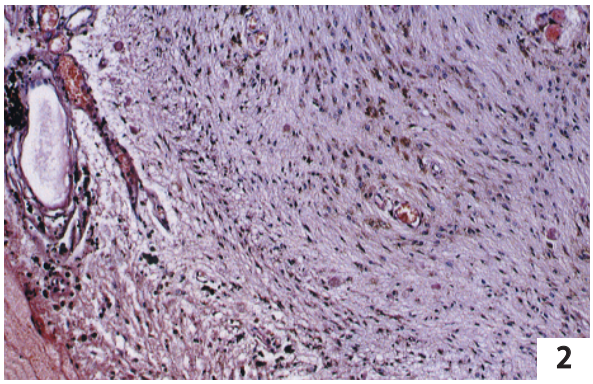
This report deals with the unusual histopathological feature of the extensive hemosiderin accumulation within tumour cells in an adult case of cerebellar pilocytic astrocytoma presenting with posttraumatic intratumoral hemorrhage.

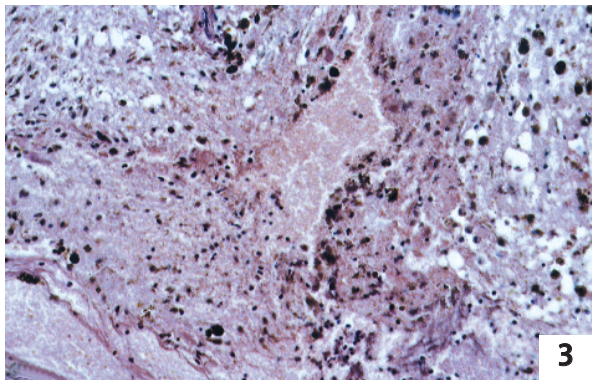
Case report

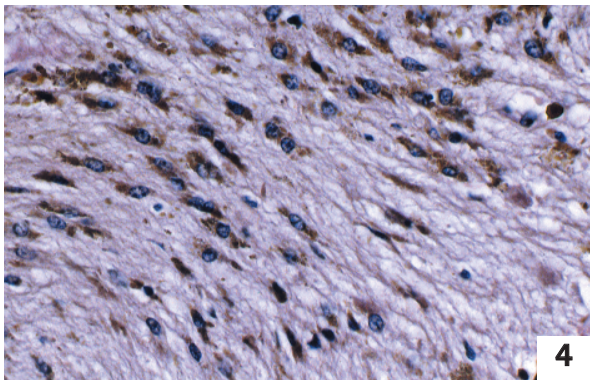
A 38-year-old man without history of neurological disorders presented with a head injury and blunt contusion in the occipital region after an automobile collision. No evidence of neurological dysfunction was observed by physical examination. The Rtg of the cranium was normal. Computed tomography (CT) scan of the head showed in the right cerebellar hemisphere and the vermis a hypodense cystic structure of 2 cm in diameter with contrast enhanced peripheral zone, causing slight compression of the fourth ventricle (Fig. 1a); a hemorrhage into a preexisting lesion was suggested. Magnetic resonance imaging (MRI) performed 8 days later demonstrated a spherical structure hypointense on T1- and hyperintense on T2-weighted images with a thin peripheral rim of low intensity signal (Fig. 1b). Three weeks after the head trauma the surgery from the occipital approach was performed. Hemorrhagic lesion with appearance of an old hematoma was encountered in the right cerebellum and evacuated and the abnormal-appearing surrounding tissue was completely dissected. In the three years follow-up the patient remains in good health without radiological signs of lesion recurrence.

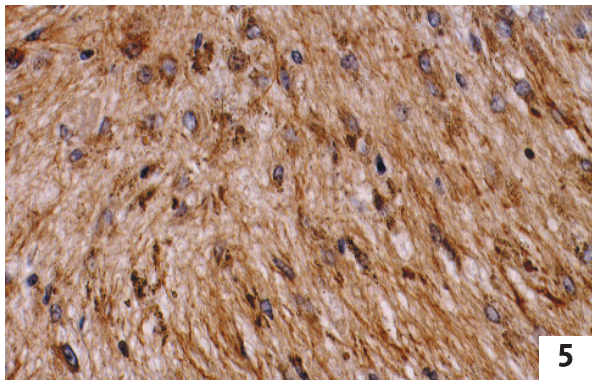
Material and methods

The surgically obtained tissue was fixed in 10% buffered formalin and routinely embedded in paraffin. The sections for histological examination were stained with hematoxylin and eosin (H&E), Prussian blue for iron and following the method of Fonatana-Masson with potassium permanganate bleach for melanin. Immunohistochemical studies were performed on paraffin sections with application of antibodies against glial fibrillar acidic protein (GFAP), HMB-45 antigen and ferritin, using the streptavidin-biotin-peroxidase









