



Regression: An Atypical Presentation of Lupus Cerebritis

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Received date: March 28, 2017; Accepted date: April 21, 2017; Published date: April 26, 2017

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Abstract

Neurologic manifestations in systemic lupus erythematosus (SLE) ranges broadly from more common manifestations such as headaches, mood disorders, cognitive dysfunction, cerebrovascular disease to rarer ones including Guillan Barre syndrome, myasthenia gravis and autonomic dysfunction.

We present a case of a 39 year old Hispanic female with newly diagnosed SLE who presents with childlike behaviour. She had serologic evidence of lupus activity and all infectious etiology was ruled out. She had a protracted course but symptoms were eventually controlled with intravenous steroids, cyclophosphamide, rituximab and intravenous immunoglobulin.

This case is reported because regression has not previously been documented as one of the possible manifestations of neuropsychiatric SLE.

Introduction

Systemic Lupus erythematosus (SLE) is a chronic inflammatory connective tissue disease characterized by autoantibodies and immune complexes [1]. The term cerebritis (LC) simply implies that there is active inflammation occurring in the cerebral cortex. However, LC falls under the definition of Neuropsychiatric SLE (NPSLE) as defined by the American college of Rheumatology in 1999. NPSLE can be the initial presentation of SLE or can occur at any point during the course of the disease [2]. It is estimated that the prevalence of NPSLE ranges widely from 12-95% in SLE patients [3,4]. Neurologic manifestations can be nonspecific such as headaches and irritability, focal for example cranial nerve palsy and a cerebrovascular event or lastly psychiatric and present with depression and personality disorders [1,2]. In a meta-analysis performed by Unterman et al, the most common presentations were headaches, mood disorders, seizures, cognitive dysfunction and cerebrovascular diseases. Myelopathy, plexopathy and Guillain Barre Syndrome are the least frequent syndromes. We present the case of a 39 year old previously healthy Hispanic female who presents with childlike behavior.

Case Presentation

A 39 year old female presented to our facility brought in by her husband for change in behavior, compulsiveness, disorganization and culminating in childlike behavior. These included sitting on the floor, expressing she is 3.5 years old, babbling speech and repeating what is said to her in a singsong voice or as part of a rhyme. However it was reported that she did have occasional lucid moments. Prior to this, patient had no history of any neuropsychiatric conditions. She had been diagnosed with SLE few months previously, after she had presented with malar rash and right eye vision loss due to retinal

vasculitis and was started on oral prednisone 60 mg a day with some improvement in her symptoms.

At presentation her vitals were only significant for tachycardia. There was no leukocytosis. She had high titers of anti-nuclear antibody (ANA), anti- double stranded (ds) DNA antibody, low Complement 4 (C4) levels, positive anti Ro and La and anti ribonucleoprotein (RNP) antibodies. Cerebrospinal fluid (CSF) analysis was negative for any infectious pathology and anti-N-Methyl-D-aspartic acid (NMDA) receptor antibodies were negative. Other sources of infection including respiratory, urinary and intra-abdominal were ruled out. Urine porphyrins was within normal limits. Magnetic resonance imaging and computed tomography were both negative for an acute intracranial pathology and electroencephalogram showed no seizure activity.

The patient was given one dose of cyclophosphamide and high dose intravenous methylprednisolone for three days. She experienced some improvement but her behavioral changes had not fully resolved at discharge. She was readmitted to the medical intensive care unit one week later for a relapse in regressive symptoms; and received IVIG infusion for 5 days and intravenous methylprednisone 40 mg once a day. Seven days after admission patient had minimal improvements in her mental state. Rituximab 100 mg IV was infused after hepatitis B and C serologies were checked and found to be negative. Her mood and agitation were controlled by psychotropic medications such as quetiapine. Patient began to show some improvements in her concentration and her speech. Patient was able to recall 2 out of three objects and her babbling and sing-song response to questions was decreased. She was discharged home on day 12 to receive the second dose of rituximab outpatient two weeks from first dose.

One month after discharge, she was back to her baseline mental status.

Discussion

The exact pathogenesis of LC and NPSLE as a whole is unknown however; multiple factors have been implicated including, circulating immune complexes, anti-neuronal antibodies, antiphospholipid antibodies, focal vascular events and cytokine release [1-5]. The role of IgG anti neuronal antibodies was demonstrated by Bluestein et al. who showed that antineuronal antibodies were higher in the CSF of SLE patients with active neuropsychiatric presentation compared to SLE patients without active neuropsychiatric disease. It appears as though these antibodies cross the blood brain barrier either via vesicle formation or via the choroid plexus [6,7]. In addition, the presence of immune complexes leads to an inflammatory response causing a break in the blood brain barrier [8]. Focal vascular events may explain cerebrovascular events, cranial neuropathies and plexopathies but is unlikely to explain the more diffuse NS symptoms such as cognitive dysfunction and mood disorders as these are unrelated to brain cell death [7].

Over recent years, the role of cytokines have been investigated in the pathogenesis of NPSLE lupus [9-11]. In a study by Wang et al., they compared the levels of certain cytokines, Interleukin (IL)-1 β , IL-8, IL-6, and interferon (IFN) γ in the serum and CSF of patients with NPSLE, those with lupus but without CNS symptoms, patients with intracranial infection and normal controls. The outcome of their findings suggested that IL-6 has a role in increasing blood brain barrier permeability and resulting in brain injury, IL-1 β is nonspecific for NPSLE and IFN γ plays a role in inducing multiple ischemic foci. Finally they proposed that elevation of IL-6 and 8 may increase the risk of NPSLE [10]. Other cytokines implicated include IL-2,10, tumor necrosis factor α and IFN α [11].

There are no definitive diagnostic criteria however, in a patient with neuropsychiatric manifestations, a history of SLE and laboratory findings demonstrating low complement levels and high titres of implicated antibodies (lupus anticoagulant, antiphospholipid, antineuronal, anti-ribosomal P, anti-ganglioside, anti-cardiolipin and brain lymphocyte cross reactive antibodies) and cytokines NPSLE should be suspected especially when other more common etiologies such as cerebral ischemia/hemorrhage and infections have been ruled out [7,8].

Treatment depends of the severity of the disease and symptoms. Those presenting with migraines, anxiety or mood disorder may be treated symptomatically. Individuals with seizures, cerebrovascular events should also be treated as per standard guidelines, bearing in mind that long term anticoagulation may be needed for those with antiphospholipid syndromes [12]. The main stay of diffuse NS lupus such as cognitive dysfunction as in our patient is immunosuppressants

starting with steroids; however, in more severe or refractory cases cyclophosphamide is the second line of treatment [12]. Several case reports have been published in which IVIG has provided resolution of symptoms [5,8,9]. Other therapeutic approaches have included rituximab, intrathecal methotrexate, azathioprine and plasmapheresis [12].

To the best of our knowledge, this is the first reported case of refractory NS symptoms presenting with regression and requiring four different immunosuppressive agents to obtain resolution of symptoms.

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