CASE REPORT

Idiopathic intracranial hypertension as an initial presentation of systemic lupus erythematosus

Keisha Maloney

University of the West Indies,
Kingston, Jamaica

Correspondence to
Dr Keisha Maloney,
keisha.maloney@uwimona.
edu.jm

SUMMARY

A 14-year-old girl with no known illness presented with a several week history of headaches and vomiting. The patient also reported having joint pain and swelling to the wrists and knees. She had no prior history of headaches, use of hormonal contraception or other medications, recent weight changes or family history of autoimmune disease. Blood pressure, temperature, height and weight were normal. She was alert, there was alopecia, cervical lymphadenopathy, symmetrical synovitis to the wrists, bilateral papilloedema and cranial nerve VI palsy. Laboratory investigations revealed a normochromic normocytic anaemia, leucopenia and lymphopenia. Serum chemistries were normal. CT of the brain was normal. Lumbar puncture revealed an opening pressure of greater than 300 mm H₂O; cerebrospinal fluid (CSF) analysis was normal. HIV antibodies were non-reactive. Despite treatment with acetazolamide she developed somnolence. Hence MR venography was performed which showed no evidence of cerebral vein thrombosis. Further investigations revealed a positive direct coombs test, positive antinuclear antibodies (ANA) positive antidouble-stranded DNA (dsDNA) and false positive VDRL. Complement levels were reduced. Anti-Smith, anticardiolipin antibodies and lupus anticoagulant were negative.

BACKGROUND

Systemic lupus erythematosus (SLE) is a chronic systemic inflammatory disease which may affect multiple organ systems. It is associated with increased morbidity and mortality.¹ Neuropsychiatric manifestations are common in SLE and are associated with a worse prognosis, higher mortality and more cumulative organ damage.^{2,3}

Idiopathic intracranial hypertension (IIH) is considered a rare neuropsychiatric manifestation of SLE. In this case, we report a patient with IIH as an initial presenting manifestation of SLE.

CASE PRESENTATION

- ▶ Presenting features: headache, vomiting and arthralgias
- ▶ Medical history: none
- ▶ Social history: attends school, non-smoker, no use of alcohol, no use of recreational/illicit drugs ever
- ▶ Family history: no history of autoimmune disease or neurological disease

INVESTIGATIONS

Blood and urine investigations

- ▶ Complete blood count—normochromic normocytic anaemia.
- ▶ Erythrocyte sedimentation rate—115 mm/hr.
- ▶ Serum urine chemistry—normal.
- ▶ Acute and convalescent sera—negative.
- ▶ HIV antibodies—negative.
- ▶ Antinuclear antibody—positive.
- ▶ Double-stranded DNA (dsDNA)—positive.
- ▶ Complement levels (C3 <30 mg/dL (90–180 mg/dL) and C4 was low at 9.76 mg/dL (10–40 mg/dL))—low.
- ▶ Urinalysis and microscopy showed 10–12 red blood cells, 0–1 white cell count and 1+ protein.
- ▶ Anti-Smith, anticardiolipin antibodies and lupus anticoagulant were negative.
- ▶ Serological Venereal Disease Research Laboratory (VDRL) test was positive with negative fluorescent treponemal antibody (FTA) test.

Cerebrospinal fluid (CSF) investigations

- ▶ CSF analysis (cell count 0, CSF protein 2.45 g/dL, CSF glucose 60 mg/dL with serum glucose of 121.8 mg/dL, CSF Gram stain negative, CSF culture negative, CSF acid-fast stain negative, CSF cryptococcal antigen negative, CSF herpes simplex virus PCR negative, CSF VDRL negative.)

Imaging investigations

- ▶ CT of the brain showed mild generalised cerebral atrophy with no intracranial haemorrhage or infarct.
- ▶ MR venography which showed no evidence of cerebral vein thrombosis.

DIFFERENTIAL DIAGNOSIS

- ▶ SLE with idiopathic intracranial hypertension.
- ▶ SLE with acute cerebrovascular event (ischemic cerebral vascular disorder, cerebral vein thrombosis, intracranial haemorrhage).
- ▶ SLE with meningitis (aseptic and bacterial meningitis).

