Desmoplastic Cerebral Astrocytoma of Infancy. A Clinicopathological Analysis

Shoutian Zhu, Hongqi Shi, Shanxian Lou, Lixia Wang, Qingwei Liu

Department of pathology, Zhejiang Provincial Jinhua Central Hospital, Jinhua ZheJiang 321000, P.R.China

Abstract **Purpose** To investigate the clinicopathological features, immunohistochemistry(IHC) and differential diagnosis of desmoplastic cerebral astrocytoma of infancy (DCAI). **Methods** The clinical presentation, radiologic finding, histological features, immunostaining of 1 case of DCAI was analyzed with review of literature. **Results** A 17-month-old female infant presented with a generalized weakness of bilateral lower extremities for 15 days. Brain MRI showed a well-circumscribed dural-based cystic-solid mass, which was 5.6 cm in its largest diameter, lying in the posterior fossa, compressing the ipsilateral cerebellum hemisphere and extended into the spinal canal. The wall of the cyst and cortical solid component was enhanced intensely by contrast medium. It had a biphasic histologic pattern consisting of neoplastic astrocytes embedded in a desmoplastic stroma, resembling a cellular, mesenchymal tumor, raising the differential diagnosis of meningeal neoplasm but the strong GFAP immunostaining gave unequivocal support to the glial nature of the tumor cells. Meanwhile, it positively expressed S-100 protein and vimentin. **Conclusions** DCAI is a rare tumor that presents itself as a hemispheric mass of voluminous size in infants. Histologically, the tumor cells are arranged in fascicle and whorls forming storiform pattern resembling a meningioma or fibrous histocytoma. It should be distinguished from meningioma, DIG, PXA, Gliofibroma and its diagnosis relies on its unique clinical presentation, radiologic finding, histological features, immunostaining and the presence of large amounts of redundant and sometimes extensively duplicated basal membran material and collagen between nonpleomorphic and nonlipidized astrocytes, corresponding to the reticulin fibers seen by light microscopic analysis between the S-100 protein and GFAP–positive cells.

Key Words Infants; Astrocytoma; Immunohistochemistry

The desmoplastic cerebral astrocytoma of infacy (DCAI) is a rare neoplasm arising in the cerebral hemispheres especially in fronto-parietal areas, within the first two yeas of life. no report has been found yet to deal with DCAI involving cerebellum. We just present such a case involving posterior fossa attached to cerebellar tentorium.

MATERIAL AND METHOD

Clinical material

A 17-month-old girl was admitted to the hospital because of generalized weakness of bilateral lower extremities for 15 days. Physical examination: alert, stable vital signs (T 37.2℃, P 112/min), no abnormality found with heart and lung, normal muscle power, free articular activity, shivering of lower extremities were shown when standing.

MRI showed a well-circumscribed dura-based cystic-solid mass, about 4.8 cm×5.6 cm in size, which lay in the posterior fossa, extended into spinal canal and compressed the spinal cord. The wall of the cyst was enhanced by contrast media. Enlargement of bilateral ventricles and third ventricle with compression of fourth ventricle and cerebellar hemispheres could be observed while no shift of midline and other lesion were seen. It was diagnosed as cyst-solid mass in posterior fossa, medulloblastoma first considered, glioma to be excluded.

Surgical resection was carried out with a post–occipital midline incision. After a bone flap about 7 cm×7 cm in area removal, the dura was opened in a Y fashion, then a cyst-solid neoplasm with a complete envelope, measuring up to 6 cm×6 cm×5 cm in volume came into visual field. Surrounding with proliferative colloid, it was attached tightly with the cerebellum, and removed grossly complete-

Corresponding author: Shoutian zhu, Department of pathology, Zhejiang provincial Jinhua Central Hospital, Jinhua Zhejiang 321000, P.R.China.
E–mail: 2ST0802@sina.com

ly.

Methods

formalin fixation was employed and hematoxylin-eosin (H&E) stain was used. Immunocytochemical studies were performed on all formalin-fixed, paraffin-embedded samples about 4μm thick. Demonstration of GFAP, S-100 protein, Vim, NSE, NF, Syn, EMA was attempted using the S–P method, and the immunohistology kits was obtained from Zhongshan biologic technical company in Beijing.

RESULT

Gross Findings

The tumor was well demarcated, with a complete envelope, measuring about 6.0 cm×5.5 cm×4.0 cm in dimension. The cross-section was cyst- solid, with an unilocular cyst about 1.2cm in diameter. The rest was solid, rubbery in consistency and grey-white in colour. There was no gross evidence of haemorrhage or necrosis.

Microscopic Findings

It had a biphasic histologic pattern consisting of neoplastic astrocytes embedded in a desmoplastic stroma (Fig.1), resembling a cellular mesenchymal tumor. The main portion was composed of cells arranged in fascicles or in a storiform or whorled pattern (Fig.2), sometimes with desmoplastic cirrhosis interstitium, scattered with giant pleomorphic glioma cells with rich cytoplasm, giant, eccentic nuclei (Fig.3). No mitosis was observed but interstitial gliosis was obvious.

