

Intracranial hypertension with delayed puberty: a rare presentation of juvenile onset systemic lupus erythematosus

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ABSTRACT An adolescent boy presented with headache, bilateral papilloedema, growth retardation and absent secondary sexual characteristics. The diagnosis of intracranial hypertension was confirmed by increased intracranial pressure and normal neuroimaging of the brain except for partial empty sella and prominent perioptic cerebrospinal fluid (CSF) spaces. Evaluation showed an erythrocyte sedimentation rate of 150 mm/hr, positive antinuclear antibody, anti-dsDNA and antiribosomal P protein. Renal biopsy revealed diffuse segmental proliferative lupus nephritis (LN) class IV-S (A), which confirmed the diagnosis of systemic lupus erythematosus (SLE). Treatment of LN with intravenous pulse methylprednisolone and cyclophosphamide normalised the patient's CSF pressure and symptoms. In cases of intracranial hypertension, SLE must be considered. Growth retardation and absence of secondary sexual characteristics could coexist and may be presenting features of SLE. These manifestations point to advanced grades of LN, which could be asymptomatic and may be missed without a renal biopsy.

Keywords: antinuclear antibody, cyclophosphamide, erythrocyte sedimentation rate, methylprednisolone, papilloedema
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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by diverse autoimmune manifestations encompassing almost all organ systems. Neuropsychiatric lupus may range from subtle cognitive or behavioural disorders to coma and death.⁽¹⁾ Intracranial hypertension (IH) is included among the rare neuropsychiatric manifestations of SLE.^(2–4) We present the case of a 14-year-old boy who presented with features of IH and had a short stature. On evaluation, he was found to have SLE and lupus nephritis (LN). However, IH has not been included as one of the neuropsychiatric syndromes in the American College of Rheumatology (ACR) 1999 nomenclature for neuropsychiatric lupus.⁽⁵⁾

CASE REPORT

A 14-year-old boy presented with fever, headache and vomiting that lasted six months despite the use of analgesics. He was diagnosed to have hypothyroidism four months ago, and was prescribed replacement thyroxine. He was in a euthyroid state at the time of presentation. His height and weight were two standard deviations below the average. There was no history of blurring of vision, diplopia, seizures, behavioural abnormalities, arthritis, skin lesions, photosensitivity or reduction in his urine output. On examination, he was febrile with pallor, oral ulcers and absent secondary sexual characteristics (Tanner stage 1). His blood pressure was normal, and a neurological examination was unremarkable except for the presence of bilateral papilloedema. Visual acuity was normal, but a perimetry revealed bilateral

concentric visual field constriction. Fluorescein angiography showed increased hyperfluorescence extending beyond the disc margins, which confirmed the diagnosis of papilloedema. Magnetic resonance (MR) imaging of the brain revealed the classic features of IH: a partial empty sella (Fig. 1), prominent perioptic cerebrospinal fluid (CSF) spaces and buckling of optic nerves.⁽⁶⁾ MR venogram provided no evidence of sinus thrombosis, and a CSF tap showed an opening pressure of 270 mm of water with a normal composition.

Laboratory investigations revealed microcytic hypochromic anaemia, haemoglobin of 9 gm%, platelet count of 1,00,000/mm³, white blood cell (WBC) count of 9,110/mm³, lymphocyte count of 3,000/mm³ and an erythrocyte sedimentation rate (ESR) of 150 mm/hr. As the patient was an atypical patient for developing IH, he was further evaluated. Routine urine examination showed the presence of albumin (+), no red blood cells, 6–8 WBCs per high power field and granular casts. Liver and renal function tests, including serum albumin (3.8 gm%) were within normal limits. Antinuclear antibody was positive, with an index of 22.7 (negative < 1.4), while anti-dsDNA was positive at 57.67 IU/mL (negative < 20 IU/mL), antiribosomal P protein was strongly positive (+++) and anti-La antibody (SS-B) was positive (++) . Serum complement levels of both C3 and C4 were low. C-reactive protein was elevated at 12 mg/L (N ≤ 6 mg/dL). Anticardiolipin and lupus anticoagulant antibodies were negative. Anti-neutrophil cytoplasmic antibody (both c-ANCA and p-ANCA), Venereal Disease

