Progressive Encephalopathy in an MS Patient Responsive to Plasma Exchange

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Case History
In 2009, this thirty-three year old gentleman with a ten-year history of Multiple Sclerosis and relapsing course, had an episode of marked deterioration of cognitive function, with decreased muscle strength, balance, and walking abilities that progressed over three months. The patient had received a total of 77 infusions of natalizumab to date, with brief interruptions, after doing well in clinical trial with natalizumab and having failed interferon therapy previously.

This patient received his last natalizumab infusion in the fall of 2009 and sought opinion elsewhere one month later at which time he was briefly treated with cyclophosphamide due to complaints of worsening motor and cognitive status and belief that he had experienced breakdown disease. Within three months the patient returned to our center where he was admitted due to continued progression of encephalopathy and motor disturbance. Magnetic resonance imaging of the brain showed new lesions from prior scans.

Due to concern of Progressive Multifocal Leuкоencephalopathy, lumbar puncture was performed (and subsequently repeated) revealing negative polymerase chain reaction for JC virus in the spinal fluid (on two occasions). The patient's encephalopathic status markedly improved with Plasma Exchange Therapy. Because he responded with dramatic improvement, continued pulse treatment with plasma exchange was maintained thereafter, through 2012. Of note, the patient also initiated glatiramer acetate therapy in March 2010, and has done well on this combination.

Objective
To describe a case of progressive encephalopathy in the setting of natalizumab therapy that responded to plasma exchange, including magnetic resonance imaging, and discussion of management.

MRI at presentation
FLAIR T2 MRI showing new confluent lesions

Subsequent Imaging
Follow-up FLAIR T2 MRI revealed improvement of some of the patient's lesions from imaging performed circa presentation with encephalopathy; this was coupled with clinical stabilization in the setting of continued plasma exchange and glatiramer acetate therapy

Discussion
It is unclear why this patient had such a fulminating clinical and radiographic presentation, and the timing of his presentation and cessation of natalizumab therapy raises a number of diagnostic and treatment dilemmas.

Plasma exchange constitutes an extracorporeal blood purification technique designed to remove large molecular weight particles from plasma. The removal of circulating autoantibodies, immune complexes, cytokines, and other inflammatory mediators is thought to be the principal mechanism of action of plasma exchange.

This patient's response could indicate a mechanism of action of plasma exchange, namely the removal of pathogenic humoral and plasma factors. This therapy has also been used in cases of worsening status in multiple sclerosis patients treated with natalizumab, particularly in the diagnosis and treatment of progressive multifocal leukoencephalopathy.

Improvement with this therapy in multiple sclerosis with acute exacerbations has been described as rapid and associated with male sex. Despite this small sample size of one, we believe chronic treatment may be of benefit.