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Case Report

A severe case of systemic lupus erythematosus with increased pressure communicating hydrocephalus

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Abstract

Normal/increased pressure hydrocephaly is an unusual manifestation of systemic lupus erythematosus (SLE), and the pathogenesis is still unclear. We report the case of an 18-year-old white female with severe refractory renal and pulmonary involvement who developed stupor during intensive immunosuppressive treatment. Enlarged ventricles on imaging and increased intracranial pressure with the exclusion of infectious and hemorrhagic/thrombotic processes suggested increased pressure communicating hydrocephalus associated with SLE. Few case reports are reviewed, and potential pathophysiologic mechanisms are discussed.

Keywords: Hydrocephalus, increased pressure communicating, systemic lupus erythematosus

Introduction

During any time point in the course of systemic lupus erythematosus (SLE), up to 75% of patients show neuropsychiatric involvement, one of the major causes of morbidity and mortality in SLE (1). Neuropsychiatric lupus includes various syndromes affecting central, peripheral, and autonomic nervous systems, but increased pressure communicating hydrocephalus is a rarely recognized complication in SLE. We report the development of increased pressure communicating hydrocephalus in SLE in concomitance with severe renal and pulmonary involvement and discuss the underlying pathophysiologic mechanisms.

Case Presentation

An 18-year-old female was diagnosed as having SLE with polyarthritis, photosensitivity, lymphopenia, and anti-nuclear antibody (ANA) positivity in 1/1280 titer, and she was treated with hydroxychloroquine. One year after diagnosis, she presented with pretibial edema. Laboratory evaluation revealed pancytopenia, hypocomplementemia, positive anti-dsDNA, 3.7 g/day proteinuria, and active urinary sediment with a serum creatinine of 0.8 mg/dL. Coombs' tests, antiphospholipid antibodies, and lupus anticoagulant were negative. Renal biopsy revealed class IV lupus nephritis (activity index: 15/24, chronicity index: 4/12). Pulse methylprednisolone (1 g/day, 3 days) and 500 mg intravenous (iv) cyclophosphamide (CYC) treatment was started; however, creatinine increased up to 2 mg/dL. Plasmapheresis and repeat pulse methyprednisonole (3 days) were also unsuccessful. Along with maintenance methylprednisolone at 1 mg/kg/day, she received 2 more cycles of 500 mg iv CYC biweekly. Subsequently, she developed hemoptysis. Thoracic computed tomography (CT) revealed bilateral consolidations. Besides ventilatory support, hemodialysis, and antibiotics, she received pulse corticosteroids and iv immunoglobulin. Pulmonary functions improved; however, recurrent hemoptysis and daily hemodialysis requirement continued. Finally, rituximab (2 infusions of 500 mg, 2 weeks apart) was initiated. Within 2 weeks, hemoptysis disappeared, hemodialysis was reduced to 3/week. Although clinically stable, 3 weeks after 1st dose of rituximab, stupor and slurred speech emerged. Neither focal neurologic deficits, meningeal irritation signs, nor fever was detected. Except moderate uremia, there was no other metabolic/hemodynamic disturbances. Cranial CT showed enlarged lateral ventricles without hemorrhagic, parenchymal, or venous/arterial lesions (Figure 1). A ventricular drainage catheter was placed. Intracranial pressure (ICP) was measured as 320 mmH_2O. Cerebrospinal fluid (CSF) was normal without pleocytosis (protein=10 mg/dL). Gram/acid-fast stain examinations, aerobic/fungal cultures, Mycobacterium tuberculosis polymerase chain reaction were all negative. As no other explanatory cause was detected, the condition was regarded as SLE-associated increased pressure communicating hydrocephalus. Recent intensive immunosuppressive (IS) treatment and the lack of evidence hindered further immunosuppresion. Initially, mental status improved; however, within 3 days, deterioration occurred. CSF examinations and CT were repeated. Signs of superimposed infection or hemorrhage was absent. Despite all supportive measures, the patient died a week after the onset of hydrocephalus.

