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Letters to the Editor

Cerebral venous thrombosis (CVT) in systemic lupus erythematosus (SLE)



Dear Sir,

Here, we are presenting a 15-year-old girl who at the age of 13 was diagnosed to have SLE based on thrombocytopenia, arthritis, abnormal titer of ANA (>1/1000, homogenous pattern with normal range of <1/10), and a positive anti-dsDNA (55 U/ml with normal range of <20). She had been treated with prednisolone 15 mg daily, hydroxychloroquine 200 mg twice a day, folic acid, and calcium-D daily. Two years ago, she was admitted to the hospital because of severe thrombocytopenia and was treated with intravenous immunoglobulin.

On 24 April 2012, she was admitted in the academic hospital of Gorgan, Northeast of Iran for headache, horizontal diplopia that worsened with right gaze, and recurrent vomiting.

Examination on admission revealed temperature of 37 °C orally, blood pressure of 120/70 mmHg, pulse rate of 75 bpm, and respiratory rate of 15/min.

Mucocutaneous examination showed no malar rash and discoid rash and no oral ulcer. Fundoscopy revealed bilateral papilledema. No arthritis was present. She was completely oriented and conscious (GCS:15/15). Neurologic examination showed right sixth cranial nerve (abducens nerve) palsy. Other neurologic examinations including fundoscopy were normal and no other neurological deficit was seen. No remarkable finding in physical examination of other systems was reported.

Laboratory investigation showed: white blood cells = 5400/mm³, hemoglobin = 10.2 g/dl (normal range of 11.7–15.3), mean corpuscular volume (MCV) of 75 fl (normal range of 78–98), platelet count of 244,000/mm³, anti-dsDNA of 10.9 U/ml (<20 negative), lupus anticoagulant of 30 s (normal range of 31–44), anti-β₂ glycoprotein IgG of 6.9 RU/ml (<20 negative), anti-β₂ glycoprotein IgM of 5.8 RU/ml (<20 negative), anticardiolipin antibody IgG of 6.9 U/ml (<12 negative), anticardiolipin antibody IgM of 4.8 U/ml (<12 negative), erythrocyte sedimentation rate of 61 mm/h (normal range of 1–20), C₃ of 0.335 g/l (normal range of 0.89–1.87), C₄ of 0.075 g/l (normal range of 0.165–0.380), and other laboratory tests were at the normal range.

Imaging studies such as abdominopelvic sonography and echocardiography were normal. In endoscopy examination, nodular gastritis and hemorrhagic duodenitis were reported. Lateral and left sigmoid sinus thrombosis was seen in brain MRI and MRV. The diagnosis was cerebral venous thrombosis as a rare manifestation in SLE. As seen in MRI imaging (Fig. 1), a thrombotic lesion was seen in the left sigmoid sinus and in MRV imaging (Fig. 2) filling defect was seen in left transverse sinus.

The patient was treated with continuous heparin infusion and later with warfarin, dexamethasone, and hydroxychloroquine. A dramatic improvement was seen in her condition the day after starting heparin, and she recovered completely within 2 weeks. She was discharged from the hospital with Tab. Prednisolone 50 mg daily and Tab. Warfarin 5 mg daily aimed at an international normalized ratio (INR) target of 2.5, and Tab. ASA 80 mg daily and hydroxychloroquine 200 mg twice a day. Work-up for antiphospholipid syndrome was done two months later that showed no abnormality. Also, she had been evaluated for antithrombin III, protein C and S deficiency, and factor V Leiden mutation that no abnormality was detected. Prednisolone was gradually tapered to 2.5 mg daily.

