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Case report

Intracranial hypertension as the first manifestation of systemic lupus erythematosus: A case report

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ABSTRACT

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple systems and organs, including the central and peripheral nervous systems. Papilledema and idiopathic intracranial hypertension, in the absence of space-occupying lesions or other detectable causes, is a rare manifestation. We report the case of a young woman with chronic headache, papilledema, and intracranial hypertension on examination, in whom a de novo diagnosis of systemic lupus erythematosus and class V lupus nephritis was made. It is important to recognize this association when the review of systems supports it.

Case report: A 19-year-old Colombian woman with recent hypothyroidism presented with a chronic severe headache and was found to have papilledema. She reported several systemic symptoms including hair loss, skin dryness, and edema. Brain MRI and lumbar puncture were conducted, with high opening pressure noted but no significant abnormalities. She was diagnosed with Systemic Lupus Erythematosus (SLE) based on symptoms and positive autoimmune markers. Treatment with methylprednisolone and other medications led to an improvement in her symptoms, and a renal biopsy confirmed lupus nephritis class V. The comprehensive treatment regime effectively managed her symptoms.

Conclusion: In the case of papilledema with idiopathic intracranial hypertension, always carry out an in-depth review by systems to rule out SLE as a cause.

1. Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disease with a chronic, remitting, and relapsing course with manifestations in multiple organs, which can range from mild to life-threatening symptoms [1]. It predominantly affects women between puberty and menopause.

It is explained by the breakdown of self-tolerance and systemic inflammation mainly because of hyperactivation of peripheral B and T cells, resulting in high levels of pathogenic autoantibodies, tissue deposition of immune complexes, and, ultimately, injury of multiple and diverse organs, where the most common are the cutaneous and musculoskeletal [2]. The diagnosis of SLE is made

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according to the clinical manifestations and laboratory tests to detect serological changes regarding decreased complement levels and elevated autoantibodies [3].

Intracranial hypertension (IH) is not included among the diagnostic criteria defined by the American College of Rheumatology (ACR) as one of the neuropsychiatric manifestations of lupus [4]. However, literature suggests an association between these two entities causing leading experts to reconsider this concept. Although there are previous reports of idiopathic intracranial hypertension associated with lupus, the pathogenesis is unclear [5]. Some mechanisms could be aseptic meningitis, depot of immune complexes on the arachnoid villi, or the micro-occlusion of these villi [6].

In recent years, treatment strategies have made significant advances to provide patients with these two entities with a better prognosis; but there are still many challenges in the definitive diagnosis and treatment [7]. The following describes the case of a patient in whom a de novo diagnosis of SLE was made, with papilledema and intracranial hypertension as index finds.

2. Case description

A 19-year-old Colombian woman, mixed race, with a recent diagnosis of hypothyroidism in substitution with Levothyroxine, had a year of oppressive headache in the nasal bridge, irradiated to the left upper orbital region and the occipital region that relieved with the use of NSAIDs and Acetaminophen. The headache occurred six days a week, sometimes associated with nausea, photophobia, and phonophobia, without visual acuity or diplopia alterations. In a routine ophthalmology consultation, two days before she was admitted, they found papilledema in the left eye fundus, which is why she was referred to the emergency room. In the review of systems, the patient reported a two-year history of hair loss with alopecia, xeroderma, onycholysis, and koilonychia, with unintentional weight loss of approximately 4 kg asthenia and adynamia. Additionally, one month before admission, she presented edema in the lower limbs with prolonged standing and facial edema in the left side.

On physical examination, the patient was admitted alert, without alteration in higher mental functions, no compromise of the cranial nerves, preserved strength and sensitivity, and without meningeal signs. We documented areas of capillary fragility with ecchymosis on the arms' skin. A brain MRI was performed, which incidentally reported an anomaly in the right frontal venous development, without space-occupying lesions or other alterations. A lumbar puncture was performed, finding an opening pressure of 40 cm H2O. The cytochemistry of the cerebrospinal fluid (CSF) had no alterations, and the microbiological studies were negative (Table 1). After the lumbar puncture, the patient presented improvement of the symptoms, and it was decided to start management for intracranial hypertension with Acetazolamide. At the same time, during hospitalization, she had high blood pressure, for which the laboratory tests described in Table 2 were performed. The autoimmune profile showed positive complement consumed, with positive ENAS, Anti-DNA, and ANA. ANCA and Antiphospholipid antibodies were negative. Rheumatology made a de novo diagnosis of Systemic Lupus Erythematosus (SLE) due to alopecia, renal (proteinuria and hypoalbuminemia), and neurological (papilledema with IH), immunological (hypocomplementemia, positive ANA, Anti-Ro, Anti-Sm, Anti-RNP and Anti-DNA by EIA) involvement, with a SLEDAI-2K of 18 points. Management was begun with pulses of methylprednisolone 1 g for three days followed by prednisone 50 mg per day (previous deworming). A new ophthalmological examination was performed, which documented a pink disc in the fundus, erased borders in both eyes with 10 % excavation, macula, and normal vessels, without alterations on the Ishihara test or afferent pupillary defect. Nephrology performed percutaneous renal biopsy guided by ultrasound which reported a class V lupus nephritis, without interstitial fibrosis or atrophy, with an activity index of 0/24 and a chronicity index of 0/12 (Fig. 1a–c). Mycophenolate Mofetil at a dose of 2 g, Chloroquine 150/250 mg, Prednisone 50 mg daily, Acetazolamide, Losartan, Levothyroxine, and replacement of Calcium + Vitamin D were started, with adequate response and symptoms control. The patient did not experience any adverse effects from the medication.

