Lhermitte-Duclos Disease

Lhermitte-Duclos disease (LDD) is a rare benign cerebellar lesion of uncertain pathogenesis and is widely regarded as a hamartomatous mass lesion. There is distortion of the normal cerebellar laminar cytoarchitecture with appearance of thickened cerebellar folia giving a laminated or striated appearance in magnetic resonance imaging (MRI), which has a striking imaging appearance, and is diagnostic of this condition. Although it follows an indolent course, ventricular obstruction necessitates cerebrospinal fluid shunting, and excision may be indicated in progressive lesion. The lesion has characteristic spectroscopic findings that can be useful in decision making and long-term follow-up.

Lhermitte-Duclos disease was first documented as a unique entity in 1920.[1] This rare disease is characterised by disarrangement of the normal cerebellar architecture and appearance of numerous abnormal ganglion cells. Various terms have been used to describe the disease including dysplastic angliocytoma, benign hypertrophy of the cerebellum, hamartoma of the cerebellum, purkinjeoma, diffuse ganglioneuroma of the cerebellar cortex. In line with this confusion, the pathogenesis remains uncertain. LDD is recognised as a single disease entity based on its characteristic histological structure in the World Health Organisation classification of brain tumours. LDD occurs mainly in young adults with no sex preference, and usually manifests as symptoms of increased intracranial pressure, but not always cerebellar symptoms. LDD is frequently associated with megalencephaly, megalocephaly, hydrocephalus, heterotopia, and hydromyelia, and more rarely with polydactylia, neurofibromatosis, mental retardation, spongioblastoma, multiple hemangiomas, partial gigantism, dysplastic body, metastaticperithelioma, hyperplastic tongue, seizures.[2] Coexistence of Cowden disease or multiple hamartoma syndromes, an autosomal dominant disorder of the skin and mucous membranes, with LDD has been described[3] suggesting that this constellation of diseases represents a phakomatosis. In this syndrome, thyroid disorders are also common, and malignancies of the breast, colon and adnexa may also occur.[4]

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Due to the inherent beam hardening artifacts in the posterior fossa with computed tomography, MRI is certainly the imaging modality of choice. On T1-weighted images, the striations have been described as hypointense and isointense, respectively, to cerebellar grey matter.[5] On T2-weighted images, the lesions are well-circumscribed and have a unique striated pattern consisting alternating bands of high signal intensity and normal signal intensity relative to cerebellar grey matter [Figure 1].[6] Majority of the lesions appear very mild or with no enhancement following administration of intravenous gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA). The lack of contrast enhancement suggests insignificant disturbances of the blood-brain barrier and/or absence of extracellular oedema. The characteristic non-enhancing gyriform patterns correspond to the enlargement of cerebellar cortical folia. The enlarged folia lose their secondary foldings and asymmetrically widen the affected cerebellar hemisphere.[7] Kulkantrakorn *et al*.[4] reported that the high signal intensity band seen on T2-weighted images corresponded to the inner molecular layer and the granular cell layer. Loss of central white matter within the folia also contributed to this appearance. The outer portion of the folia consisting of the outer molecular layer and leptomeninges within effaced sulci create the band isointense to cerebellar gray matter on T2-weighted images. Magnetic resonance spectroscopy shows decrease in N-acetyl aspartate (NAA)/creatinine (Cr) and NAA/choline (Cho) ratios with near normal values of Cho/Cr, which could be attributed to a lack of neuronal architecture (a hallmark of hamartoma) and/or the presence of embryonic neural tissue, which fails to express NAA. If Cr is taken as an internal standard, the near normal values of Cho/Cr ratios in LDD indicate a lack of cell turnover or proliferation, and the pathology is unlikely to be tumorous. These results are in favour of 'benign' hamartoma rather than a tumour.[8-10] In other cerebral neoplasia, a decrease in NAA or NAA/Cr ratio associated with an increase in Cho or Cho/Cr ratio is often reported.[11] This combination has also been described in cerebellar tumours.[12] On the other hand, decreased Cho/Cr ratios are not observed in cerebral malignant tumours, where increases in Cho levels are associated with enhanced membrane turnover. Lactate, normally undetectable in the brain, accumulates in

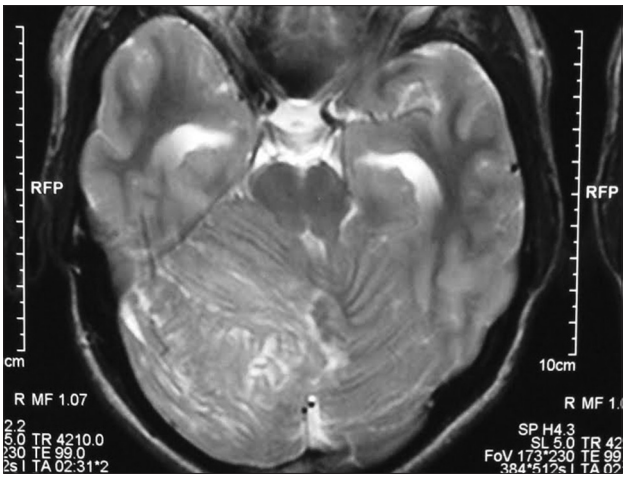

Figure 1: Magnetic resonance imaging (T2-weighted axial) showing typical 'tiger stripe' pattern of cerebellar folia in Lhermitte-Duclos disease

cysts, necrotic tissue, or within active tumours because of the high rate of glycolysis. Hence, the lactate peak suggests altered anaerobic metabolism. The elevated lactate level is due to an abnormal high glucose metabolism with the LDD, rather than representing high lactate level in cystic or necrotic components of LDD.[6,8] Combined with the histopathologic findings of no necrotic areas within the LDD lesion; the elevated lactate levels do not represent cell death. Therefore, LDD has some characteristics of tumours such as decreased NAA and increased lactate, but not increased levels of Cho.

The diagnosis of LDD can now frequently be made using MRI, and this advance has markedly improved the prognosis for the disease. Patients with LDD may demonstrate the typical striated pattern of hyperintensity on T2-weighted images and corresponding hypointensity on T1-weighted images, as well as the typical absence of enhancement following Gd-DTPA administration. In addition, the lack of restricted diffusion on diffusion-weighted MRI, and associations of decreases in the NAA/Cr and NAA/Cho ratios with near normal values of Cho/Cr, as well as an obvious lactate peak may suggest a benign hamartoma. Recent studies of the biology of the PTEN pathway[13] explain why LDD is a hamartoma, and not a tumour: 11C-methionine positron emission tomography shows the lesion of LDD as a high uptake area.[14]

Some patients with LDD become symptomatic and require resection of the cerebellar mass. Neurological deterioration or increase in the size of cerebellar mass during follow-up would automatically qualify for surgical decompression. The nature and scope of surgery can be decided, based on the clinical presentation and diagnostic features on neuroimaging.

The histopathological features of this disease are classical. Macroscopically there is thickening of the cerebellar folia which appear pale. Microscopically, enlargement and distortion of cerebellar folia is seen. Proliferation of dysplastic ganglion cells is seen in the granular layer along with the enlargement of the molecular layer with abnormal myelinated bundles. Purkinje cell layer is disrupted.

Typical course of LDD consists of insidious expansion of the posterior fossa mass, which may require surgical decompression. Surgical decompression improves quality survival from 2.5 to 11 years.[15]

Lhermitte-Duclos disease is a hamartomatous mass lesion of the cerebellum having a striking imaging appearance. Although it follows an indolent course, ventricular obstruction necessitates cerebrospinal fluid shunting and excision may be indicated in progressive lesion.

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