Case report

LUPUS JOURNEY: THE CHALLENGE OF OBSTRUCTIVE HYDROCEPHALUS

ABSTRACT

Systemic lupus erythematosus (SLE) is a complex autoimmune condition known for its diverse clinical presentations. Neuropsychiatric SLE refers to neurological or psychiatric symptoms that arise once other potential causes have been ruled out. While hydrocephalus occurring in the context of SLE is exceedingly rare and its underlying mechanism remains elusive, its recognition is crucial for informed management decisions.A 20-year-old female patient, diagnosed with SLE, had been under our rheumatology clinic's care for two years. She recently presented with confusion, which emerged a year after her initial diagnosis. Brain tomography revealed obstructive hydrocephalus, and subsequent investigations ruled out other potential causes, linking the condition to her clinical SLE.

Keywords:lupus, SLE, hydrocephalus, obstructive, NPSLE, systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematosus (SLE) is a profound systemic autoimmune disorder marked by dysfunction in multiple organs, presenting with a diverse array of clinical manifestations(1). Neuropsychiatric systemic lupus erythematosus (NPSLE) encompasses neurological or psychiatric symptoms observed during the course of SLE, after excluding other potential causative factors through clinical, laboratory, and imaging evaluations(2).The literature reports an estimated prevalence of neuropsychiatric syndrome among patients diagnosed with SLE as 80%, with a prevalence rate of 28% at the time of diagnosis(3).NPSLE may manifest in the clinic with involvement of the peripheral or central nervous system (CNS) in either an isolated or diffuse manner. Diagnosis poses a significant challenge for rheumatologists, as specific and sensitive laboratory or cerebrospinal fluid (CSF) biomarkers are lacking, along with guiding criteria(4).Aseptic meningitis, cerebrovascular disease, encephalopathy, and movement disorders have all been documented as CNS involvements in NPSLE. However, hydrocephalus occurring in the course of the disease is exceptionally rare in the literature, with its mechanism not yet fully elucidated, and a clear treatment plan remains elusive(5). In this instance, we will discuss the case of a female patient diagnosed with SLE presenting with the rare and perplexing phenomenon of increased pressure hydrocephalus, alongside our own experience in managing such patients.

CASE PRESENTATION

A 20-year-old female patient had been under the care of our rheumatology clinic for two years following a diagnosis of SLE. She was diagnosed two years ago following symptoms of polyarthritis, oral ulcers, malar rash, lymphopenia, thrombocytopenia, and positivity for anti-

nuclear antibodies (ANA) at a titer of 1/1280, as well as anti-double stranded DNA (anti ds-DNA)(6).While the patient was being managed with hydroxychloroquine following the diagnosis, she presented to our clinic one year later with complaints of nausea, vomiting, polydipsia, and polyuria. Blood tests at this time revealed negative results for antiphospholipid antibodies (APA) and lupus anticoagulant, and no metabolic or hemodynamic disorders were detected apart from mild uremia.Following the onset of confusion upon admission, the patient, who did not present with focal neurological deficits, fever, or signs of meningeal irritation, underwent a brain computed tomography (CT) scan to evaluate potential intracranial pathologies. The CT scan revealed enlarged lateral ventricles, unaccompanied by parenchymal, hemorrhagic, arterial, or venous lesions. (figure 1) The patient was referred to neurosurgery for consultation. A ventricular drainage catheter was inserted by the neurosurgeon, and the intracranial pressure was measured at 270 mmH_2O. No cellular increment was detected in the CSF and all Gram stain, acid-fast stain, fungal and bacterial cultures, as well as mycobacterium tuberculosis polymerase chain reaction samples, returned negative results.As no other explanatory cause for hydrocephalus could be identified, the patient's condition was assessed as increased pressure hydrocephalus associated with SLE. Following the insertion of the ventricular drainage catheter by the neurosurgeon, the patient's clinical status significantly improved within three days.The nausea, vomiting, polyuria and polydipsia, likely caused by ADH deficiency stemming from hydrocephalus, subsided. As the patient's condition improved, the ventricular drainage catheter was removed, and following its removal, the patient's neurological status was closely monitored by the neurosurgery team. A follow-up brain CT scan was conducted on the patient, whose neurological examination showed no deterioration, revealing minimal enlargement of the ventricles. (figure 2) After two more days of monitoring with the drainage catheter closed, it was removed. The patient's neurological status remained stable, and in response to the developing NPSLE situation, a regimen of three 1 gram/day pulse doses of methylprednisolone followed by 1 mg/kg methylprednisolone therapy was initiated.The steroid dose was gradually reduced and adjusted during follow-up. Additionally, mycophenolate mofetil was introduced to the patient's regimen as an immunosuppressive agent. Over a period of seven months under maintenance methylprednisolone, hydroxychloroquine, and mycophenolate mofetil, there was no recurrence of hydrocephalus. Currently, the patient is being jointly monitored by the rheumatology and neurosurgery clinics.

