Case Report
Cerebellar liponeurocytoma with unusually histopathology: a case report

Xiaomei Ma1, Yin Wang2, Huimin Liu1, Hongyu Yu1, Weiqing Li1, Chunyan Xia1

1Department of Pathology, Changzheng Hospital, Second Military Medical University, Shanghai 200003, China; 2Department of Neuropathology, Huashan Hospital, Fudan University, Shanghai 200003, China

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Abstract: Cerebellar liponeurocytoma (LPN) is a rare central nervous system tumor. We encountered a 45-year-old woman with cerebellar LPN who had a three months history of headaches and mild ataxia. MRI revealed a mixed signal tumor in the cerebellar vermis. The tumor was totally removed. Histologically, a highly cellular neoplasm composed of monomorphic small round neuronal cells mixed with lipomatosous cells. There was “Starry sky appearance” structure in the tumor. At high magnification, there were two different type histopathological morphologies. One was more than one large cell in one lacuna with clear cytoplasm. Another was huge cell with mononuclear or polynuclear and abundant mucinous cytoplasm. There were neuropil-like islands. Immunohistochemistically, neuronal cells were diffuse positive for Syn and NeuN. The lipomatosous cells were positive for Syn, NeuN and GFAP. The “Starry sky appearance” cells were positive for GFAP and S100 and negative for Syn and NeuN. The proliferation index was about 2%. The pathological diagnosis was cerebellar LPN. The patient underwent radiation therapy after operation and no recurrence follow-up of 32 months. We do not know the “Starry sky appearance” cells were what really. Moreover, we listed the different diagnosis of cerebellar LPN in pathology.

Keywords: Cerebellar liponeurocytoma, histopathology, different diagnosis

Introduction

Cerebellar liponeurocytoma (LPN) is a rare central nervous system tumor first described by Bechtel et al [1] composed of densely packed neuronal cells admixed with foci of well-differentiated adipocyte-like cells. It was defined as grade I under the heading of glioneuronal tumors in 2000 edition of the World Health Organization (WHO) classification and assigns as grade II in 2007 WHO classification because of the rate of recurrence in the long-term clinical follow-up. In this paper, we report a new case of cerebellar LPN with special histological features which never been described in the literature.

Case report

Clinical summary

A 45-year-old previously healthy woman, presented with a three months history of headaches, vertigo and unsteadiness of gait now and then. General physical examination and neurological was unremarkable. Computed tomography (CT) scanning revealed a well-demarcated, hypodense lesion within the cerebellar vermis. Magnetic resonance imaging (MRI) scan showed a heterogeneous mass measuring 4 × 3.5 cm, characterized by discrete hyperintensity on T1-weighted images and high signal intensity on T2-weighted images (Figure 1). Several central parts of the lesion were very hyperintense on both T1 and T2 weighted sequences suggesting the presence of fat within the tumor. Intra-operative frozen section was reported as low-grade glioma being consistent with ependymoma. The patient underwent a gross total resection of the tumor.

Histopathological findings

Microscopically, the tumor was purple colored. Microscopic examination revealed a highly cellular neoplasm composed of monomorphic small round neuronal cells and focal lipomatosous cells and characterized by a single cyto-
plasmic vacuole displacing the nucleus to the periphery mimicking mature fat cells (Figure 2A). There was some single lipomatous cell distributed in the neuronal cells. No fresh tumor tissue was available to stain with oil red O for detecting lipid droplets or performing ultrastructural examination. In some areas the nuclei appeared more elongated and hyperchromatic. Perivascular hyaline deposits and pseudorosettes (Figure 2B) and clear cytoplasm resembling homoplastic oligodendrocytes were noted (Figure 2C). The tumor also has many morphological similarities to medulloblastoma.

There were some structures appeared as rosettes or micronodules bordered or inhabited by monomorphic small cells with a nucleus-free center which so-called neuropil-like islands (Figure 2D) exhibited granular matrix. Moreover, there was “Starry sky appearance” structure, like Burkitt lymphoma, in the tumor. At high magnification, there were two different type histopathological morphologies. One was more than one large cell in one lacuna with clear cytoplasm. Another was huge cell with mononuclear or polynuclear and abundant mucinous cytoplasm (Figure 2H).

There were a few foci of endothelial proliferation, calcification and mucoid degeneration in the stroma. Focal necrosis was present (Figure 2I). It was absent mitotic figures.

