Case Report

A Rare Case Report on Lhermitte-Duclos Disease: An Intraoperative and Radiopathological Diagnosis

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Abstract

Background: Lhermitte-Duclos Disease (LDD), also known as dysplastic gangliocytoma of the cerebellum, is a very rare tumor of the cerebellum, with only about 300 cases reported worldwide. It is a slow-growing benign tumor causing diffuse enlargement of the cerebellum due to granular layer hypertrophy.

Case Report: We present a case of a 30-year-old female with symptoms of giddiness, focal convulsions, and loss of consciousness, along with positive cerebellar signs. On MRI, an ill-defined intra-axial lesion showed classical alternating light and dark “tiger stripe” patterns with no contrast enhancement. Frozen and histopathological evaluations confirmed the diagnosis, as there was the presence of atypical ganglion cells replacing the internal molecular layer. The patient underwent total tumor resection.

Conclusion: Lhermitte-Duclos disease is a rare lesion that unilaterally enlarges the cerebellum but maintains the foliar architecture. It is identified as a component of Cowden syndrome, an autosomal dominant cancer predisposition disorder. Recognition of the histological characteristics of this uncommon condition and maintaining a heightened suspicion are imperative for an accurate diagnosis. This should prompt comprehensive examinations to rule out manifestations of associated Cowden syndrome. Lhermitte-Duclos Disease is an infrequent occurrence, and understanding its histological attributes and aligning them with radiological findings is crucial, particularly in small biopsy samples, to ensure a precise diagnosis.

Keywords:

Lhermitte-Duclos Disease, Cerebellum, Histopathology

Introduction

Lhermitte-Duclos Disease (LDD) is a condition stemming from an uncommon benign lesion of unknown origin. It is also referred to as dysplastic gangliocytoma of the cerebellum, marked by an alteration in the typical cytoarchitecture of the cerebellar layers. When observed on magnetic resonance imaging (MRI), the lesion presents as a non-enhancing mass within the cerebellar

hemisphere, displaying a striated pattern [1]. In the majority of instances, it is linked to genetic mutations affecting the tumor suppressor gene PTEN. These mutations interfere with the phosphatidylinositol-3'-kinase (PI3K) pathway, resulting in heightened cell proliferation and disrupted neuronal migration [2].

Magnetic resonance imaging (MRI) is the diagnostic modality of choice and reveals characteristic non-enhancing gyriform patterns with the enlargement of cerebellar folia. The most common presenting symptoms are ataxia, seizures, or those related to raised intracranial pressure. It sometimes presents with psychiatric symptoms. It is considered a grade 1 tumor and is usually treated by surgical resection in symptomatic cases. We present this case report because of its rarity and unique diagnostic features.

Case Report

A 30-year-old female presented to the neurosurgery OPD with a history of giddiness, followed by one episode of focal convulsion and loss of consciousness for 10 minutes. She also complained of headaches and had one episode of vomiting. She did not have any history of fever, vision, or hearing abnormalities. No difficulty in walking was reported. On examination, the Glasgow Coma Scale was graded as E4V5M6, with normal tone and power in both upper and lower limbs. Deep tendon reflexes exhibited a normal response (Grade 2). Except for the Romberg test, the following cerebellar signs were positive in the patient: dysdiadochokinesia, finger-to-nose test, and finger-to-finger test. MRI revealed a large, ill-defined intra-axial lesion in the right cerebellum with a ribbon-like alternating pattern of high and low signal intensities (Fig. 1).

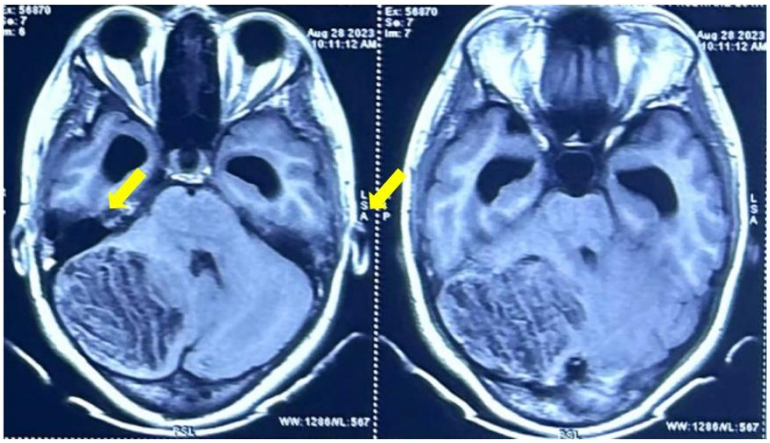

Figure 1: A large, diffuse, ill-defined intra-axial lesion was noted in the right cerebellum, appearing iso to hypointense on T1W and hyperintense on T2W, with ribbon-like high and low-intensity signals (Arrow).

The patient was operated on, and we received a sample for frozen examination, which showed the proliferation of dysplastic ganglionic cells along with mild vascular proliferation under microscopy (Fig. 2). Postoperatively, paraffin sections of the frozen tissue and histopathology samples revealed an increased number of dysplastic ganglion cells replacing the internal granular layer. Dysplastic ganglion cells showed hyperchromasia and prominent nucleoli, interspersed with small neurons (Figs. 3, 4). A rare finding of a decrease in the number of Purkinje cells was also noted (Fig. 3). Based on the radiological findings, intraoperative frozen section findings, and histopathological examination, we reported this case as Lhermitte-Duclos Syndrome and advised PTEN mutation studies.