DISCUSSION

NPSLE has been linked to elevated mortality and morbidity rates among patients. CNS involvement, a hallmark of NPSLE, can be observed to varying extents in up to 75% of patients(5).However, hydrocephalus is exceedingly rare, and its underlying mechanism remains unclear. Proposed developmental mechanisms include meningeal inflammation, vasculitis, microthrombi formation due to phospholipid antibodies, and lupus activity(7).Among the reported cases, microinfarctions resulting from organized thrombus formation and leptomeningeal cell infiltration, along with concomitant aseptic meningitis, have been identified as key contributors to the pathogenesis of hydrocephalus(8).

A review of the literature revealed ten reported cases of increased pressure hydrocephalus occurring in the course of SLE thus far. Notably, one of these cases, reported from our country, documented hydrocephalus development despite the patient receiving intensive immunosuppressive therapy. Tragically, the patient succumbed despite effective cerebrospinal

fluid drainage(9).In another case, cerebellar ataxia was observed alongside hydrocephalus, prompting a biopsy from the cerebellar vermis. The biopsy revealed findings consistent with fibrinoid necrosis, indicative of vasculitis(10).The patient underwent intravenous cyclophosphamide treatment, resulting in regression of cerebellar edema. In our case, clinical stabilization was achieved through pulse steroids and mycophenolate mofetil, which was initiated during follow-up.

The literature identifies increased APA at medium or high titers, prior or recurring NPSLE events, heightened SLE activity, or organ damage resulting from SLE activity as risk factors for the development of hydrocephalus in the context of SLE(11).In our case, APA tested negative, ruling out antiphospholipid syndrome-associated hydrocephalus, a well-documented syndrome. Furthermore, our patient had no history of prior NPSLE events, and SLE activity had escalated just before the onset of hydrocephalus.

Recent studies have suggested a close association between hydrocephalus development in the context of SLE and CNSinfections(12). However, due to the broad spectrum of symptoms and findings associated with SLE, distinguishing between infection, hydrocephalus, or overlap syndromes can be challenging when CNS involvement occurs. In our case, CSF samples collected from the ventricle yielded no microbial growth, and there was no evidence of aseptic meningitis. Additionally, the patient presented no systemic signs of infection, leading to the initial consideration of obstructive hydrocephalus.

Although evidence of inflammation and thrombosis implicated in the pathogenesis is limited, there remains insufficient data regarding the efficacy of anticoagulant or immunosuppressive therapy in the absence of APA and concurrent thrombotic events. Effective CSF drainage and, if warranted, shunt surgery appear to constitute the primary treatment modalities in such cases.While studies in the literature demonstrate the superior efficacy of intravenous cyclophosphamide over high-dose steroids in the induction treatment of NPSLE, such specificity has yet to be established for hydrocephalus within this spectrum. In our case, the patient's clinical condition improved with pulse steroids administered adjunctively to surgery(13).

To the best of our knowledge, our case represents the eleventh reported instance in the literature of obstructive hydrocephalus occurring in the course of SLE and the third case documented in our country(9, 14). The manifestation of obstructive hydrocephalus in the context of SLE can present a perplexing clinical scenario for rheumatologists. The objective of reporting this case is to raise awareness regarding this phenomenon. In the management of SLE patients, particularly in instances of heightened disease activity where symptoms and findings suggest NPSLE, it is crucial to recognize the diverse presentation of this condition. Management of such cases necessitates a multidisciplinary approach involving rheumatology, infectious diseases, and neurosurgery.

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FIGURE LEGENDS

Figure 1. enlarged lateral ventricles, unaccompanied by parenchymal, hemorrhagic, arterial, or venous lesions.

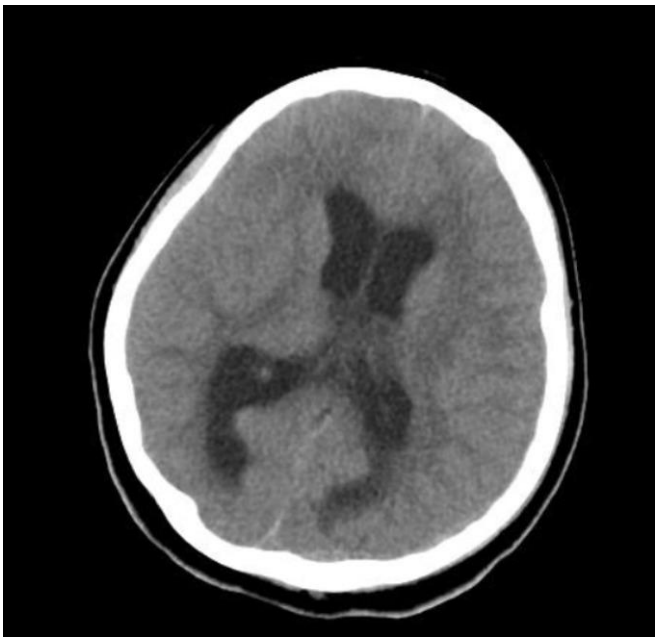

Figure 2. Cranial CT revealing minimal enlargement of the ventricles