TREATMENT

Pulse methylprednisone 1 g was subsequently administered for 3 days followed by prednisone 1 mg/kg/day.

OUTCOME AND FOLLOW-UP

The patient had rapid symptom improvement postmethylprednisone pulse with resolution of

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papilloedema and was discharged on prednisone 60 mg daily and hydroxychloroquine sulfate 200 mg daily.

Unfortunately the patient defaulted from follow-up and was non-compliant with medical therapy and had a relapse of IIH after 1 year requiring hospitalisation and administration of methylprednisone pulse. On this admission the patient was noted to have subnephrotic range proteinuria (2.5 g urine protein : creatine ratio) and was diagnosed with lupus nephritis (class IV) on renal biopsy. Serum creatine remained within normal limits.

DISCUSSION

The patient fulfilled American College of Rheumatology (ACR) diagnostic criteria for SLE.^{4 5} She had (1) haematological manifestations (haemolytic anaemia with reticulocytosis, leucopenia and lymphopenia), (2) positive ANA, (3) positive dsDNA (4) symmetrical arthritis and (5) neuropsychiatric manifestation of SLE—headache due to IIH.

IIH is defined as an elevated intracranial pressure but no clinical, laboratory or radiological evidence of hydrocephalus, infection, tumour or vascular abnormality. The modified Dandy criteria describe clinical, laboratory and radiological findings required for a diagnosis of IIH. The criteria required are (1) symptoms and signs of increased intracranial pressure (eg, papilloedema and headache), (2) CSF pressure >250 mm H₂O in the lateral decubitus position, (3) no localising signs with the exception of sixth nerve palsy, (4) normal CSF composition, (5) normal-to-small (slit) ventricles on imaging with no intracranial mass, (6) no unexplained symptoms or signs, (7) exclusion of other causes on specific forms of imaging in particular MRI/venography should be included to rule out intracranial venous sinus thrombosis.⁶ Our patient met all criteria for a diagnosis of IIH.

Nervous system disease involvement in SLE varies widely and may occur in up to 50% of patients from the time of diagnosis.⁷ The ACR has developed case definitions for 19 neuropsychiatric syndromes as shown in box 1.⁵

Headache (including migraine and IIH) has been classified by the ACR as a neuropsychiatric manifestation of SLE. Headache is a common neuropsychiatric manifestation of SLE; however, IIH is rarely a presenting manifestation of SLE.⁸

The cause of IIH is unknown; however, multiple associations have been made with IIH in particular weight gain, obesity, female gender, venous outflow abnormalities and rarely SLE.^{9 10} The pathophysiology of IIH in SLE remains unknown.

We reviewed the number of cases in which IIH is described in SLE by conducting a MEDLINE search for patients using the following descriptors “idiopathic intracranial hypertension” “intracranial hypertension”, “lupus”, “systemic lupus erythematosus” and “pseudotumor cerebri”; cases which included cerebral venous thrombosis were excluded. Within these articles we found 37 cases of IIH associated with SLE as shown in table 1.^{11–29} All patients reported were women with the exception of two men.

Headache was the most common symptom in this group of patients occurring in 86.5% of patients. The kidney was the most commonly involved organ (54.1%). Serological flare (elevated dsDNA, low complement) was evident in most of the patients (81.1%). Almost all cases reported were treated successfully with glucocorticoid therapy or with combination of glucocorticoid and other drugs as in this case. Most patients responded well to the therapy with good outcome.

Serological flare correlates with disease activity in SLE³⁰; the review analysis suggests that there may be more than an association between IIH and SLE and that IIH may occur directly as a result of SLE disease activity. This review also suggests an association with renal involvement; the associations of lupus

Box 1 Neuropsychiatric syndromes observed in SLE—ACR Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature

Central nervous system

Aseptic meningitis
Cerebrovascular disease
Demyelinating syndrome
Headache (including migraine and benign intracranial hypertension)
Movement disorder (chorea)
Myelopathy
Seizure disorders
Acute confusional state
Anxiety disorder
Cognitive dysfunction
Mood disorder
Psychosis

Peripheral nervous system

Acute inflammatory demyelinating polyradiculoneuropathy
Guillain-Barré syndrome
Autonomic disorder
Mononeuropathy, single/multiplex
Myasthenia gravis
The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum 1999.
ACR, American College of Rheumatology; SLE, systemic lupus erythematosus.

serological flare with SLE and renal involvement in SLE has been well established in the literature.³¹

To our knowledge there have been no documented reports of intracranial hypertension in patients with SLE in Jamaica or the Caribbean.

