A Case of Rare Inflammatory Brainstem Syndrome: Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids

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Clinical Description

We report a case of a 23-year-old female with subacute onset of dysarthria, ataxia, vertigo, and bulbar involvement with magnetic resonance imaging (MRI) brain [Figure 1] showing diffuse T2 and fluid-attenuated inversion recovery hyperintensities involving the pons which appeared slightly expanded, with punctate foci of restricted diffusivity manifested as hyperintense signals on diffusion-weighted imaging images, with contrast enhancement and preservation of transverse pontine fibers. She had no history of or predilection to allergies. Her laboratory screening included complete blood count, renal and liver function, creatine kinase, C-reactive protein, erythrocyte sedimentation rate, serum protein electrophoresis, immunofixation, thyroid function test, lipid profile, Vitamin B12, and urinalysis. Autoimmune serological evaluations included antinuclear, antineutrophil cytoplasmic antibody (c and p), rheumatoid factor, complement levels, lupus anticoagulant, anti-beta-2-glycoprotein-1 and anticardiolipin antibodies, angiotensin-converting enzyme, anti-aquaporin-4 antibody, thyroid autoantibodies, and onconeural antibodies. Microbiological examination included hepatitis C, hepatitis B, human immunodeficiency virus, venereal disease research laboratory, *Treponema pallidum* hemagglutination, and *Borrelia burgdorferi* serological evaluations. Results for all these laboratory tests were normal or negative. She responded dramatically to pulse followed by maintenance corticosteroid treatment. In view of clinical features, typical MRI findings, not consistent with multiple sclerosis (MS), negative vasculitis and autoimmune markers, and good response to steroids, the patient was provisionally diagnosed as a case of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS). Six-month follow-up showed remarkable clinical and radiological improvements.

Discussion/Commentary

CLIPPERS is a central nervous system (CNS) inflammatory disease affecting the brainstem, cerebellum, and spinal cord, which was defined in 2010 by Pittock *et al.*[1] Clinical diagnostic criteria[2] include as follows: (a) subacute pontocerebellar dysfunction, (b) CNS symptoms responsive to corticosteroid therapy, (c) absence of peripheral nervous system disease, and (d) lack of alternative better explanation. Imaging criteria include as follows: (a) homogeneous, gadolinium-enhancing nodules without ring enhancement or mass effect predominating in the pons and cerebellum, measuring <3 mm in diameter, (b) marked improvement with corticosteroid treatment, (c) homogeneous T2 signal abnormality and (d) spinal cord lesions with similar T2- and gadolinium-enhancing lesions. Neuro-pathological criteria include as follows: (a) dense lymphocytic inflammation

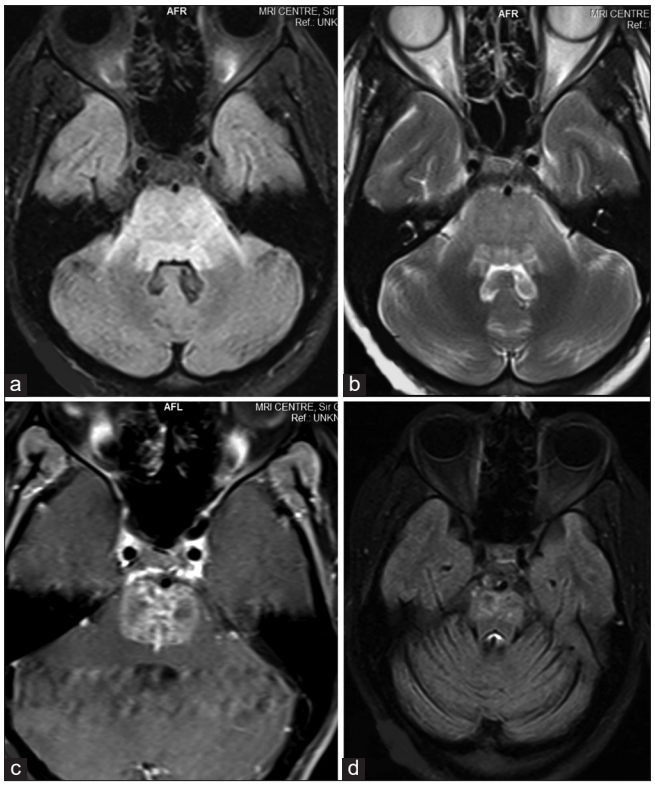

Figure 1: (a) Axial fluid-attenuated inversion recovery showing pontine hyperintensity extending into middle cerebellar peduncles without associated mass effect, (b) axial T2-weighted sequence showing diffuse lesions with altered signal intensity involving pons, (c) axial gadolinium-enhanced T1-weighted image showing patchy spot-like and curvilinear postgadolinium punctuate enhancement "peppering" the pons and spreading into the cerebellar peduncles with sparing of transverse fibers, and (d) axial fluid-attenuated inversion recovery on follow-up after 6 months showing significant regression of altered signal in pons, atrophy of anterior half of pons with sparing of the nuclei

with perivascular predominance and parenchymal diffuse infiltration, (b) T-cells predominating infiltration (CD4 > CD8) with variable macrophage components, (c) absence of myelin loss or focal secondary myelin loss, and (d) lack of alternative better explanation. Cerebrospinal fluid is usually noncontributory.

The presence of a perivascular and parenchymal inflammatory cell infiltrate and clinical response to immunosuppression suggests an autoimmune or other inflammatory-mediated pathogenesis. The location of the inflammatory infiltrate suggests that the target autoantigen is likely to be located in perivascular regions. Differentials include MS, glioma, lymphoma, autoimmune disorders, vasculitis, sarcoidosis, neuro-Behcet's disease, histiocytosis, and Bickerstaff's encephalitis. Pittock *et al*. suggested that CLIPPERS diagnosis could be made without brain biopsy if clinical and MRI features of the disease were present and if alternative diagnoses are excluded. Corticosteroid responsiveness is prompt with significant clinical and radiographic response, with relapses known when steroids are withdrawn or tapered below 20 mg PO daily. Patients require long-term maintenance immunosuppressive agents.

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.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

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