

A RARE CAUSE OF HYDROCEPHALUS : LHERMITTE DUCLOS DISEASE

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ABSTRACT

Background: Lhermitte Duclos Disease (LDD) is a rare disorder of unknown pathogenesis. It generally affects middle-aged patients and is categorized as a WHO grade 1 tumor. LDD commonly presents with symptoms related to increased intracranial pressure.

Magnetic resonance imaging is the appropriate technique allowing preoperative diagnosis with the characteristic striated pattern of exaggerated folia appearance on T2 weighted image. The principal histological abnormalities are expansion and massive replacement of the internal granular cell layer by large neurons with vesicular nuclei and prominent nucleoli. Surgery is the treatment of choice. The prognosis is excellent.

Case report: A 41-year-old male was referred to our hospital with loss of consciousness and dizziness lasting for one week. Physical examination revealed left cerebellar signs. In the ophthalmological examination, bilateral papillary oedema was observed. Cranial magnetic resonance imaging revealed a non enhancing striated lesion in the right side of the cerebellum with Hydrocephaly.

A subtotal craniectomy and partial resection of the left cerebellar tumor were performed. The histological and immunohistochemical profile was that of a dysplastic gangliocytoma.

Conclusions: LDD or dysplastic cerebellar gangliocytoma is a rare benign cerebellar mass, probably hamartomatous, with a characteristic aspect magnetic resonance imaging.

Surgery is the only treatment approach that avoids the complications.

Key words: Lhermitte, Duclos, gangliocytoma, dysplastic.

INTRODUCTION

LDD also known as dysplastic gangliocytoma of the cerebellum is a rare cerebellar disease of unknown pathogenesis, probably hamartomatous [1]. It includes an overgrowth of cerebellar ganglion cells, which replace granular and purkinje cells [2]. LDD was first reported by Lhermitte and Duclos in 1920 [1]. The disorder often occurs in the third or fourth decade [3] and may be part of Cowden's syndrome [4]. The tumor causes the development of expansive processes in the posterior

cranial fossa and frequently gives symptoms of intracranial pressure or cerebellar dysfunction [2].

CASE REPORT

A 41-year-old male was referred to our institution complaining of holocranial headache and progressive vision diminution for the last 3 years. He presented 12 hours before admission, with loss of consciousness and dizziness lasting for one week. Physical examination revealed left cerebellar signs such as ataxia, dysmetria and dysidiadochokinesia. Cranial nerves, motor and

sensory functions were intact. Bilateral papillary oedema was noted in the ophthalmological examination. No other hamartomatous lesions were found. The patient had no family history for Cowden syndrome.

Cranial magnetic resonance imaging revealed a non enhancing striated lesion in the right side of the cerebellum. The lesion had layers of hypo- and iso-intense signals on T1 weighted images, hyper and iso-intense signals on T2 weighted images [Figure 1].



Figure1: T2-weighted axial magnetic resonance image. The mass is predominantly hyperintense with the typical alternate high and normal signal intensity bands. The fourth ventricle is compressed.

Hydrocephaly was also noted. The tumor had a mass effect on the fourth ventricle, cerebellar aquaduct and the brainstem.

Magnetic resonance spectroscopy revealed decreased N-acethyl aspartate and N-acethyl aspartate/creatinine without increased choline/creatinine ratio. A subtotal craniectomy and partial resection of the left cerebellar tumor were performed. The tumor surface was yellowish white. The histologic examination revealed loss of cerebellar architecture with enlarged cerebellar stratum granulosum showing sheets of large cells with enlarged vesicular nuclei, prominent nucleoli and abundant cytoplasm without mitosis [Figure2,3]. Purkinje cells were absent. Immunohistochemistry showed membranous immunoreactivity of these cells by synaptophysin, indicating their neuronal nature [Figure 4]. Some cells were positive for neurofilament.

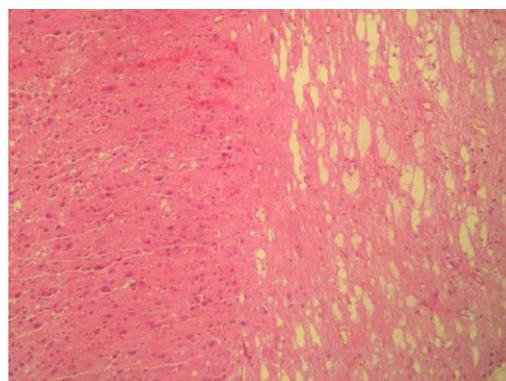


Figure 2: Atypical neurons dominate within the granular cell layer (HE stain, ob. x 20).

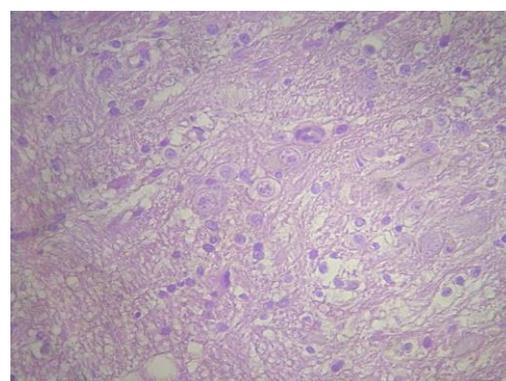


Figure 3: Neurons are considerably larger than ordinary granular cell neurons. The atypical neurons show an eccentric nucleus with a prominent nucleolus within their eosinophile cytoplasm (HE stain, ob. x 40).