In conclusion, IIH is a rare presenting manifestation of SLE. We suggest that particularly in young women with clinical findings of intracranial hypertension who lack other typical associations of IIH (weight gain, obesity and venous outflow abnormalities) that SLE should be included in the diagnostic investigations.

Learning points

- ▶ In young women with clinical findings of intracranial hypertension, systemic lupus erythematosus (SLE) should be included in the diagnostic investigations particularly if the patient has no typical causal associations of intracranial hypertension such as weight gain, obesity and venous outflow abnormalities.
- ▶ Although headache is a common neuropsychiatric symptom of SLE, intracranial hypertension is a rare cause of headache in SLE and should be considered in the differential diagnosis of headache in a patient with SLE.
- ▶ There may be an association of renal disease with intracranial hypertension in patients with SLE hence patients with SLE with the rare presentation of intracranial hypertension should be closely followed for this complication.

Table 1 Characteristics of patients with SLE and IIH

Series	Number	Gender	Ethnicity	Headache	Visual symptoms	Papilloedema	NI	RI	Thrombocytopenia	APLA	Haemolysis	Leucopenia	Serological flare	Treatment	Follow-up
Bettman <i>et al</i> ¹¹	1	F	Afro-American	0 (1)	0 (1)	0 (1)	0 (1)	1 (1)	NR	NR	0 (1)	1 (1)	1 (1)	Steroids	Resolution
Carlow and, Glaser ¹²	1	F	NR	0 (1)	0 (1)	0 (1)	0 (1)	1 (1)	1 (1)	NR	NR	1 (1)	1 (1)	Steroids	Resolution
Del Guidice <i>et al</i> ¹³	3	3F	3 Afro-America	2 (3)	2 (3)	0 (3)	1 (3)	1NR 2 (2)	0 (3)	3NR	2NR 1 (1)	0 (3)	1NR 2 (2)	1 Steroid bolus, 3 (3) steroids	3 (3) Resobtion
Li and Ho ¹⁴	3	3F	3 Asiatic	1 (3)	0 (3)	0 (3)	0 (3)	3 (3)	2NR 1 (1)	2NR 0 (2)	NR	1NR 0 (2)	3 (3)	3 (3) Steroids	3 (3) Resobtion
Chevalier <i>et al</i> ¹⁵	1	F	Caucasian	1 (1)	0 (1)	0 (1)	0 (1)	NR	NR	0 (1)	1 (1)	1 (1)	1 (1)	Steroids	Resolution, relapse 1 year later
Vachvanichsanson <i>et al</i> ¹⁶	1	M	NR	1 (1)	0 (1)	0 (1)	1 (1)	1 (1)	1 (1)	NR	1 (4)	1 (1)	1 (1)	Steroids and acetazolamide	Resolution
Siberberg and Laties ¹⁷	4	4F	4NR	3 (4)	3 (4)	1 (4)	2 (4)	3 (4)	1 (4)	4NR	2 (3)	1 (4)	1NR 2 (3)	4 (4) Steroids	4 (4) Resolution
Green <i>et al</i> ¹⁸	3	3F	3NR	3 (3)	1 (3)	1 (3)	1 (3)	1 (3)	2 (3)	2 (3)	0 (1)	0 (3)	3 (3)	3 (3) Steroids, 1 (3) acetazolamide, 1 (3) IG	(3) Mild pailloedema, (3) Resobtion, 1 (3) Relapes 4 years later
Padeh and Paswell ¹⁹	1	F	Ashkenazi	1 (1)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	NR	0 (1)	1 (1)	Steroids bobs and steroids	Resolution, relapse 6 months later
Chaves-Carballo, <i>et al</i> ²⁰	1	F	Arab	1 (1)	0 (1)	0 (1)	1 (1)	1 (1)	NR	NR	NR	NR	1 (1)	Steroids bolus and steroids	Resolution, relapse 20 months later
Yoo <i>et al</i> ²¹	1	F	NR	1 (1)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	NR	1 (1)	Steroids and acetazolamide	Resolution, relapse
Komura <i>et al</i> ²²	1	F	NR	1 (1)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	1 (1)	1 (1)	Steroids bobs and steroids	Resolution
Sbeiti <i>et al</i> ²³		F	NR	1 (1)	1 (1)	0 (1)	0 (1)	0 (1)	NR	1 (1)	0 (1)	1 (1)	1 (1)	Steroid	Resolution
Herrero <i>et al</i> ²⁴	1	F	NR	1 (1)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	1 (1)	Steroids and acetazolamide	Resolution
Kuyucu <i>et al</i> ²⁵	1	F	NR	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	1 (1)	0 (1)	1 (1)	Steroids bobs, steroids and acetazolamide	Resolution
Hershko <i>et al</i> ²⁶	10	9F, 1M	6 Arab, 4 Jewis	10 (10)	5 (10)	1 (10)	5 (10)	6 (10)	4 (10)	9 (10)	1 (10)	3 (10)	7 (10)	Steroids 9 (10), acetazolamide 10 (10) azathioprine 2 (10)	6 (10) Resolution, 4 (10) visual defects, 3 (10) relapes
Barahona-Hernando <i>et al</i> ²⁷	1	F	Caucasian	1 (1)	0 (1)	1 (1)	0 (1)	0 (1)	0 (1)	1 (1)	0 (1)	0 (1)	1 (1)	Steroids bolus, steroids, VPS	Resobtion

