M.H. Harirchian MD[1]
A. Bayati MD[2]
D. Ghanbarian MD[2]
H. Ghanaati MD[3]

Cerebral Venous Thrombosis in a Patient with Clinically Isolated Syndrome Suggestive of Multiple Sclerosis

Cerebral venous thrombosis (CVT) may occur at any age and may be idiopathic or secondary to various causes. It has been described in patients with multiple sclerosis (MS) as well. On the other hand, because of the variations of MS per presentations, coincidence of other neurological disorders in MS patients could be ignored. Therefore, more clinical and paraclinical evaluations should be considered in MS patients with any new atypical symptom.

We report a rare case with symptoms and signs of inflammatory demyelinating disease as clinically isolated syndrome (CIS) suggestive of MS onset. This case developed CVT after lumbar puncture and during high-dose methylprednisolone pulse therapy.

Keywords: Multiple Sclerosis, Venous Thrombosis, Corticosteroid, Spinal Puncture, Coagulation Disorders

Introduction

Cerebral venous thrombosis (CVT) is an infrequent condition. A large number of causes and risk factors have been described, such as the hematological hypercoagulable state, malignancy, vasculitis and oral contraception consumption; however, it is idiopathic in approximately 20% of cases.[1]

On the other hand, multiple sclerosis (MS) could be presented with a wide range of central and even peripheral nervous system symptoms and signs, so coincidence of other neurological disorders in MS patients could be ignored. Therefore, more clinical and paraclinical evaluations should be considered in any MS patient with new atypical symptoms. One important issue in this regard is repeated MRI in MS patients which could be advised in these situations:

1. Establishment of dissemination in time in the clinically isolated syndrome (CIS).
2. Evaluation of drug efficacy which seems to be limited to clinical trials.
3. In the beginning and during treatment with natalizumab.
4. In order to rule out other associated disorders especially in patients with atypical presentations.

Cerebral venous thrombosis is one of the disorders that can complicate the course of disease in MS patients. Of course in a patient with white matter disease and venous thrombosis, collagen vascular disorders such as Behcet's disease and systemic lupus erythematosus (lupoid sclerosis) should be considered first,[2,3] but the coincidence of MS and a hypercoagulable state due to coincidence of a primary cause, or secondary to medical interventions should be considered as well. CVT must always be suspected in MS patients when:

1. Postural post lumbar puncture headache evolves into a severe continuous headache.

1. Associate Professor of Neurology, Iranian Center of Neurological Research, Tehran University of Medical Sciences, Tehran,Iran.
2. Department of Neurology, Tehran University of Medical Sciences, Tehran,Iran.
3. Associate Professor, Department of Radiology, Tehran University of Medical Sciences, Tehran,Iran.

Corresponding Author:
Mohammad Hossein Harirchian
Address: Iranian Center of Neurological Research, Imam Khomeini Hospital, Keshavarz Blvd., Tehran, Iran.
Tel:+9821-6691-2274
Fax:+9821-66591319
Email: harirchm@sina.tums.ac.ir

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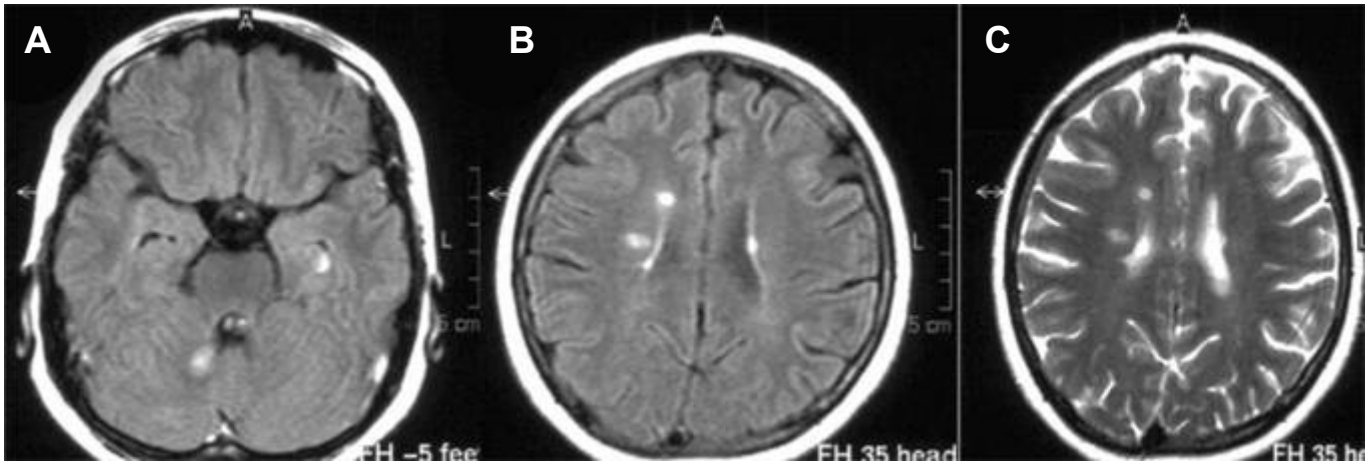