Immunohistochemically, the monomorphic small round cells demonstrated neuronal differentiation characterized by widespread immu-
Figure 2. A. Cerebellar liponeurocytoma was a highly cellular tumor composed of adipocytes in a background of small round neoplastic cells (H&E, × 100). B. Perivascular hyaline deposits and pseudorosettes were noted mimicking clear cell ependymoma (H&E, × 100). C. The tumor cells showed a clear cytoplasm and perinuclear halos on paraffin sections ('honeycomb' appearance) resembling neoplastic oligodendrocytes (H&E, × 400). D. Monomorphic
small tumor cells with a nuclear-free center formed neuropil-like islands (H&E, × 400). E. “Starry sky appearance” structure, like Burkitt lymphoma, was been seen (H&E, × 100). F. At high magnification, the “Starry sky appearance” cells were cytoplasmic vacuole with unclear membrane (H&E, × 400). G. Another different “Starry sky appearance” structure was been seen. There was an adipocyte cell in the upper right (H&E, × 100). H. At high magnification, the “Starry sky appearance” cells were large with mononuclear or polynuclear and abundant mucinous cytoplasm (H&E, × 400). I. Necrosis was focal present (H&E, × 100). J. The small neural cells were positive while the “Starry sky appearance” cells were negative for Syn (immunostain, × 400). K. The small neural cells were positive while the “Starry sky appearance” cells were negative for NeuN (immunostain, × 400). L. The small neural cells were negative while the “Starry sky appearance” cells and adipocytes were positive for GFAP (immunostain, × 400). M. The proliferation index Ki67 was about 2% (immunostain, × 400).

Because it was easy to relapse, it was included in WHO classification as grade II. The treatment and prognosis were different from the ordinary medulloblastoma and central neurocytoma. So the pathological diagnosis is very important. Pathologic examination revealed a highly cellular neoplasm composed of morphomorphic small round neuronal cells mixed with lipomatous cells and characterized by a single cytoplasmic vacuole displacing the nucleus to the periphery. Immunohistochemically, neuronal cells were diffuse positive for neural markers such as NSE, Syn, MAP-2. The majority of cases observed focal GFAP positive indicating astrocytic differentiation and even with predominant pilocytic pattern and myoid differentiation [3]. Some cases showed that the lipid vacuoles progressively accumulate and coalesce within cells retaining neurocytic features, indicating tumoral lipidization rather than true adipose metaplasia [4]. Fatty acid binding protein 4 (fatty acid binding protein 4, FABP4) may be specifically expressed in the cerebellum fat neuroblastoma, and medulloblastoma is not expressed [5].

The most challenging aspect of the differential diagnosis based on histopathology is to distinguish disease entity from neurocytoma/extraventricular neurocytoma, medulloblastoma, ependymoma, lymphoma, oligodendroglioma, astroblastoma and glioneuronal tumor with neuropil-like islands.

(1) neurocytoma/extraventricular neurocytoma: The localization, the histopathology of monomorphic small round neuronal cells and immune positivity for neural markers of the two entity tumors were similar, but neurocytoma had no lipidized cells resembling mature adipose tissue. (2) Medulloblastoma: (xanthomatous histiocyte or contain adipocyte in ordinary medul-
loblastoma): The most important differential diagnosis is that of medulloblastoma with lipidized cells. It is important to note that xanthomatous histiocytes, as occasionally observed in ordinary medulloblastoma, are not considered evidence of lipomatous differentiation.

In these lesions, the adipose tumor cells are usually more diffuse tumor cells are usually more diffusely distributed, but may also show the typical clustering like seen in the liponeurocytoma. Tumor cell atypia, mitotic and necrosis are more common in medulloblastoma. Most important the growth fraction is in the range of 15-40%, which is incompatible with the diagnosis of liponeurocytoma. Syn and NeuN are negative. The prognosis is poor with WHO grade IV.