Continued

Table 1 Continued

Series	Number	Gender	Ethnicity	Visual symptoms			Thrombocytopenia	APLA	Haemolysis	Leucopenia	Serological flare	Treatment	Follow-up
				Headache	Headache	Headache							
Xue <i>et al</i> ²⁸	1	F	Asian	1 (1)	1 (1)	1 (1)	0 (1)	0 (1)	0 (1)	1 (1)	0 (1)	Steroid, mannitol	Resolution, improved papilloedema
Mathew and Cherian ⁹	1	M	Asian	1 (1)	0 (1)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)	Steroid bobs, steroids, CYC	Resolution
Our patient	1	F	Afro-Caribbean	1 (1)	0 (1)	1 (1)	0 (1)	1 (1)	1 (1)	1 (1)	1 (1)	Steroid bobs, steroids and acetazolamide	Relapse

The number of patients with a reported characteristics (out of the total number of patients in which the characteristics is analysed) is presented.

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REFERENCES

- Petri M. Epidemiology of systemic lupus erythematosus. *Best Pract Res Clin Rheumatol* 2002;16:847–58.
- Hanly JG, Urowitz MB, Sanchez-Guerrero J, *et al*. Neuropsychiatric events at the time of diagnosis of systemic lupus erythematosus: an international inception cohort study. *Arthritis Rheum* 2007;56:265–73.
- Bernatsky S, Clarke A, Gladman DD, *et al*. Mortality related to cerebrovascular disease in systemic lupus erythematosus. *Lupus* 2006;15:835fa–9fa.
- Tan EM, Cohen AS, Fries JF, *et al*. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271–7.
- ACR Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 1999;42:599–608.
- Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology* 2002;59:1492–5.
- Bruyn GA. Controversies in lupus: nervous system involvement. *Ann Rheum Dis* 1995;54:159–67.
- Unterman A, Nolte JE, Boaz M, *et al*. Neuropsychiatric syndromes in systemic lupus erythematosus: a meta-analysis. *Semin Arthritis Rheum* 2011;41:1–11.
- Wall M. Idiopathic intracranial hypertension. *Curr Neurol Neurosci* 2008;8:87–93.
- Brazis PW. Pseudotumor cerebri. *Curr Neurol Neurosci* 2004;4:111–16.
- Bettman JW Jr, Daroff RB, Sanders MD, *et al*. Papilledema and asymptomatic intracranial hypertension in systemic lupus erythematosus. A fluorescein angiographic study of resolving papilledema. *Arch Ophthalmol* 1968;80:189–93.
- Carlow TJ, Glaser JS. Pseudotumor cerebri syndrome in systemic lupus erythematosus. *JAMA* 1974;228:197–200.
- DelGiudice GC, Scher CA, Athreya BH, *et al*. Pseudotumor cerebri and childhood systemic lupus erythematosus. *J Rheumatol* 1986;13:748–52.
- Li EK, Ho PC. Pseudotumor cerebri in systemic lupus erythematosus. *J Rheumatol* 1989;16:113–16.
- Chevalier X, de Bandt M, Bourgeois P, *et al*. Primary Sjogren's syndrome preceding the presentation of systemic lupus erythematosus as a benign intracranial hypertension syndrome. *Ann Rheum Dis* 1992;51:808–9.