Systemic lupus erythematosus (SLE) could involve any organs of the body including the nervous system which in turn may lead to diverse neurological and psychiatric manifestations. Neuropsychiatric presentations of SLE have been reported in a high proportion of SLE patients (accounts for 5–7% of mortality in SLE) but the outcome has not been fully studied yet.¹

Thrombotic events like deep vein thrombosis (DVT) occur in renal, vena cava, extremities, and mesenteric vein in about 10–20% of the SLE patients but cerebral venous thrombosis (CVT) is rarely reported.^{2,3} Symptoms and signs of CVT can be divided into three major syndromes: isolated intracranial hypertension syndrome, focal syndrome, and encephalopathy.⁴

In clinically suspected CVT patients, the absence of clear demonstration of flow and intraluminal venous thrombus by CT or MRI is the most important finding for confirming the diagnosis.⁵

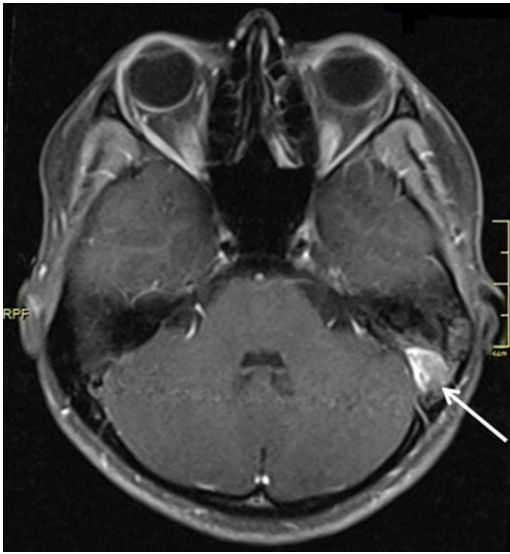


Fig. 1 – A T1-weighted image of brain MRI showed thrombosis of left transverse sinus.

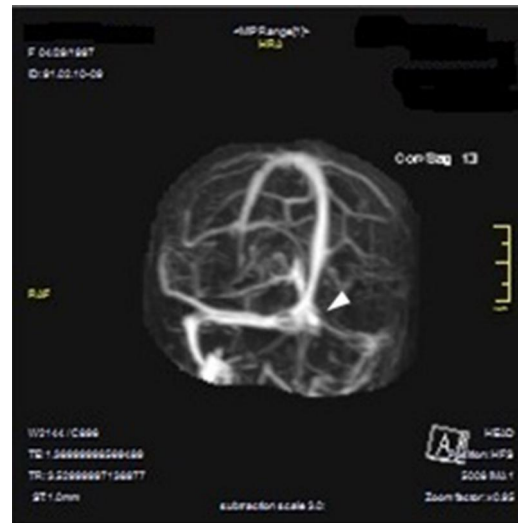


Fig. 2 – MRV showed the absence of normal signal and filling defect in left transverse sinus.

There is no simple confirmatory laboratory test that can confidently rule out CVT in acute phase of the disease. Routine blood studies consist of complete blood count (CBC), chemistry panel, prothrombin time, and activated partial thromboplastin time for patients with suspected CVT.⁵

The finding of these tests may suggest the presence of conditions that contribute to the development of CVT and rule out other causes such as hypercoagulable state, infection, or inflammatory process.⁵

Searching for a thrombophilic state, either genetic or acquired, should be done in all patients. Screening should include, antithrombin, protein c, s, factor V Leiden, prothrombin G20210A mutation, lupus anticoagulant, anticardiolipin, and anti- β_2 glycoprotein-I antibodies. The mortality and morbidity rate of CVT is high, but usually has a favorable prognosis. Approximately 5% of patients die in the acute phase of the disorder.⁵

The main treatment option to achieve these goals is anticoagulation, using either heparin or low molecular weight (LMW) heparin.⁶ Seizure prophylaxis is recommended only for patients with both seizure at presentation and subtemporal lesions such as edema, infarction, or hemorrhage on CT or brain MRI.⁵

Anticoagulation with warfarin is suggested for at least three months after acute CVT, aiming at an INR target of 2.5.^{7,8}

In patients with idiopathic CVT, 6–12 months of oral anticoagulation and indefinite oral anticoagulation for patients with either recurrent CVT is recommended.⁷

Serial assessment of visual fields and visual acuity is recommended for children with CVT during follow-up, particularly during the first year.⁵

In this case, the imaging studies revealed abnormality in the brain structures as a cerebral venous thrombosis recovered after heparin therapy. So, suspicious to thrombotic events in SLE cases could be considered as the cornerstone to diagnose these disorders.