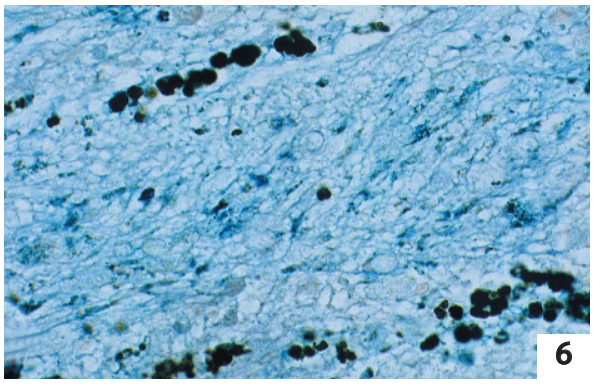


Fig. 2. Compact bundles of pilocytic astrocytoma cells showing fine pigmentation and perivascular hemosiderin depots in the surroundings of an old hemorrhage. H&E, x 100

Fig. 3. Hemorrhages and coarse hemosiderin depots within loose-textured areas of the tumour. H&E, x 200

Fig. 4. Accumulation of yellow-brown pigment granules in the cytoplasm of neoplastic astrocytes. H&E, x 400

Fig. 5. GFAP-immunoreactive tumour cells with co-localisation of the granular pigment. x 400

Fig. 6. Prussian blue positive stains of the fine granules in tumour cells and the coarse hemosiderin depots. x 400

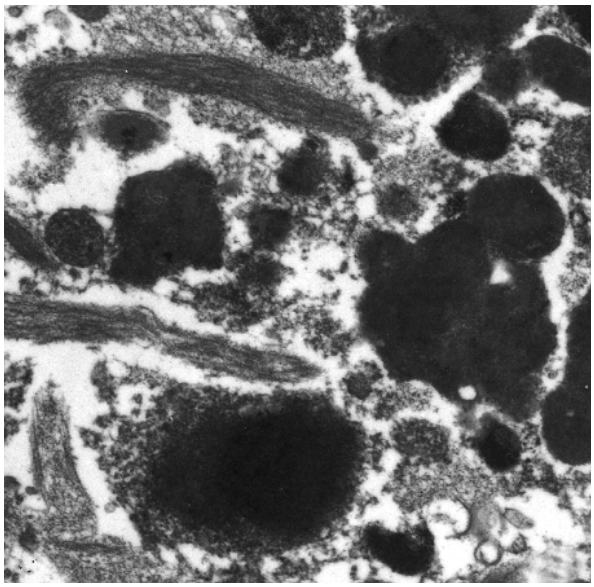


Fig. 7. Accumulation of variably sized, heterogeneously osmophilic, not membrane bound pigment granules in tumour cell cytoplasm containing bundles of intermediate filaments. x 20000

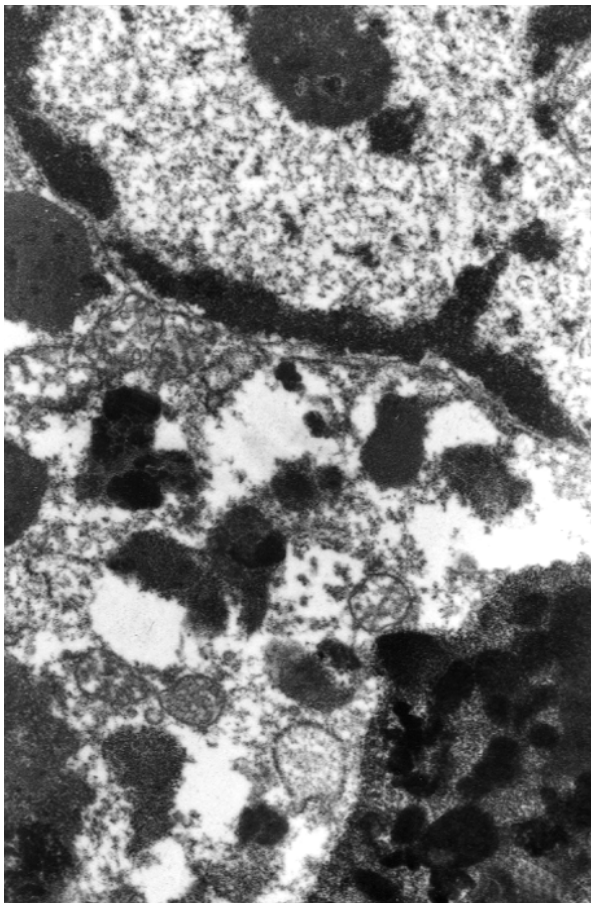


Fig. 8. The cytoplasm of macropahage loaded with coarse hemosiderin granules. x 10000

complex method with DAB as chromogen (all antibodies provided from DAKO). For electron microscopy the small specimens of formalin-fixed paraffin-embedded tissue was deparaffinized, postfixed in 2.5% buffered glutaraldehyde and in 1.0% osmium tetroxide, dehydrated in graded alcohols and embedded in Epon 812. Ultrathin sections were stained with uranyl acetate and lead citrate and examined in electron microscope JEOL 1200EX.