Fig. 1: The initial brain MRI of the patient. The findings are highly suggestive of a demyelinating disorder.
A. FLAIR image shows infratentorial signal abnormalities in the right superior cerebellar peduncle, right cerebellum and left temporal lobe.
B and C. FLAIR and T2WI show multiple periventricular flame shaped signal abnormalities.

2. New focal lesion, especially hemiparesis, during pulse therapy.

3. Seizure episodes.

The coincidence of CVT and MS has been already described in literature.[4-6] Associated thrombophilia is the cause of thrombosis in much of these patients.

It has been suggested that the inflammatory infiltration in MS plaques located close to small or medium-sized veins could have a role as well. Of course, this inflammatory process is not only restricted to demyelinating plaques but also affects the normally appearing white and grey matter and meninges. The exact pathogenesis of cerebral venous thrombosis in multiple sclerosis patients is still unclear.[6]

We here report a rare case with symptoms and signs of inflammatory demyelinating disease as clinically isolated syndrome (CIS) suggestive of MS onset. This patient developed CVT after lumbar puncture and during high-dose methylprednisolone pulse therapy.

Case presentation

Our patient was a 43-year-old, right-handed, married woman who was admitted with blurred vision in the right eye. On admission, she had a right retrobulbar optic neuritis and tandem gait ataxia. She had neither a history of oral contraceptive consumption nor any other cardiovascular risk factors. There was no family history of neurological diseases. Brain MRI, accomplished using echo speed 1.5-tesla machine, disclosed hypersignal plaques in the white matter, which were suggestive of a demyelinating disease (Fig. 1). The venous sinuses were patent. Routine investigations for vasculitis (including ESR, CRP, RF, ANA, anti DNA, anticardiolipin antibody, VDRL, urine analysis, C_3, C_4 and CH_{50}) were negative.

A lumbar puncture was performed and the cerebrospinal fluid (CSF) analysis was within normal limits. Oligoclonal bands and IgG index were negative as well. She received high-dose methylprednisolone (1 g/day) for 5 days. Five days later, she developed a continuous headache followed by hemiparesis, decreased level of consciousness and seizures. Repeated brain MRI and magnetic resonance venogram (MRV) showed superior sagittal sinus thrombosis and ischemic changes in the parietal lobe (Fig. 2). Routine blood and hypercoagulable work-up were normal. Intravenous heparin was started and then replaced with an oral anticoagulant. After a few days, she recovered from her initial neurological state and was discharged from the hospital with no neurological deficit after 2 weeks.

Discussion

Combination of CVT and MS has already been reported in more than a couple of patients. Some of them were bedridden, patients with oral contraceptive consumption, or with other hypercoagulable states. In patients without these risk factors it has been suggested that the inflammatory infiltration in MS plaques located close to small or medium-sized veins could have a role as well. Of course, this inflammatory process is not only restricted to demyelinative plaques but also affects the normally appearing white and grey matter and meninges.[6] There are

reports in the literature that suggest a possible role for corticosteroids in the occurrence of deep venous thrombosis in these patients.[5-8] It has been suggested that lumbar puncture could be one of the thrombophilic factors in MS patients. After dural puncture the decrease of cerebrospinal fluid pressure induces a rostrocaudal sagging effect with traumatic damage to the fragile venous endothelial wall, and may trigger a venous vasodilatation with resultant stasis.[5,8-11]

Our patient was a CIS case with her first presentation of white matter disease suggesting multiple sclerosis. There was no positive history of oral contraceptive consumption or vascular risk factor. The thrombophilia work up state and vasculitis tests were normal. There are few case reports of CVT in CIS patients without associated hypercoagulable risk factors.[12] We consider the lumbar puncture followed by corticosteroid treatment as the main cause of CVT in our patient.

We agree that the sequence of "lumbar puncture followed by corticosteroid treatment, especially when corticosteroid is administered for the first time" may be a contributory risk factor for the development of CVT especially when associated with other risk factors.[10-12]

In patients with demyelinating and hypercoagulable disorders, some possibilities should be considered, but it seems that high dose corticosteroid therapy after lumbar puncture may be a considerable risk factor especially when associated with other predisposing causes. Indeed CVT must always be suspected when postural post-LP headache evolves into a severe continuous headache, particularly when there is a sequence of LP followed by high dose corticosteroid treatment.