(3) Lymphoma: Monomorphic small cells demonstrate the typical angiocentric infiltration pattern where tumor cells form collars within concentric perivascular reticulin deposits. The “Starry sky appearance” structure like the Burkitt lymphoma was been seen in our case. The lymphoma was invaded and usually with mitotic feature and large geographic necroses which was not be seen in the cerebellar LPN. Lymphoma was positive for lymphoma markers and negative for GFAP and neural markers. (4) Oligodendrocytic tumor: Some tumor cells have round or oval nuclei and often show a clear cytoplasm and perinuclear halos on paraffin sections ('honeycomb' appearance) resembling neoplastic oligodendrocytes. While it usually occurred in the cerebral hemispheres without lipoma-like components characterized by widespread immunopositivity for GFAP but neural markers; (5) Clear cell ependymoma: This variant appears to be preferentially located in the supratentorial compartment of young patients. Clear cell ependymomas had monomorphic small cells and display an oligodendroglia-like appearance with clear perinuclear halos. There was no lipoma-like cells. Ependymal and perivascular rosettes were immunoreactivity positive for GFAP, epithelial membrane antigen (EMA) and negative for neural markers. (6) Astroblastoma: Unipolar cytoplasmic processes in astroblastoma anchor neoplastic cells to stromal blood vessels in formations of pseudo-papillary appearances. Manifesting signet-ring or adipocyte-like features has been described. Mitotic activity, cytoplasmic atypia and necrosis could be seen in high grade astroblastoma. It was positive for GFAP, vimentin, S-100 and EMA, and negative for neural markers. (7) Glioneuronal tumor with neuropil-like islands: It was rare infiltrating astrocytomas, usually have focal, round oval islands composed of a delicate, neuropil-like matrix with granular immunohistochemistry for synaptophysin and at least focal nuclear for NeuN consist mainly of GFAP-positive. In our cerebellar LPN case, neuropil-like islands could be seen. While glioneuronal tumor with neuropil-like islands had no adipose cells.

Only in Giordana’s [6] case, lipidized cells expressed neither glial nor neuronal antigens. These cells were positive for vimentin. Some cells were stained with macrophage markers. There is no consensus about the lipidization that other than being true metaplasia either it is the end result of cellular metabolism or the differentiation of the neuroectodermal cells to different lines. In our case, the lipidized cells were positive for neural markers and glial markers. The “Starry sky appearance” cells were positive for glial antigens and negative for neuronal antigens.

In this study, we described the histopathological structures such as neuropil-like islands and “Stars” structure like Burkitt lymphoma. We unsure such cells were what really. Combining morphological and immunohistochemical results of these cells, we hypothesized that they may be related to the tumoral adipose cells or others. This idea needs further study confirmed.

Because of the rarity of this tumor are the lack of systematic follow-up data, survival and recurrence rates must be interpreted with some caution. The cerebellar LPN patients underwent gross total resection of the tumor usually with good prognosis, but easy to relapse in situ local and sometimes involving the structure of supratentorial. Despised being clinically progressive, recurrent liponeurocytomas did not show histological features of malignant progression. Early recurrence may even be associated with a relative increase in the lipomatous component. There was no indication of age or gender affecting clinical outcome. While some scholars believed that mitotic figures, vascular proliferation and a high proliferation index had relationship with clinical behavior. They proposed cerebellar LPN may have different grade. It was concluded that LPN is an uncertain malignant
potential lesion when mitoses are present and MIB-1 positive cells constitute more than 10% of total neoplasia cells [7]. Interestingly, the proliferation index of recurrence cases were less than 5% [8], and by the high proliferation index cases which was > 10% were no recurrence in the literature [9]. Radiotherapy or not postoperative was contain controversial currently [7, 10]. Some scholars have proposed the proliferation index contributed to the decision to use adjuvant radiotherapy after gross total resection. In the literature, there were 9 cases in the 10 recurred cerebellar LPN cases had no radiotherapy after gross total resection. Based on clinical follow-up research, most scholars supported radiotherapy postoperative or relapse after surgery.

In short, the cerebellar LPN is a rare and newly identified neoplasm. A highly cellular neoplasm composed of monomorphic small round neuronal cells mixed with lipomatous cells by widespread immunopositivity for synaptophysin was the histological characterized. There were some structures such as neuropil-like islands and “Stars” like structure, like Burkitt lymphoma had not been described in the literature. What was it need further study. Surgical resection was the preferred treatment method. Prognosis is good. It had high recurred rate. Radiotherapy maybe was necessary post operation. The histology and grade remains to be further study. Based on the clinical characteristics of supratentorial LPN reports, LPN or central LPN maybe more accurate than cerebellar LPN?

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Chunyan Xia, Department of Pathology, Changzheng Hospital, Second Military Medical University, 415 Fengyang Road, Shanghai 200003, China. Tel: 86 21 81886121; Fax: 86 21 81886124; E-mail: xia.chunyan1971@126.com (CYX); maxiaomei2001@126.com (XMM)

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