Results

The histological examination revealed characteristic features of pilocytic astrocytoma with compact fibrillar and loose-textured areas and with broad hemorrhagic changes within the tumour tissue and adjacent leptomeninges (Fig. 2). Most prominent perivascular and intraparenchymal hemorrhages and abundant accumulation of coarse hemosiderin depots were seen in loose-textured areas of the tumour (Fig. 3) and around the conglomerates of leptomeningeal blood vessels. Intratumoral blood vessels were numerous and showed thin or hyalinized walls, often with abnormally convoluted, glomeruloid pattern. Widespread granular eosinophilic bodies and less infrequent Rosenthal fibers were seen in the neoplastic tissue. Besides the ordinary hemorrhagic changes, there was massive pigmentation of the cytoplasm of pilocytic astrocytes caused by intracellular accumulation of hemosiderin granules, especially in the compact areas of the tumour (Fig. 4). Furthermore, similar intracytoplasmic load by hemosiderin granules was also observed within normal astrocytes of Bergmann glia layer in a small fragment of the cerebellar cortex.

Immunohistochemistry demonstrated GFAP immunoreactivity in the tumour cells with co-localization of granular pigment (Fig. 5). The cells were negative for HMB-45 antigen. Finely dispersed pigment granules in the tumour cells and coarse depots of hemosiderin were blue stained for iron with Prussian blue (Fig. 6) and were immunopositive for ferritin. Staining by the Fontana-Masson method was negative for melanin, showing no bleaching reaction with potassium permanganate. Ultrastructural examination

revealed the cytoplasm of the tumour cells containing both bundles of intermediate filaments and pigment granules of variable size and density, consistent with hemosiderin. The granules were composed of electron-dense small particles within heterogeneously osmophilic matrix and were not membrane bound (Fig. 7). Aggregates of coarse hemosiderin granules within the perivascular macropahages showed a similar ultrastructural appearance (Fig. 8). The melanosomes and premelanosomes were not found.

Discussion

The pigmented neoplasms with an extensive hemosiderin load of the tumour cells is only exceptionally described [11,19]. The distinction between hemosiderin and neuromelanin or melanin pigmentation of tumour cells may be difficult in routine examination although prior intratumoral hemorrhage could facilitate recognition of intracellular hemosiderin pigment. In the present case, the accumulation of hemosiderin granules within the cytoplasm of neoplastic astrocytes was confirmed by positive staining for iron, positive immunoreactivity for ferritin, negative reactions for melanin and by ultrastructural study. A similar pattern of hemosiderin pigmentation in the cytoplasm of Bergmann glia, as evidenced in this case, could indicate the common mechanism of posthemorrhagic cytosiderosis in both the neoplastic and normal astrocytes. Hemosiderin accumulation by subpial and Bergman astroglia, leading to the feature of superficial hemosiderosis following subarachnoid hemorrhages is a well-known phenomenon [13,14]. Intracellular deposition of hemosiderin granules may be also found within astrocytes in the surroundings of intracerebral hemorrhages [9]. In any hemorrhage the hemosiderin formation takes place most rapidly in cells rich in ferritin, i.e, macrophages and microglia [12]. In the present case, pigmented neoplastic astrocytes in the surroundings of the hemorrhage were immunoreactive for ferritin protein, indicating that tumour cells may produce this protein in response to regional iron overload. Incorporation of the iron particles to ferritin could be also thought as a protective mechanism for the cells exposed to the noxious action of free iron [14].

The present case of cerebellar pilocytic astrocytoma was characterized by asymptomatic course until intratumoral hemorrhage occurred. The lesion on CT likely representing a cystic lesion with hemorrhage was unexpectedly found in this case after head trauma. Pilocytic astrocytomas often have a cystic feature and other regressive changes, especially in cerebellar tumours with a longstanding indolent course [2,3]. Microscopically, the marks of slowly growing tumor, including numerous eosinophilic granular bodies and abnormal tumor vasculature with glomeruloid pattern and hyalinization of the blood vessels were evident in the examined case.

Despite rich vasculature and proliferative and regressive changes of the blood vessels, the pilocytic astrocytomas are only rarely associated with gross intratumoral hemorrhage [2,3]. To our knowledge, only three cases of cerebellar pilocytic astrocytoma presenting with spontaneous hemorrhage [5,16,21] and other 5 cases of the hemorrhages into pilocytic astrocytoma located in the hypothalamus [4,8], cerebral hemispheres [6,15] and medulla [18] have been described in literature. The reported cases of hemorrhages to cerebellar pilocytic astrocytoma concerned 9-, 13- and 14-year-old children, in whom the cerebellar hemorrhage with acute apoplectic onset was a first manifestation of the tumour [5,16,21].

This report illustrates the presumable causative relation between a head injury and intratumoral hemorrhage in an adult case of clinically asymptomatic cerebellar pilocytic astrocytoma. Abnormal tumor vasculature, cystic changes and trauma-produced hemodynamic disturbances are thought to be the most important factors implicated in the hemorrhagic event in this case. The histological pattern of pigmented pilocytic astrocytoma is consistent with massive intracellular and perivascular deposition of hemosiderin within the tumour in consequence either of gross traumatic or/and continuous small hemorrhages.

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