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Lhermitte-duclos disease (dysplastic cerebellar gangliocytoma): a case report

Aribah Atiq[1], Usman Hassan[2], Noreen Akhtar[3], Sajid Mushtaq[4]

1 Department of Histopathology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan; **2-4** Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan

Correspondence: Aribah Atiq. **Email:** aribah.atiq@yahoo.com

Abstract

Lhermitte-Duclos disease (LDD) is a relatively uncommon condition of the cerebellum. It is generally characterised as a hamartomatous lesion of posterior fossa and is common in the third and fourth decades of life. According to the World Health Organisation, it is classified as a grade I tumour with potential for recurrence. Otherwise, this disease is generally associated with good prognosis. Malignant transformation of LDD has not yet been reported. However, genetic counselling of the patient is recommended with active surveillance. Since LDD is believed to be a pathognomonic feature of Cowden syndrome, which is a multi-system autosomal dominant hereditary disorder characterised by multiple hamartomas and an elevated risk of benign and malignant neoplasms, we decided to report this important entity considering its rarity and high clinical significance.

Keywords: Lhermitte-Duclos disease, Cowden syndrome, dysplastic cerebellar gangliocytoma, PTEN

Introduction

Lhermitte-Duclos disease is a rare disease of the cerebellum, originally described by Lhermitte and Duclos in 1920. It is generally seen in young patients, mostly

in their third and fourth decades of life. Lhermitte-Duclos syndrome is also known as dysplastic cerebellar gangliocytoma. It is now considered a slowly growing hamartomatous lesion of cerebellar cortex that results in the thickening of cerebellar folia.[1,2,3] It is strongly believed to be associated with Cowden syndrome and predisposes patients to high risk of benign and malignant neoplasms. This tumour can show PTEN mutation and germline alterations in SDHB-D and PIK3CA/AKT1. [4,5] We encountered a similar interesting case in our centre, which was sent to us from an outside neurosurgery centre by a neurosurgeon. The case is reported as Lhermitte-Duclos disease (dysplastic cerebellar gangliocytoma).

Case Report

A 33-year-old man presented to the neurosurgery department of a neurosurgery hospital with complaints of headache and diplopia. Clinical examination revealed ataxic gait and cerebellar signs. Family history was negative for any benign and malignant neoplasm. MRI examination of the brain revealed a mildly enhancing diffuse lesion in the right cerebellar region. The lesion had a specific gyriform pattern with prominent and thickened cerebellar folia. The lesion was hypointense on TI sequences and hyperintense on T2 sequences. The patient underwent right suboccipital craniotomy and the mass was excised. (Fig 1 & 2).

The gross specimen was sent to the pathology department of Shaukat Khanam Memorial Cancer Hospital and Research Centre on September 14, 2017. The submitted tissue composed of multiple fragments aggregately measuring 7.2cm x 5.4cm x 3.3cm. Microscopic examination revealed cerebellar tissue with expansion of internal granular layer and hypermyelination of molecular layer with scattered dysplastic ganglion cells of varying sizes and shapes. There were white vacuoles in the molecular layer and white matter with dilated ectatic vessels. (Fig 3, 4, 5, 6)

Immunohistochemistry showed positive expression of ganglion cells with synaptophysin. No high-grade features, such as mitoses, necrosis, or vascular endothelial proliferation, were identified. Final diagnosis of dysplastic cerebellar gangliocytoma was made, keeping in view the radiological and histological features.

Discussion

Lherrmite-duclos disease (Dysplastic cerebellar gangliocytoma) is a rare neoplasm with a frequency of five cases per million population per year. The prevalence of this disease is not known, however, 230 cases have been reported in medical literature. [6] It is most frequently seen in the third and fourth decades of life. [7] There is no gender predisposition. [8] LDD is considered as a hamartomatous lesion of cerebellar cortex. It has a strong association with Cowden syndrome and an elevated risk of developing other benign and malignant neoplasms.[9, 10] Cowden disease is associated with a germline mutation in PTEN gene (located at locus 10q23.2), recently identified as a major predisposition factor for Cowden syndrome.[11] Lhermitte-Duclos disease also shows a germline loss of PTEN allele, and with the loss of remaining allele, leads to abnormal growth of granule cells. However, PTEN is not the only mutation seen in LDD, other mutations reported in LDD are EGRF, SDHB-D and PIK3CA/AKT1.[12, 13,14)]

Clinical presentation of this disease is variable but patients mostly present with signs and symptoms of mass effect, i.e. cranial nerve palsies and occlusive hydrocephalus. In a case reported by Rheinboldt et al, a 33-year-old woman presented with headache, dizziness and ataxia. Radiology revealed a 6-cm mass in superior right cerebellar hemisphere with cortical involvement. The lesion was hypo and hyper intense on T1 and T2 respectively. On histology, the lesion showed widening of molecular layer of cerebellar cortex with replacement by abnormal ganglion cells. These features and findings are surprisingly similar to

the findings seen in our patient, as our patient was also 33-years-old with similar radiological and histological features as described by Rheinboldt et al [15]. However, in our case, the patient was a male.

