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A Rare Case of Anti Dopamine D-2 receptor antibody encephalitis

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Abstract

Regional encephalitic syndromes described previously under various names which include basal ganglia encephalitis and encephalitis lethargica specifically affect basal ganglia (1).

These disorders are proposed to be autoimmune in etiology (1) basal ganglia encephalitis (BEG) patients present with subcortical features which include movement disorders like dystonia, parkinsonism or chorea (2). These patients also present with hypersomnolence and psychiatric features like emotional lability and attention deficit, psychosis & obsessive compulsive disorder.

Response to immunotherapy, histopathology of basal ganglia revealing lymphocytic cuffing and inflammatory CSF(lymphocytic pleocytosis & oligoclonal bands) support autoimmune process which targets grey matter neurons (1,3). FDG-PET done in these patients mostly demonstrate basal ganglia hypermetobolism.

MRI in some of these patients reveals T2 weighted hyperintensity, basal ganglia swelling and sometimes signal change in brainstem with basal ganglia gliosis and atrophy on follow up scan (1,4). In view of important role of dopamine as neurotransmitter and its impact on movement and psychiatric disorder, Dale et al. did analysis on dopamine receptor as target for auto antibodies in these patients (4) .

Case Report

A 43 year old female with underlying hypertension presented with sub acute onset dysarthria, dysphagia and drooling of saliva of 5 days duration without any history of fever, rash, polyarthralgia, loss of consciousness, seizure, diplopia, facial weakness, numbness, limb weakness, bladder/bowel symptoms with examination revealing her to be conscious, comprehending verbal commands but little agitated, producing incomprehensible sounds with bilateral 9^{th} and 10^{th} cranial nerve palsy, generalized rigidity all over, brisk reflexes all over with upgoing plantars and rest of the examination was normal.

Investigations revealing normal CBC, KFT, LFT, Lipid Profile, routine urine examination, chest x-ray, ECG. Widal, brucella, vasculitic profile, wilson's profile, TSH, Ft4, Anti TPO. CPK, lactate, iron profile, iPTH, tumour markers, triple serology was normal. USG abdomen/ pelvis/ breasts, USG Doppler neck, CECT chest abdomen pelvis, CT Head, MRA MRV Brain were normal. MRI brain was showing bilateral basal ganglia (caudate and lentiform nuclei) hyperintense signal changes without restricted diffusion or abnormal susceptibility. CSF

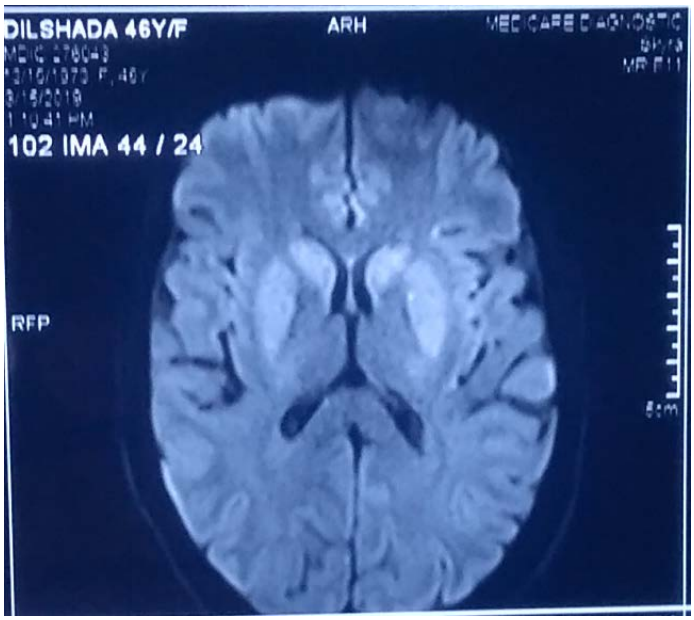
showing neutrophilic pleocytosis, normal sugar, protein, ADA, Gram Staining, AFB Staining, fungal staining and CBNAAT negative, CSF HSV PCR negative. Paraneoplastic profile, autoimmune profile of CSF was negative except anti D2 receptor antibody.

