Sir,

Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) is a rare autosomal dominant neurodegenerative disease resulting from heterozygous mutations in the colony-stimulating factor 1 receptor gene.\(^1\) ALSP is a challenging diagnosis in the absence of pathological or genetic confirmation because of its varied clinical presentation and imaging features. We report a case of ALSP in a 54-year-old lady presenting with predominant language disturbance in the form of logopenic variant of primary progressive aphasia (LvPPA) with no similar family history. Magnetic resonance imaging (MRI) brain showed frontoparietal predominant periventricular and corpus callosum signal changes with diffusion restrictions suggestive of leukodystrophy where eventually genetic testing aided in the final diagnosis.

The frequency of ALSP is variable and ranges from 0.6% to 10% of all leukoencephalopathies.\(^2\) The mean age of onset in a cohort of 119 patients was 43 years (range 18–78 years) with a disease duration of 6.8 years and no difference between genders.\(^3\) Predominant language impairment is extremely rare, and only a handful of cases are reported so far.\(^4,5\) Imaging features of ALSP are patchy to diffuse nonenhancing diffusion restricted lesions predominantly affecting the frontoparietal regions. Thinning of the corpus callosum and occasional lesions in pyramidal tracts are also evident.\(^6,7\)

A 54-year-old female, born to nonconsanguineous parents right-handed, undergraduate, home-maker presented with decreased speech output for 1.5 years and naming deficits. Gradually, she had a considerable reduction in verbal communication which progressed to pointing to the objects accompanied by a decreased interest in family issues. Difficulty in cooking and fluctuating behavioral disturbance with episodes of aggressiveness were observed. Partial dependence on the activity of daily living was reported. She had no major medical comorbidities and normal menstrual history. There was no family history of similar illness among her first- and second-degree relatives.

She was apathetic and had psychomotor slowing. The comprehensive cognitive assessment revealed impaired attention, memory disturbances (immediate, delayed, and remote) which improved with clues, digit forward recall adequate up to three words and digit backward recall-0, visuospatial deficits, grossly impaired frontal lobe functions, and calculation deficits. Language evaluation revealed word-finding pauses in spontaneous speech with no agrammatism, fair auditory word recognition for everyday used objects, difficulty in following complex commands, impaired repetition for greater than three-word phrases, semantic paraphasias in object naming, with phonemic cues being facilitatory for word recall and intact object knowledge. The generative naming and phonemic fluency were significantly reduced. She could consistently follow only the final aspects of a verbal command or select the second choice among the binary options, or repeat the final words of a question reflecting the possibility of a phonological working memory deficit.\(^8\) Reading and writing were also impaired. The Aphasia Quotient was 50.1, suggestive of moderate-severe language impairment. No signs of dysarthria or verbal apraxia of speech were present. Due to significant apathy, inattention, and behavioral disturbances, a detailed assessment of semantic memory could not be done. In the background of the word-finding difficulty and impaired repetition with otherwise fluent speech and semantic knowledge, a provisional clinical diagnosis of LvPPA was considered with odd features of inattention, apathy, and behavioral disturbance.

Clinical Dementia Rating scored 3 suggestive of severe dementia. Other system examinations were normal. Based on the history and clinical examination, a provisional clinical diagnosis of LvPPA was considered with some odd features. Routine blood investigations and investigations like autoimmune and paraneoplastic panel, anti-thyroid peroxidase (TPO) titers, serum venereal disease research laboratory (VDRL), human immunodeficiency virus (HIV), and electroencephalogram (EEG) were normal. MRI brain showed symmetric periventricular and deep white matter hyperintensity in T2-weighted images (T2WI) and corresponding patchy areas of diffusion restrictions involving periventricular and deep white matter in diffusion-weighted images sequence (DWI) with corresponding apparent diffusion coefficient (ADC) reduction. No areas of any blooming were noted on the susceptibility weighted image sequence (SWI). Midsagittal fluid-attenuated inversion recovery (FLAIR) image showed patchy involvement of the corpus callosum with sparing of subcortical white matter. Time-of-flight (TOF) angiography study showed a normal circle of Willis. Positron emission tomography-computed tomography (PETCT) brain fused images axial sections showed an asymmetrical decrease in tracer uptake in the left parietal-temporal region as compared to the right side. Following the investigations, a diagnosis of adult-onset leukodystrophy was suspected. Whole exome sequencing revealed a heterozygous pathogenic CSF1R mutation in exon 14 of variation c.1969+1G>A of...
Figure 1: Noncontrast computed tomography (a) axial image showed symmetrical periventricular and deep white matter hypodensities with cerebral atrophy. Coronal plain T1 (b) image showed hypointense signal involving periventricular and deep white matter. Axial T2w (c) section showing symmetric periventricular and deep white matter hyperintensity. Axial ADC (d) and DWI (e) sections showed corresponding patchy areas of diffusion restrictions involving periventricular and deep white matter. Axial Fluid Attenuated Inversion Recovery (FLAIR) (f) image showed hyperintense signal involving similar areas and ex-vacuo prominence of bilateral lateral ventricles. No areas of any blooming were noted on SWI sequence (not shown). Midsagittal FLAIR (g) & Axial (high frontoparietal) (h) image showed patchy involvement of corpus callosum with sparing of subcortical white matter. TOF Angiography study (i) showed normal circle of Willis. PET-CT Brain Fused images axial sections [j (1-4)] showed diffuse decrease in tracer uptake in left parietal, temporal region (Blue arrow) as compared to the right side without any increased uptake in periventricular and deep white matter.
There are no conflicts of interest.

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There are no conflicts of interest.

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