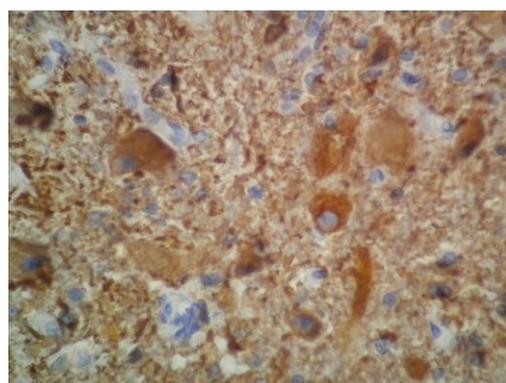


Figure 4: The dysplastic ganglion cells are strongly immunopositive for synaptophysine (Ob. x 40).

DISCUSSION

LDD or dysplastic cerebellar gangliocytoma is a rare benign cerebellar mass, probably hamartomatous, of unknown pathogenesis, composed of abnormal ganglion cells, which corresponds to WHO grade I tumors [5, 6].

LDD was first reported by Lhermitte and Duclos in 1920. Since then, several other cases have been reported with the use of different names [7]. The association between LDD and Cowden syndrome was first described by Padberg in 1991[2].

The pathogenesis of LDD is unknown. Until today, there is controversy if it is a hamartomatous lesion, a development anomaly, a manifestation of phacomatosis or a low grade neoplasm [7]. It can occur in a family context or have a sporadic form. LDD can be associated with Cowden's disease in 40% of cases [8]. This finding supports the hamartomatous hypothesis [9]. They are classified by some authors as a phacomatosis [10]. These two diseases can be associated with PTEN genetic defects [3, 11].

LDD can be accompanied by many abnormalities such as megalencephaly, hydromyelia, heterotopia, microgyria, polydactyly, leontiasis ossea and multiple hemangiomas [7]. In our patient, we did not find features of Cowden syndrome. Evaluation of PTEN mutation was not performed [11].

As in our case, LDD generally presents in patients in the third and fourth decades of life [2], but it can occur at any age [7, 12]. There is no clear sex preference [7, 12].

Patients with LDD may be asymptomatic or they commonly present with symptoms of hydrocephalus, increased intracranial pressure, cerebellar signs and cranial nerve deficits [2]. Usually, patients have long-standing symptoms that have been present for years, indicating the slowly progressive nature of this disease [11].

Magnetic resonance imaging is the appropriate diagnostic tool since it can show unilateral, non enhancing cerebellar vermian-hemispheric mass with a layered appearance consisting of alternating bands of relative iso-, and hypointensity to the normal brain on T1 weight, and relative hyper and isointensity on T2 weight images [7, 12]. Cystic and necrotic areas are absent [2], calcifications are unusual [2]. Magnetic resonance imaging is better than computed tomography for the diagnosis of LDD [7].

Magnetic resonance spectroscopy also helps guide diagnosis with decreased N-Acetyl Aspartate and increased lactate level without elevation of the lipid levels. Also in contrast to the tumoral lesions, lack of increased choline/creatinine ratios in LDD is striking [7]. Nagaraya et al reported decreased levels of N-Acetyl Aspartate/creatinine.

The main macroscopic finding of the disease is the focal, hemispheric, or diffuse thickening of the cerebellar folia and nearly total disappearance of the arbor vitae cerebelli [7].

Microscopically, the dysplastic gangliocytoma causes diffuse enlargement of the molecular and internal granular layers of the cerebellum which are filled by abnormal ganglion cells of varying sizes [13, 2]. An important diagnostic feature is the relative preservation of the cerebellar architecture, in which folia are enlarged and distorted but not obliterated. A layer of abnormally myelinated axon bundles in parallel arrays is often observed in the outer molecular layer. Scattered cells morphologically consistent with granule neurons are also sometimes found under the pia or in the molecular layer. The resulting structure of these dysmorphic cerebellar folia has been referred to as inverted cerebellar cortex. Purkinje cells are reduced in number or absent. Calcification and ectatic vessels are commonly present within the lesion. Vacuoles are sometimes observed in the molecular layer and white matter [13]. The lack of mitosis and low level of proliferative activity are also consistent the hamartomatous nature of this lesion [2].

The dysplastic neuronal cells are immunopositive for synaptophysin [13]. Occasional ganglion cells expressed neurofilament protein [1]. Immunohistochemistry also demonstrates loss of PTEN protein expression in most dysplastic cells [13].

The process can be misinterpreted as gangliocytoma, ganglioglioma or even astrocytoma [14]. Dysplastic gangliocytoma of the cerebellum overlaps somewhat with conventional gangliocytoma, but is obviously a malformative process, whereas ganglion cell tumors are cellular, tumorous masses. Dysplastic gangliocytoma also has an interface with the white matter that is more linear and abrupt than even the most well-circumscribed ganglion cell tumor [14]. Ganglioglioma shows greater cellular pleomorphism, a variably collagenous stroma, focal chronic inflammation, frequent cyst formation, extension into the leptomeninges, cells appearing morphologically intermediate between ganglion cells and astrocytes, and a clearly defined glial component. The latter is conspicuously absent in dysplastic gangliocytoma. Unlike astrocytoma, the cells of dysplastic gangliocytoma are uniforme, larger, rounded and more neuronal in configuration. Immunohistochemistry resolves the issue [14].

The treatment is based on surgery [3]. The lesion usually merge with the normal cerebellar parenchyma and often, no tumour mass can be found during surgical exploration [15]. This can lead incomplete resection and recurrence [7].

Complete resection is associated with a excellent prognosis [3]. Recurrence is possible [4]. Malignant transformation has not been reported.

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