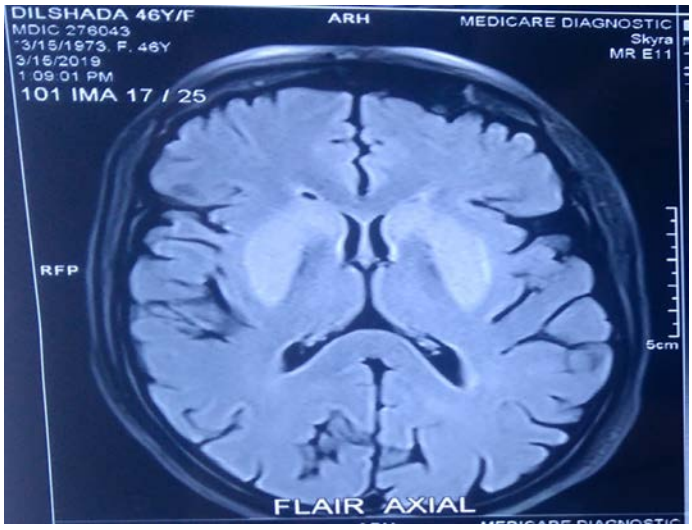
Patient was managed with ryles tube feeding, antiparkinsonian drugs in view of parkinsonian features and on the line of autoimmune encephalitis, she was given 5 doses of IV methyl prednisolone 1g/day with no improvement. Patient was then given IVIG 400mg/kg/day for 5 days and there was dramatic improvement in her symptoms and signs and within 10 days patient was able to take orally.

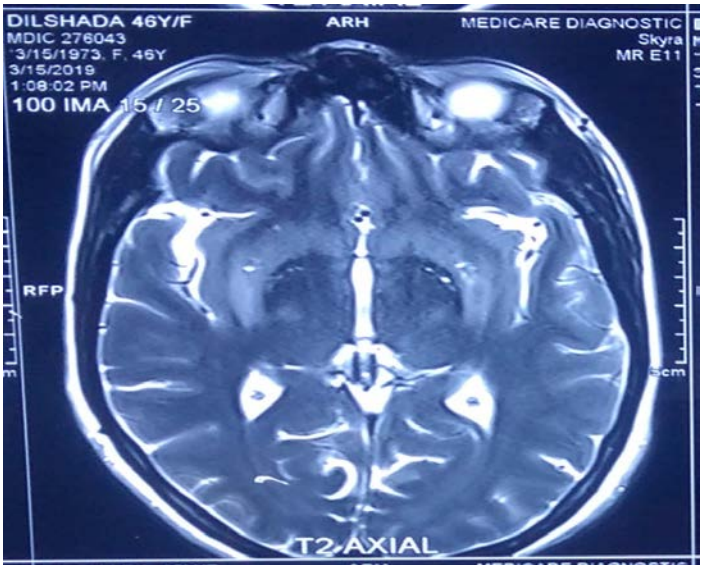
Discussion

In humans there are five subtypes of dopamine receptors which are rhodopsin like seven transmembrane G protein coupled receptors, and are divided into 2 groups D1 like group (D1R, D5R) and D2 like group (D2R, D3R, D4R) on the basis of their structural biochemical and pharmacological properties (5,6). Dopamine receptor expression, innervation in humans are prominent in the brain, important in regulation of psychological and neuromuscular functioning like behavior, learning , working memory, gross and fine motor control(6)

Dale et.al in a survey found that out of 17 children with basal gangalia encephalitis 12 were negative for Anti-N-methyl-D-aspartate receptor (anti-NMDA-R) antibodies but had elevated IgG antibodies to extracellular dopamine 2 receptor (D2R) against 67 pediatric controls which were negative for IgG antibodies to D2R. In D2R positive patients, no binding was demonstrated to dopamine 1,3, or 5 receptors, NMDA-R or dopamine transporter immunolabelling was grossly decreased in D2R knockout brains providing further evidence of the role of D2R as target antigen basal ganglia encephalitis patients diagnosed recently who received early immune therapy have shown complete clinical recovery and a reduction in antibody titres (4). On the contrary patients diagnosed retrospectively who received only steroids without immunomodulatory therapy had residual psychiatric, neurological symptoms and high titres of antibody. Some patients who persisted with anti D2R have shown subsequent relapse seen in autoimmune encephalitis (unpublished data). These antibodies bind to extracellular domain of D2R but their pathogenicity is yet to be demonstrated further study is needed to evaluate role of antibodies in adults and other disease subtypes.







Images A, B & C (Diffusion/ FLAIR/ T2) MRI Brain Images Showing bilateral caudate nucleus and putamen hyperintensities.

Dale et.al recently found in a survey that in 12 children this encephalitis and anti D2 antibodies were associated with many types of movement disorders which may co-exist in same patients included tremor, dystonia, parkinsonism, oculogyric crisis and or chorea (7), frequently accompanied by a gitation psychosis, anxiety and sleep disturbances. In 50% of patients MRI brain was normal, when abnormal findings were localized to basal gangalia patients showing response to immune therapy but residual cognitive, motor, psychiatric deficits were seen. In 120 patients mostly children with encephalitis associated with abnormal movements or basal gangalia MRI abnormalities all were negative for D2 antibodies (Armangue et al., data unpublished).

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