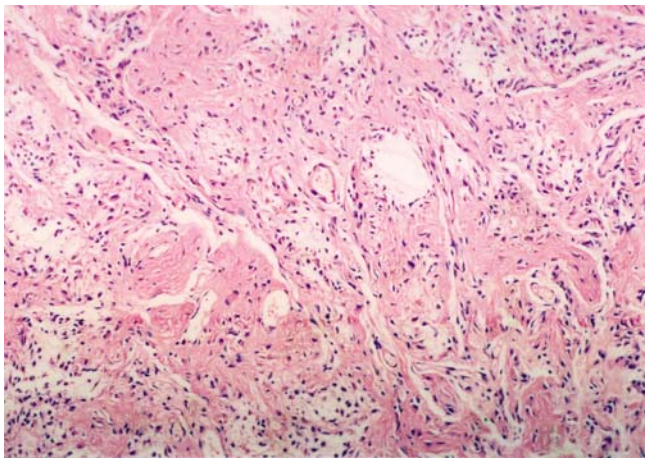

Fig.1 Consisting of neoplastic astrocytes embedded in a desmoplastic stroma (HE, 10×5)

Immunohistochemical Findings

GFAP, Vim and S-100 protein were all expressed in the tumor cells but no expression of NSE, NF, Syn, EMA were found.

Pathological diagnosis: desmoplastic cerebral astrocytoma of infacy.

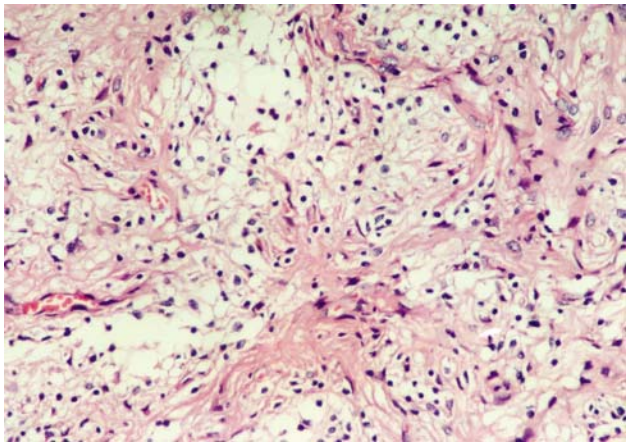

Fig. 2 The main portion was consisted of cells arranged in fascicles or in a storiform or whorled pattern (HE, 10×10)

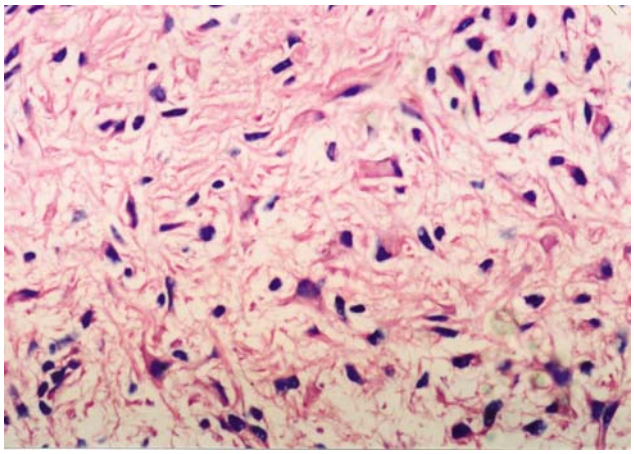

Fig. 3 Scattered with giant pleomorphic glioma cells with rich desmoplastic cirrhosis interstitium (HE, 10×40)

DISCUSSION

Diagnosis

DCAI is rare tumor that occurs in infants within the first two years of life, characterized by a massive, often cyst-solid, supratentorial lesion usually in the frontoparietal region[1,2], most rare in cerebellum [3]. It has a biphasic histologic pattern with neoplastic astrocytes, which arranged in fascicles or in a storiform or whorled pattern and desmoplastic stroma[4]. Immunohistochemical stainings for GFAP,