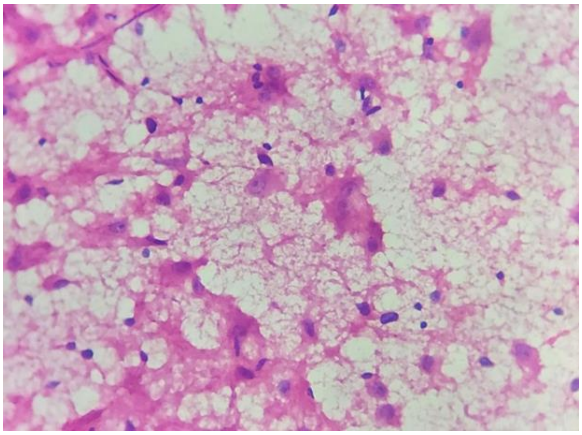

Figure 2: Dysplastic ganglionic cells scattered with neurons in a fibrillary background in cytological smear (H&E stain; 400x).

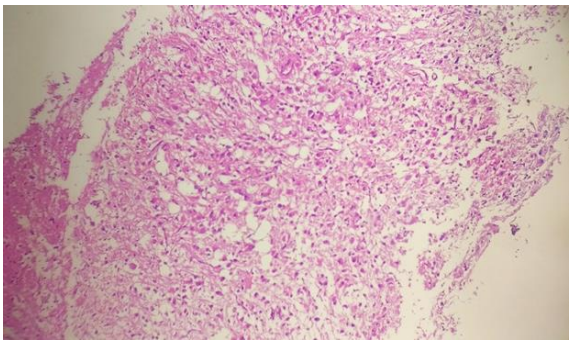

Figure 3: Section shows replacement of the internal granular layer with proliferation of ganglion cells and absence of the Purkinje layer (H&E stain; 100x).

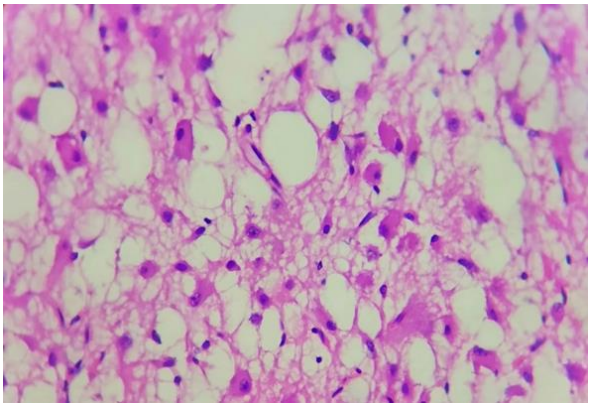

Figure 4: Section demonstrated dysplastic ganglion cells showing occasional prominent nucleoli scattered among dysplastic neuronal cells (H&E stain; 400x).

Discussion

While classified as a WHO grade I tumor, its histology suggests it is more likely a hamartoma characterized by enlarged and abnormally developed cerebellar folia containing dysplastic cells, rather than neoplastic cells [3]. Presently, it is recognized to be connected with Cowden syndrome, and both conditions are correlated with germline mutations on the PTEN gene. Moreover, sporadic instances exist that do not feature a PTEN mutation and lack the Cowden syndrome phenotype, particularly when the

onset occurs in childhood [4]. While MRI is highly sensitive in revealing the enlarged folia, indistinct radiographic findings and varied presentations can occasionally add complexity to the diagnosis, being sometimes misdiagnosed as gliomas or medulloblastomas [5]. Therefore, in the absence of indicative clinical data, awareness of this rare lesion is crucial for achieving an accurate pathological diagnosis. Kulkantrakorn et al. have delineated the MRI characteristics corresponding to dysplastic-hypertrophied cerebellar folia, which represent histopathological features observed in this condition [7].

Under microscopy, there is evident enlargement of the molecular and internal granular layers, with a notable preservation of the cerebellar foliar architecture. The molecular layer appears widened due to the presence of numerous enlarged and irregularly myelinated axons, often arranged in parallel arrays, originating from the abnormal hypertrophied neurons constituting the internal granular layer. Additionally, the absence of Purkinje cells, calcification of vessel walls, and vacuolar changes within the molecular layer are occasionally noted [7, 8]. In the medical records of the patient, there were no indications of other primary or secondary tumors. Upon further assessment regarding hamartomatous lesions and family history, no potential association with Cowden syndrome was identified. However, our patient was not tested for a PTEN mutation.

Conclusion

For pathologists, diagnosing LDD can pose significant challenges in the absence of comprehensive clinical data. Nonetheless, identifying the disease is of paramount importance, not only to distinguish it from other cerebellar tumors but also to prompt thorough clinical examinations regarding Cowden syndrome, a genetic disorder marked by numerous noncancerous growths and an increased susceptibility to specific cancers in various organs. While many reports emphasize the radiological aspects, it is critical for pathologists to recognize the diverse clinical and histopathological presentations of this rare lesion, especially to distinguish it from low-grade glial and neuronal tumors. Even in frozen sections, the changes may be subtle, and even apparently normal cerebellar tissue should be meticulously assessed for any abnormalities in the internal granular layer.

The treatment of LDD is generally decompressive surgical intervention arising due to hydrocephalus. The use of targeted therapies has been recently developed with molecules targeting the inhibition of the PI3K/Akt/mTOR pathway in LDD. These targeted therapies could potentially reduce tumor growth and improve symptoms. Drugs like sirolimus (rapamycin) and everolimus, which inhibit mTOR, are being explored for their efficacy in treating LDD.

Abbreviations:

LDD: Lhermitte-Duclos Disease

MRI: Magnetic Resonance Imaging

PTEN: Phosphatase and Tensin Homolog Deleted on Chromosome 10

OPD: Outpatient Department

WHO: World Health Organization

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Competing Interest: None Declared

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