We also agree with the recommendation that "the prophylactic low dose heparin may be warranted in MS or CIS patients who receive high dose corticosteroids after lumbar puncture.[7,12]

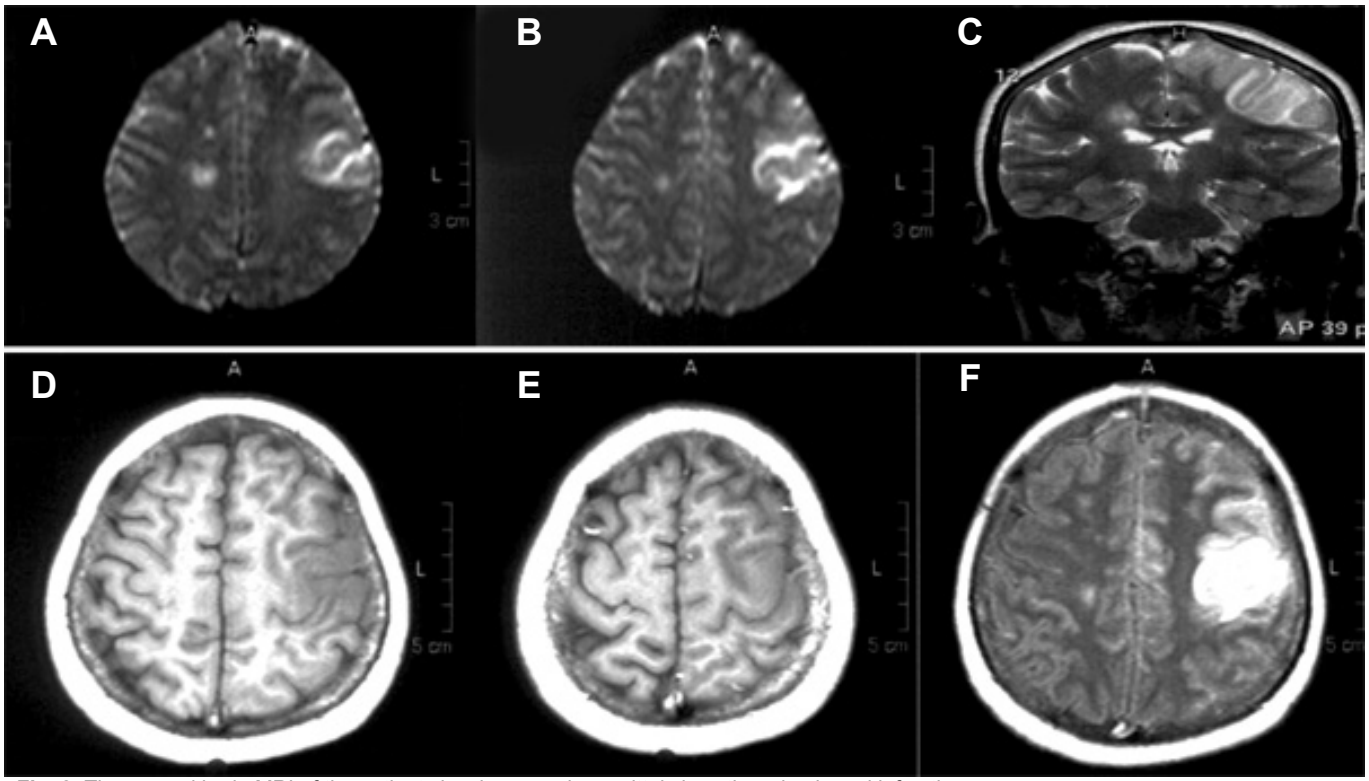

Fig. 2. The second brain MRI of the patient showing superior sagittal sinus thrombosis and infarction:
A and B. Axial DWI shows ischemic changes in cortical and subcortical areas of the left frontoparietal lobes. Some small lesions with high intensity are noted in the right central semiovale as well.
C. Coronal T2WI shows high signal intensity in cortical and subcortical areas of the left frontoparietal lobes. Some small periventricular lesions with high intensity are noted in the right central semiovale as well.
D and E. Axial T1WI shows low signal intensity in the mentioned area.
F. FLAIR sequence shows high signal intensity in the mentioned area.
Impaired flow void in the visualized part of the superior sagittal sinus is noted in C-F images. All the above findings are in favor of ischemic changes (venous infarct) in the frontoparietal lobe. According to the patient's history, periventricular lesions could be suggestive of a demyelinative lesion.

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