S-100 protein proved the glial nature of the tumor cells, while positive expression of Vim suggests desmoplastic interstitial component. No cells were found immunopositive for NSE, NF, Syn and EMA, which help to exclude a diagnosis of DIG-another CNS tumor similar to DCAI in histogenesis[5,6]. An intermingling with pleomorphic glial cells could be seen in local regions, absent of necrosis, and of favorable prognosis[7]. DCAI was first described as " superficial cerebral astrocytoma attached to dura" in 1984 [8]. Features of ultrastructure were absence of recognizable neuronal participation ,and the presence of large amounts of external cellular laminal material and collagen fibers between neoplastic astrocytes without pleomorphism or lipidized. Some of mechanisms put forward to explain the production of basal lamina and collagen in the purely astrocytic tumors include glial metaplasia, meningeal fibroblastic participation and involvement of subpial astrocytes which are known to produce basal laminal in the normal brain. Laminin, IV collagen, fibrin-connection protein which could be produced by astrocytes are all important components of basal laminal[9]. The favorable prognosis of these tumors has correlation with growth inhibition and differentiation promotion mediated by autocrine production of basal lamina component. As is shown in experiment in vivo, large amount of basal laminal proteins could be produced by immature astrocytes and leptomeningeal cells, while external cellular laminal proteins play a role in growth inhabition and differentiation promotion of neoplastic astrocytes [10]. The presence of large amounts of external laminal material and collagen fibers are corresponding to the reticulin fibers seen by light microscopic studies between the S-100 protein and GFAP-positive cells. In 1992, Losius [11] reported two cases with histopathologic, immunohistochemical, ultrasructral and molecular genetic data, and drew the following conclusions: 1)The diagnosis of DCAI requires a high index of suspicion and immunohistochemical or ultrastructral proof of astrocytic differentiation. 2) The lack of allelic loss on chromosomes 17p (including p53 tumor suppressor gene locus) and 10 seen in the cases may further distinguish the DCAI from other astrocytomas.

Differentiation

meningioma

Histologically, meningioma has originations as follows: arachnoid granula and tomenta, perivascular interstitium and choroid arachnoid cells. Clinically, it usually occurs in mid-age females, with a male to female ratio of 1 to 3, comparing little incidence in children. Any part of meninges could be involved. Besides histopathological diagnosis, imaging examination is an important complementarity. Characteristic vascular imaging features are shown by angiography. Diffuse contrast enhancement can be seen in CT or MRI, without cyst change, which is different from DACI. Laminin expression by tumor cells was observed in fibroblastic meningiomas [12], so was Vim (100% positivity) and S-100(50% positivty). There is diffuse or focal positivity of E-MA. And in none of the cells was any positivity for GFAP dectected. From the immunohistochemical expression mentioned above ,a differentiation with DCAI could be made.

DIG(desmoplastic infantile ganglioglioma)

Similar to DACI, DIG is a rare intracranial tumor of infancy within the first two years of life, characterized by solid and cystic components, voluminous size and supratentorial location [13]. In one series of 22 desmoplastic infantile gangliogliomas, all patients presented between 2 and 24 months of age (mean=6 months); with a male to female ratio of 1.4:1. It is rubbery in consistence due to diffuse and dense cirrhosis. The hallmark feature of both neoplasms is an abundant and often dense desmoplasia, imparting a characteristic firmness to the neoplasms. In the desmoplastic infantile gangliogliomas, astroglial and neuronal tumour cells in addition to variable numbers of more primitive, mitotic cells comprise the neoplastic neuroepithelial populations. With the median interval of 8.7 years (range 1 to 14.5 years) following surgery for 14 patients in this series, there were no deaths due to tumour or any evidence of tumour recurrence [14]. Both DIG and DCAI have favorable prognosis and neuronal differentiation is their only difference.

PXA(pleomorphic Xanthoastrocytoma)

PXA usually occurs in adolescents, well demarcated, and located superficially, often in temporal lobe or involved leptomeninges and subarachnoid space, possibly extended into cerebral hemispheres, with cyst-change partly. The characteristic histocytologic features are appearance of various deformative cells, with rich cytoplasm, and presenting foamy or vacuolar because of lipidosis. Many neoplastic cells, otherwise typical of PXA, expressed

GFAP, which neuronal cells with marked atypical were immunopositive for Syn and NF [15], helping defferentiation from DCAI.Prognosis study found correlation with mitosis, mitotic activity and MIB−1 labelling index whose findings related with the biological behavior[16]. It has been attractiing more and more attention that PXA may become malignant which is rare for DIG and DCAI. The essential difference is the age of detection of the PXA and the pleomorphic xanthomatous appearance of its astrocytes.

Gliofibromas

Whether it is a distinct entity [17] or a subtype of desmoplastic astrocytoma is still in unknown. Gliofibromas are rarely encountered astrocytic neoplasms characterized by an admixture of astrocytic and fibroblastic cell components. The exact nature of these rare tumors are still a matter of considerable debate. The astrocytic component of the tumor stained diffusely positive for glial fibrillary acidic protein (GFAP) and S-100 protein. Prominent reticulin staining was observed within the fibroblastic component of the tumor. The MIB1 labeling index (positive number of tumor cells divided by total tumor cells counted × 100) was low (0.9), supporting the general slow growth of these tumors. Immunohistochemical staining with antibody against p53 protein was negative. Gliofibromas seem to be a low-grade variant of an astrocytoma that shares many features with other desmoplastic astrocytic neoplasms (desmoplastic infantile astrocytoma, desmoplastic infantile ganglioglioma) requiring differentiation[18].

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