- Vachvanichsanong P, Dissaneewate P, Vasikananont P. Pseudotumor cerebri in a boy with systemic lupus erythematosus. *Am J Dis Child* 1992;146:1417–19.
- Silberberg DH, Laties AM. Increased intracranial pressure in disseminated lupus erythematosus. *Arch Neurol* 1973;29:88–90.
- Green L, Vinker S, Amital H, *et al*. Pseudotumor cerebri in systemic lupus erythematosus. *Semin Arthritis Rheum* 1995;25:103–8.
- Paddeh S, Passwell JH. Systemic lupus erythematosus presenting as idiopathic intracranial hypertension. *J Rheumatol* 1996;23:1266–8.
- Chaves-Carballo E, Dabbagh O, Bahabri S. Pseudotumor cerebri and leukoencephalopathy in childhood lupus. *Lupus* 1999;8:81–4.
- Yoo WH, Park JH, Kim HK, *et al*. Recurrent pseudotumor cerebri in systemic lupus erythematosus: a case report. *J Korean Med Sci* 2001;16:805–8.
- Komura K, Sato S, Ishida W, *et al*. Idiopathic intracranial hypertension with elevated cerebrospinal fluid level of interleukin-6 in a patient with systemic lupus erythematosus. *Clin Rheumatol* 2002;21:267–8.
- Sbeiti S, Kaye DM, Majuri H. Pseudotumor cerebri presentation of systemic lupus erythematosus: more than an association. *Rheumatology (Oxford)* 2003;42:808–10.
- Herrero A, Mera J, Zea A, *et al*. Pseudotumor cerebri and systemic lupus erythematosus. *Rev Clin Esp* 2003;203:74–6.
- Kuyucu S, Argin A, Kuyucu N, *et al*. Systemic lupus erythematosus presenting with pseudotumor cerebri: a rare association. *Turk J Pediatr* 2007;49:98–101.
- Hershko AY, Berkun Y, Mevorach D, *et al*. Increased intracranial pressure related to systemic lupus erythematosus: a 26-year experience. *Semin Arthritis Rheum* 2008;38:110–15.
- Barahona-Hernando R, Rios-Blanco JJ, Méndez-Mesón I, *et al*. Idiopathic intracranial hypertension and systemic lupus erythematosus: a case report and review of the literature. *Lupus* 2009;18:1121–3.
- Xue Z, Wang X, Liu F, *et al*. Intracranial hypertension syndrome in systemic lupus erythematosus: clinical analysis and review of the literature. *J Huazhong Univ Sci Technol Med Sci* 2009;29:107–11.
- Mathew M, Cherian A. Intracranial hypertension with delayed puberty: a rare association of juvenile onset systemic lupus erythematosus. *Singapore Med J* 2012;53:e15–17.
- Ter Borg EJ, Horst G, Hummel EJ, *et al*. Measurement of increases in anti-double-stranded DNA antibody levels as a predictor of disease exacerbation in systemic lupus erythematosus. *Arth Rheum* 1990;33:634–43.
- Mitjavila F, Pac V, Moga I, *et al*. Clinicopathological correlations and prognostic factors in lupus nephritis. *Clin Exp Rheumatol* 1997;15:625–31.

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