3. Discussion

SLE is a chronic, relapsing-remitting autoimmune disease characterized by loss of self-tolerance and systemic inflammation. Neuropsychiatric lupus consists of a wide range of neurological and psychiatric manifestations that can affect any central or peripheral nervous system structure. These have been grouped into nineteen syndromes, six of which are cognitive impairment, cerebrovascular

Table 1
Cerebrospinal fluid analysis.

CSF study	Result
Appearance	Clear
RBCs	0
WBCs	2
Neutrophils	0
Lymphocytes	2 (100 %)
CSF glucose	39.1
CSF total protein	16.6
Cryptococcal antigen	Negative
Gram staining	Negative
India ink staining	Negative
CSF bacilloscopy	Negative

Table 2
Laboratory tests.

Variable	Result
Leucocytes	4370 uL
Neutrophils	2010 uL
Lymphocytes	2000 uL
Eosinophiles	30 uL
Monocytes	320 uL
Hemoglobin	12 g/dL
Hematocrit	34.9 %
Platelets	301000 uL
Blood urea nitrogen	7.7 mg/dL
Creatinine	0.83 mg/dL
Sodium	138 mmol/L
Potassium	3.93 mmol/L
Chloride	107.4 mmol/L
Total bilirubin	0.18
Direct bilirubin	0.08
Indirect bilirubin	0.1
ALT	10.1
AST	24
LDH	215
C-reactive protein	0.04
IgG	33.47
Direct Coombs	Positive
Non-Treponemal test RPR	Negative
HIV	Negative
Erythrocyte sedimentation rate	51 mm/hour
Urinalysis	Density: 1005, pH: 7, nitrites: negative, proteins: 75, glucose: normal, ketone bodies: negative, WBC: 0–3, RBC: trace, bacteria: trace
Urine creatinine	11.25
Urine protein	32.5
Urine protein/creatinine ratio	2.9 gr
Albumin	2.89 mg/dL
C3	30.25 mg/dL
C4	3.04 mg/dL
Anti-Ro/SSA	>200 U/mL
Anti-La/SSB	12 U/mL
Anti-Sm	>200 U/mL
Anti-RNP	>200 U/mL
Anti-DNA (EIA)	67 U/mL
ANA	1:10240 dilution, speckled pattern (AC-2,4,5)
Cardiolipin IgG	10.4
Cardiolipin IgM	1.1
Anti-proteinase 3	2.8
Anti-myeloperoxidase	2.8
Beta-2 glycoprotein IgG	3.2
Beta-2 glycoprotein IgM	1.1

disease, seizures, and headache. However, intracranial hypertension is not included due to its low prevalence of 0.7 % [8–10]. It's also important to note that idiopathic intracranial hypertension has a prevalence between 0.5 and 2 per 100,000 of the general population [11].

Intracranial hypertension can be primary or idiopathic, also known as pseudotumor cerebri, in which there is an increase in intracranial pressure with normal brain parenchyma, in the absence of ventriculomegaly, infection, or base malignant neoplasia [10, 12]. It can also be secondary, either to an underlying disease such as obesity, polycystic ovary syndrome, anemia, kidney failure, obstructive sleep apnea, adrenal insufficiency, hypoparathyroidism, or systemic lupus erythematosus; to a precipitating factor, such as venous sinus thrombosis, middle ear and mastoid infections, superior vena cava syndrome, arteriovenous fistulae, hypercoagulable states, or secondary to the use of certain medications [12]. Among the ocular manifestations of SLE are keratoconjunctivitis sicca and retinal abnormalities such as hemorrhages, vasculitis-like lesions, or exudates, but papilledema is rare.