Conflicts of interest

The authors have none to declare.

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<http://dx.doi.org/10.1016/j.injr.2015.09.006>
0973-3698/

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ANSWERS

1c, 2c, 3a, 4b, 5d, 6d, 7d, 8a, 9c, 10b

- The two HLA loci most often found to be associated with TA are Bw52 and B39.
Comprehensive analysis of HLA genes in Takayasu arteritis in Japan. Kimura A, Kitamura H, Date Y, Numano F. *Int J Cardiol.* 1996;54 Suppl:S61-9.
- In a large series, Japanese patients predominantly presented with dizziness, vertigo, pulselessness, and aortic regurgitation. Indian patients (n = 102) tended to present with headache, hypertension, and left ventricular hypertrophy.
Moriwaki R, Noda M, Yajima M, et al. Clinical manifestations of Takayasu arteritis in India and Japan—new classification of angiographic findings. *Angiology* 1997;48:369–79.
- Japanese patients with TA have involvement of the ascending aorta, arch of aorta, and descending thoracic aorta; in Indian and Korean patients, the abdominal aorta is more commonly involved.
A. Hata, M. Noda, R. Moriwaki, F. Numano. Angiographic findings of Takayasu arteritis: new classification. *Int J Cardiol* 1996;54: S155–S163.
- Human heat shock protein HSP (hHSP) and mycobacterium-induced HSP (mHSP) especially 65 kDa HSP are believed to be a key part of the association between TA and tuberculosis. The other proteins are associated with Mycobacterium tuberculosis.
- involvement of the left-mid subclavian artery and involvement of the right-mid subclavian artery are the only two major Ishikawa criteria.
Ishikawa K. Diagnostic approach and proposed criteria for the clinical diagnosis of Takayasu's arteriopathy. *J Am Coll Cardiol* 1988;12:964e72.
- the EULAR/PRINTO/PRES criteria are most often used for childhood TA. Angiographic abnormalities are a mandatory criterion. Pulse deficit, elevated acute phase reactants, hypertension, blood pressure discrepancies and bruits are five additional features – of these one must be present.
Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al. Paediatric Rheumatology International Trials Organisation (PRINTO). EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. *Ann Rheum Dis* 2010;69:798e806.
- classical Takayasu retinopathy has four stages - Stage 1: distension of veins, stage 2: micro-aneurysm formation, stage 3: formation of arterio-venous anastomoses and stage 4: presence of ocular complications like cataract, rubeosis iridis, retinal ischemia, neovascularization and vitreous hemorrhage. Branch retinal artery occlusion is a rare manifestation of TA.
Hypoperfusive and hypertensive ocular manifestations in Takayasu arteritis. Peter J, David S, Joseph G, Horo S, Danda D. *Clin Ophthalmol.* 2010;4:1173-6.
- tree barking refers to the wrinkled appearance of the intima which is seen in several forms of aortitis including syphilis and TA.
- the Indian Takayasu Arteritis Clinical Activity Score (ITAS 2010) helps in assessing disease activity in TA. It has 44 items of which 7 key items (diastolic BP > 90, stroke, claudication, carotidodynia, new loss of pulses, pulse inequality and bruits) are assigned a score of 2 and all other items are assigned a score of 1.
Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010). Misra R, Danda D, Rajappa SM, Ghosh A, Gupta R, Mahendranath KM, Jeyaseelan L, Lawrence A, Bacon PA; Indian Rheumatology Vasculitis (IRAVAS) group. *Rheumatology (Oxford).* 2013;52:1795-801.
- Echo-color Doppler shows homogeneous, midchoic, circumferential wall thickening usually in the common carotid artery in TA. Moulage sign is seen in celiac sprue, MacEwan sign in radial fracture and scimitar sign in anomalous draining pulmonary vein.
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