In another case reported by Colby et al,[16] a 43-year-old patient presented with 5-cm mass within right cerebellar hemisphere with striated appearance and thickening of cerebellar folia on MRI. Histological features were again similar to that seen in our case.

Radiology is the usual diagnostic tool for this disease, with a characteristic gyriform pattern and thickened cerebellar folia. Microscopically, expansion of the granule cell layer and hypermyelination of molecular layer with abundant dysplastic ganglions are the most striking features. There are clear vacuoles, usually seen in the white matter and molecular layer. Dilated ectatic vessels and calcifications are generally seen. Features of malignancy, i.e. mitosis, necrosis and endothelial proliferation are usually absent. [12,13] Differential diagnosis includes other ganglion cell tumours as well, because morphological picture of these tumours also display dysplastic ganglions, but Lhermitte-Duclos disease is site specific and typically associated with dysplastic ganglion cells in the molecular layer.

To the best of our knowledge, the malignant transformation of this disease has not been reported yet. [12,14] After surgical resection, the disease is associated with good prognosis. Our patient was followed up till April, 2019 and he is healthy with no recurrence. However, regular follow-up is recommended as this disease is strongly associated with Cowden syndrome, with an increased risk of other benign and malignant neoplasm.

Conclusion

The case has been reported because it is a rare and distinct disease of the cerebellum. This disease needs to be diagnosed because of its relation with Cowden syndrome. It is generally associated with good prognosis. However, follow up is necessary.

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Conflict of Interest: None to declare.

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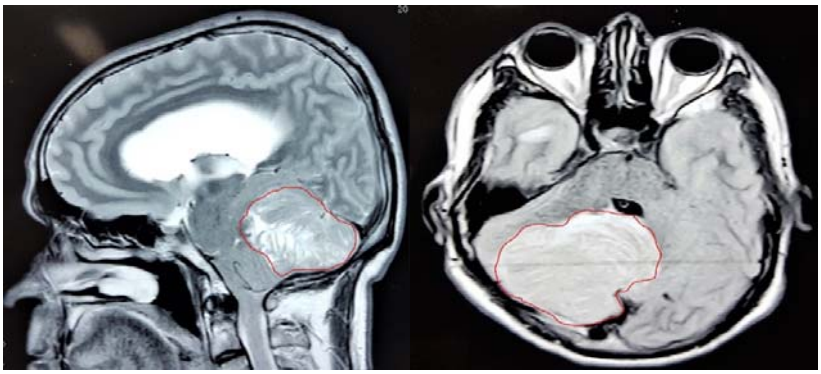
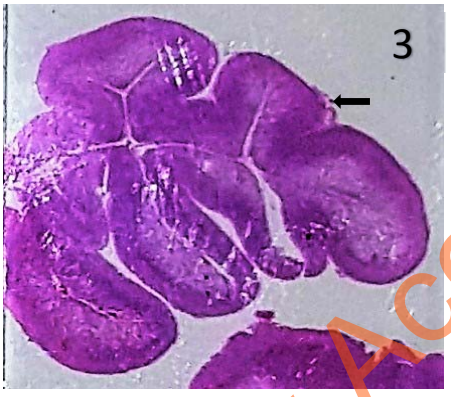


Figure 1 & 2: Intra-axial Gyriform pattern lesion with prominent and thickened cerebellar folia (marked with red ink)

Figure 3: Light microscopic picture of H&E stain showing relative preservation of cerebellar layers with thickened folia.

Figure 4: H&E stain demonstrating cerebellar tissue with relatively preserved architecture (5X).



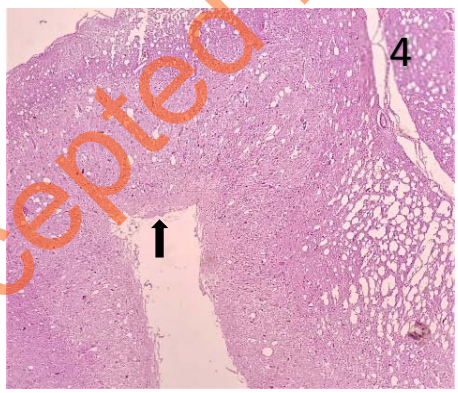


Figure 5: H&E stain showing scattered dysplastic ganglion cells of varying size and shape in the internal granular layer with axonal hypermyelination of molecular layer at 10X.

Figure 6: High power view of H&E stain showing dysplastic ganglion cells with axonal hypermyelination (40X)