Intracranial hypertension in patients with SLE is associated with nephritis, arthritis, rash, cytopenia, antiphospholipid antibody syndrome, and active lupus disease [9]. SLE rarely presents with intracranial hypertension. Some of the hypotheses proposed are the decrease in CSF reabsorption due to the disruption of the blood-brain barrier and immune-mediated damage to the arachnoid villi, apparently by anti-Ro antibodies or by vascular occlusion due to hypercoagulable states.

There are some reported cases in the literature in which SLE manifests with intracranial hypertension [13–16]. However, in most of them, there is overweight, association with other neuropsychiatric SLE syndromes, alterations in magnetic resonance images, or withdrawal of steroids as the cause [17]. Kim JM et al. [10] evaluated the CSF of 47 patients out of 1084 with SLE due to intractable headache, reporting eight patients with IH (prevalence 0.7 %). The mean interval between the diagnosis of SLE and the development of

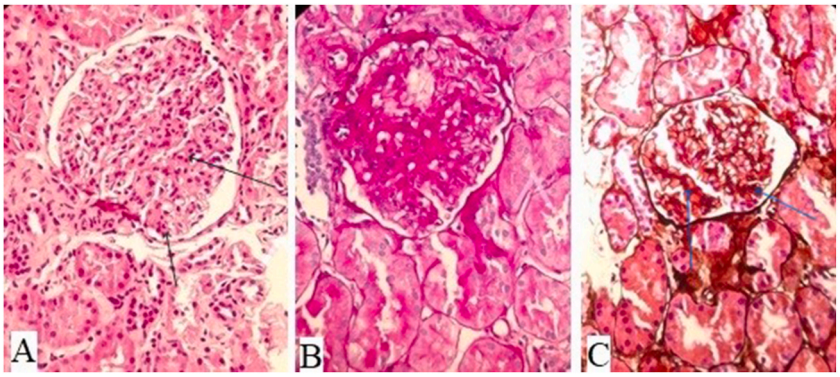

Fig. 1. Hematoxylin and eosin stain (A), Periodic acid–Schiff (PAS) stain (B), and Grocott methenamine silver (GMS) stain (C). Glomeruli with mild mesangial hypercellularity without evidence of endocapillary hypercellularity, subendothelial deposits, double contours, fibrinoid necrosis, leukocytes, karyorrhexis, "spikes," or areas of mesangiolysis. The preserved interstice presents mild edema without associated inflammatory infiltrate. There is no interstitial fibrosis or tubular atrophy.

IH was 52.0 ± 38.3 months. It is striking that they did not report obese patients in this series.

In this case report, the patient had a headache of one year of moderate intensity, was not overweight, and the finding of papilledema was incidental in a routine ophthalmological examination, for which she was timely referred to the emergency department. Considering this alteration, added to the chronic headache and a normal neuroimage, it was decided to perform a lumbar puncture that confirmed intracranial hypertension with a high opening pressure that was treated symptomatically with Acetazolamide.

To find the association between intracranial hypertension and SLE, it was necessary to conduct a detailed review of systems since the patient had presented nonspecific symptoms for two years that did not compromise her quality of life for which she had not consulted.

The treatment of intracranial hypertension associated with SLE is the same as for other causes, with carbonic anhydrase inhibitors, evacuating lumbar punctures, and steroids, in addition to treating the different manifestations of SLE. In this case, she received pulses of steroids and Mycophenolate Mofetil for the class V lupus nephritis. In other series, they have also used Cyclophosphamide [10], yet, there is no specific treatment for IH associated with SLE.

Bearing the previous in mind, we emphasize the importance of the fundus eye evaluation in the approach of headache. In the case of papilledema with idiopathic intracranial hypertension, always carry out an in-depth review by systems to rule out SLE as a cause.

4. Conclusion

In summary, while systemic lupus erythematosus (SLE) rarely presents with intracranial hypertension (IH), it's important to consider this possibility, especially in cases of unexplained headaches. This report underscores the need for a detailed evaluation, as IH may occur even without typical risk factors like obesity. Treatment involves managing both IH and underlying SLE manifestations, though specific therapy for IH in SLE is lacking. This case highlights the importance of vigilance for neurological complications in SLE patients to ensure appropriate management.

Ethical standards

This study followed the ethical standards laid down in the 1964 Declaration of Helsinki. This study was reviewed and approved by Fundación Valle del Lili's Institutional Review Board. The patient provided written informed consent to participate in this report.

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Data availability statement

The data associated with the study has not been deposited into a publicly available repository. The authors do not have permission to share data.

CRediT authorship contribution statement

Isabella Pugliese: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **María Posada:** Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Masaru Shinchi:**

Methodology, Investigation, Formal analysis, Conceptualization. **David Aguirre-Valencia:** Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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