"Shrimp Sign" in Progressive Multifocal Leukoencephalopathy

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A 47-year-old female, diagnosed with retroviral disease 6 months previously, complained of progressive weakness of the right side of her body over 2 weeks. She also had difficulty in precise movements of the affected limbs, with a history of over- and under-shooting and swaying while walking (right > left). She had no dysphagia, dysarthria, diplopia, facial weakness, or hearing loss. Examination revealed spastic speech and a flattened nasolabial fold on the right side. She had right-sided spastic hemiparesis (Medical Research Council [MRC] grade 4/5) with brisk reflexes in all limbs (right > left) and extensor plantar response. Her finger–nose–finger and heel–shin tests were abnormal bilaterally (right > left) with dysdiadochokinesia and multidirectional gaze-evoked nystagmus. The gait was wide-based ataxic with circumduction on the right.

She was evaluated for bilateral, asymmetrical, spastic ataxia syndrome. Her routine investigations were normal, and her CD4 count was 273 cells/mm^3. Magnetic resonance imaging of the brain [Figure 1] revealed asymmetrical, clearly delineated T1-hypointense and T2-hyperintense lesions in both the middle cerebellar peduncles and the cerebellar white matter, suggestive of "shrimp sign." Cerebrospinal fluid (CSF) examination showed five cells (all lymphocytes), glucose 60/98 mg/dl, and protein 104 mg/dl. Other CSF investigations, including cultures, pan-viral polymerase chain reaction (PCR), GeneXpert for tuberculosis, and India Ink stain, were negative. CSF was positive for John Cunningham (JC) virus by PCR, confirming a diagnosis of progressive multifocal leukoencephalopathy (PML).

PML is an opportunistic demyelinating disease caused by infection of the central nervous system (predominantly oligodendrocytes) by the JC virus.[1] It usually affects individuals with impaired cell-mediated immunity, with most cases reported in retroviral disease-positive individuals. Some cases have also been reported in patients with Hodgkin's lymphoma, leukemia, sarcoidosis, and patients on treatment with immune therapies like natalizumab and rituximab.[2-4] The diagnosis of PML is suspected based on clinicoradiologic findings and confirmed by CSF-JC virus positivity. Radiologically, PML lesions involve the white matter of the brain with a multifocal distribution (patchy/confluent) and typically do not enhance or have a proportionate mass effect.[1] Cerebral hemisphere lesions are more common, but cerebellar lesions can also be the presenting feature. There was absence of an imaging biomarker for the latter, and the "shrimp sign" described by Adra *et al.*[1] is an answer to that.

Diagnosing the "shrimp sign" [Table 1] requires the presence of a well-defined T2-hyperintense and T1-hypointense lesion of the cerebellar white matter, abutting but not involving the dentate nucleus (thereby outlining its serrated and curved shape and making it stand out). It is typically bilateral and asymmetrical. It was shown to have high sensitivity (85%), specificity (100%), and positive predictive value (100%) for diagnosing cerebellar PML.[1] Histopathologic studies have provided a neuropathologic basis for these findings by demonstrating the presence of widespread, severe demyelination in the cerebellar white matter, sparing the dentate nucleus.[5] Bilateral and symmetrical lesions can be found in fragile X-associated tremor/ataxia syndrome and human immunodeficiency virus-associated encephalopathy.[6] Therefore, asymmetricity of the lesions is of paramount importance to suspect PML, in contrast to symmetric involvement in Fragile X Tremor Ataxia

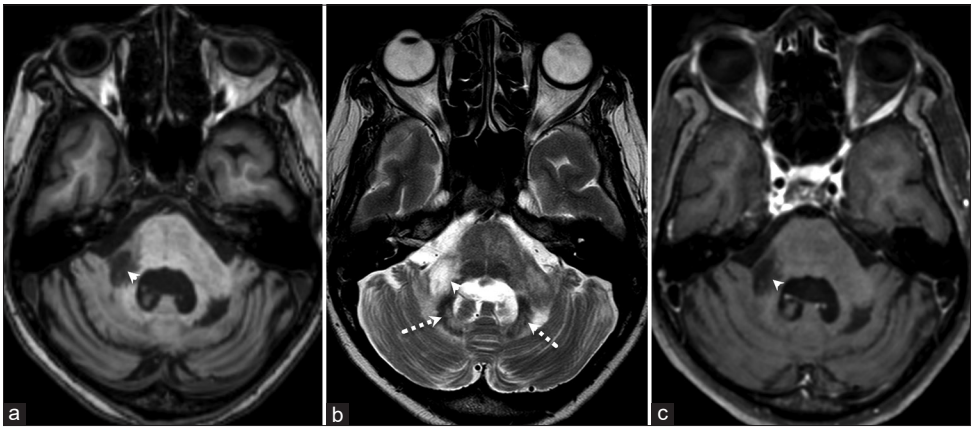

Figure 1: Asymmetrical, clearly delineated T1-hypointense (indicated by arrows in (a)) and T2-hyperintense (b) lesions are observed in both the middle cerebellar peduncles and the cerebellar white matter, adjacent to and distinctly outlining the dentate nucleus (indicated by broken arrows in (b)) on brain MR imaging. No enhancement is observed in post-gadolinium T1-weighted images (indicated by arrows in (c)). MR = magnetic resonance

Table 1: Diagnostic criteria for "shrimp sign" of cerebellar PML[1]

Core inclusion criteria	White matter lesion • Well defined • Hyperintense on T2-weighted and FLAIR sequences • Hypointense on T1-weighted sequences • Abuts and sharply demarcates the dentate nucleus • Encompasses at least 50% of the dentate nucleus
Core exclusion criteria	White matter lesion • Cavitation within the substance of lesion • Focal, diffuse, or ring enhancement • Involvement or displacement of the dentate nucleus
Compatible features	• Mottled appearance of white matter lesion • Presence of multiple noncontiguous lesions near the dentate nucleus • Involvement of white matter hilum of the dentate nucleus • Presence of other lesions in the cerebellar hemisphere or the brainstem
Permissible atypical features	• Minimal enlargement of MCP (2–3 mm) • Minimal mass effect on the fourth ventricle • Olivopontocerebellar atrophy in later stages • Faint enhancement

PML = Progressive multifocal leukoencephalopathy, FLAIR = FLuid Attenuated Inversion Recovery, MCP = Middle cerebellar peduncle

Syndrome (FXTAS). The fulfillment of the "shrimp sign" imaging criteria should be verified before diagnosing PML.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 21-Oct-2023 **Revised:** 29-Dec-2023 **Accepted:** 02-Jan-2024
Published: 16-Feb-2024

DOI: 10.4103/aian.aian_932_23