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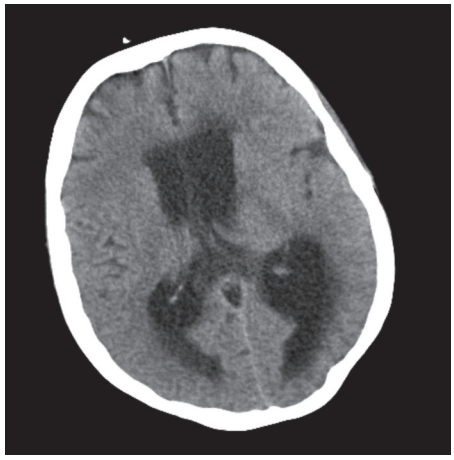

Figure 1. Cranial computed tomography (CT) in transverse view revealed ventricular dilation without widening of the sulci

Discussion

Hydrocephalus is an unusual manifestation of SLE and has challenging differential diagnosis and management. In the literature, there have been few reports of SLE complicated with normal pressure hydrocephalus (NPH) or hydrocephalus associated with bacterial/tuberculous meningitis or hemorrhage (2-4). SLE-associated increased pressure communicating hydrocephalus has been reported in only two cases so far (5). In contrast to those cases, hydrocephalus in our patient developed along with severe renal and pulmonary involvement during intensive IS therapy and was fatal despite adequate CSF drainage. Although unresponsiveness to ICP reduction suggested accompanying infectious or hemorrhagic/thrombotic processes, serial CSF analysis and cranial imaging did not reveal any pathology. Furthermore, other causes of mental status changes such as electrolyte disturbances, hypo-/hypertensive episodes and signs of SLE-associated conditions such as reversible posterior leukoencephalopathy and thrombotic thrombocytopenic purpura were absent.

The pathogenesis of SLE-associated NPH has not been fully elucidated yet. Proposed mechanisms are meningeal inflammation, vasculitis and microthrombi secondary to phospholipid antibodies, or lupus activity (2, 5, 6). Honda et al. (2) have reported dural deposition of immunoglobulins and complement components without cellular infiltration and microinfarcts in SLE-associated NPH. However, Kitching et al. showed leptomeningeal round cell infiltration and organizing thrombus in SLE-associated increased pressure communicating hydrocephalus and hypothesized that aseptic meningitis and microinfarction may play a pivotal role in the pathogenesis (5). It is unknown whether increased pressure communicating hydrocephalus is a more severe and advanced form of NPH in SLE (2-5). Interestingly, in our case, none of CSF analysis was consistent with aseptic meningitis. Moreover, a well-known associated syndrome, antiphospholipid syndrome (APS)-hydrocephalus, was absent in our patient (6). Finally, medications, accompanying uremia, and hypertension should be kept in mind as aggravating or initiating factors. High-dose corticosteroid therapy and uremia may induce cerebral edema and intracranial hypertension (7); however, no association between hydrocephalus and those conditions has been demonstrated. Similarly there is no evidence that either rituximab or CYC causes intracranial hypertension or hydrocephalus in SLE and other autoimmune diseases or malignancies.

Despite scarce evidence of inflammation and thrombus in the pathogenesis, there are no data about the efficacy of IS or anticoagulation therapy in the absence of APS or obvious thrombotic events. Prompt CSF drainage with shunt surgery and continuous pressure regulation seem to be the only effective treatment for now. Careful monitoring of infectious or hemorrhagic/thrombotic processes, blood pressure, and drug toxicity are also paramount importance.

In conclusion, neuropsychiatric symptoms in SLE patients should be evaluated promptly and carefully, considering rare manifestations of neuropscyhiatric lupus in differential diagnosis. Advanced imaging techniques and postmortem brain and leptomeningeal tissue immunohistochemical examinations may reveal the exact underlying pathogenesis of this phenomenon.

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