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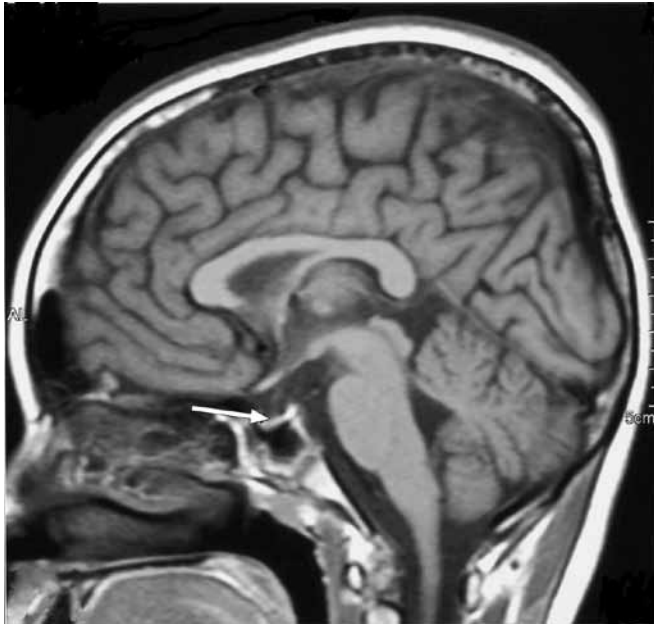


Fig. 1 Sagittal T1 MR image shows reduced size of anterior pituitary gland secondary to raised intracranial pressure (arrow).

Research Laboratory test, serologies for hepatitis B surface antigen, hepatitis C and HIV antibodies were all non-reactive. Ultrasonography of the abdomen and echocardiography examination were unremarkable. Hormone estimations showed normal growth hormone, luteinising hormone, follicle stimulating hormone and thyroid hormone levels. Fine needle aspiration cytology of the thyroid gland revealed lymphocytic thyroiditis. Anti-thyroid peroxidase antibody level was normal.

A diagnosis of SLE with IH and lymphocytic thyroiditis was made. The patient was treated with pulse methylprednisolone (25 mg/kg/day) for five consecutive days. His fever disappeared, headache subsided and papilloedema decreased in the first week of treatment. Renal biopsy showed diffuse segmental proliferative LN grade IV 1 (A), with an activity index of 5/24 and a chronicity index of 0/12. The patient was given intravenous cyclophosphamide pulse therapy of 750 mg on a monthly basis for six months along with daily oral steroids. At the four weeks follow-up, he had become totally asymptomatic, attaining clinical remission with disappearance of papilloedema, and his ESR and anti-dsDNA levels had normalised. His steroids were subsequently tapered.

DISCUSSION

While investigating the cause of IH in an atypical patient (non-obese young boy), we encountered positive antinuclear antibodies and anti-dsDNA titres, which were suspicious for SLE. The serum complements in the patient were reduced, with a mild elevation of C-reactive protein pointing toward a disease flare, which prompted a renal biopsy. The biopsy showed a class IV S (A) LN. The patient satisfied four out of 11 of the revised ACR criteria for SLE.

IH has been described as one of the neuropsychiatric syndromes in SLE. To date, approximately 25 adults and children

manifesting IH in association with SLE have been reported.^(1-4,7-9) There have been only a few reported paediatric cases where IH was the initial presenting sign of SLE,^(4,9) as in our patient. The association between SLE and IH is still unclear. The proposed mechanisms include immune-mediated injury within the arachnoid villi and consequent reduction in CSF absorption or a probable hypercoagulable state without overt vascular thrombosis, thus giving rise to micro-obliteration of the cerebral arteriolar and venous systems.^(2,8,10) Immunomodulatory drug withdrawal during the course of SLE treatment may be a predisposing or precipitating factor in the development of IH.⁽¹¹⁾ A review of 127 patients with LN has shown an IH prevalence of 4.7%. Females with serologically active lupus, severe forms of renal lesions, past history of venous or arterial thrombosis, young age and laboratory evidences of procoagulant are at increased risk of IH.⁽¹²⁾

In our patient, the antiphospholipid antibody workup was negative. Growth retardation and absence of secondary sexual characteristics are well-documented in SLE. This could be due to chronic systemic inflammatory response leading to end organ unresponsiveness (as in our patient), or associated hypopituitarism due to antiphospholipid antibody syndrome, lymphocytic hypophysitis and chronic intracranial hypertension. Antiribosomal P protein was found to be strongly positive in our patient. Like high titres of anti-dsDNA, it is usually associated with neuropsychiatric manifestations of SLE and LN, as seen in our patient.⁽¹³⁾ Treatment strategy for class IV LN with intravenous pulse methylprednisolone and cyclophosphamide was effective in normalising the CSF pressure without the use of acetazolamide or other diuretics, giving an indirect clue that IH in SLE is immune mediated. Maintenance therapy could be achieved on drugs such as oral steroids, mycophenolate mofetil or azathioprine.

In conclusion, IH could be the only presenting manifestation of SLE. Immunomodulatory drug treatment alone may suffice in normalising CSF pressure and even result in complete resolution of symptoms. Undiagnosed LN may coexist. A diagnostic renal biopsy may be needed, as the result may influence the choice of subsequent immunosuppressive therapy and renal prognosis.

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