Case Report

Bilateral Venous Infarcts Secondary To Thrombosis: Two Cases
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Abstract

Objective: To present two cases with deep-seated bilateral venous infarcts.
Case 1: An 18-year-old woman was admitted to the hospital with a state of akinetic mutism, bilateral papilledema and a left-sided hemiparesis (MRC grade 2). Her medical history disclosed multiple attacks of diarrhea during the previous week. Brain MRI showed bilateral, symmetrical thalamic lesions compatible with deep-seated venous infarcts. Brain MR venography revealed a lack of signal at the level of the left lateral and straight sinuses. Laboratory evaluation showed protein C deficiency and heterozygote factor V Leiden mutation. Following intravenous heparin administration, the acute confusional state and left-sided paresis improved.

Case 2: A 40-year-old man was admitted to the hospital with an akinetic mutism preceded by an episode of major depression of a few weeks' duration and deep venous thrombosis of the left leg. Brain MRI revealed bilateral hemorrhagic venous infarcts at the level of globus pallidus. Factor V leiden mutation was found and intravenous heparin treatment was begun without major clinical improvement.

Conclusion: Bilateral thalamic or basal ganglia infarcts are rarely seen and cerebral venous thrombosis should be considered in the differential diagnosis of such lesions.

Keywords: Thalamus, globus pallidus, venous infarct, diarrhea, Factor V Leiden mutation, Protein C deficiency

Tromboza Sekonder Bilateral Venöz İnfarktlar: İki Olgu Sunumu

Özet

Amaç: Derin yerleşimli bilateral venöz infaktli iki olgu sunmak.


Sonuç: Bilateral talamik ve bazal ganglia infarktları nadir izlenir ve bu lezyonların ayrıcı tanısında serebral venöz tromboz düşünülmelidir.

Anahtar Kelimeler: Talamus, globus pallidus, venöz infarkt, diare, Faktör V Leiden mutasyonu, Protein C eksikliği
INTRODUCTION
Isolated bilateral thalamic infarction is a rare condition that is generally considered to result from the occlusion of a common feeding artery, for which several types of anatomic variations have been reported. However, a venous etiology may be more likely as both thalami have a common venous drainage, namely the internal cerebral vein. Differential diagnosis between arterial or venous occlusion is important, as clinical improvement depends on early initiation of therapy.

CASE PRESENTATION
CASE 1:
An 18-year-old woman was admitted to the hospital with headache, disturbed consciousness, confusion, and left-sided weakness. She reported two episodes of generalized tonic-clonic seizure a day before admission. Vital parameters, namely temperature, pulse rate and arterial blood pressure, were within normal limits. Neurological examination revealed an uncooperative and drowsy patient with a lack of initiation that was considered to be compatible with akinetic mutism. Fundoscopy showed bilateral papilledema; motor examination demonstrated a left-sided hemiparesis (MRC grade 2) with increased deep tendon reflexes, extensor plantar responses on both sides.

Her medical history was remarkable for multiple attacks of diarrhea for the previous week and headaches with nausea unresponsive to analgesics for 2 years. She denied any use of oral contraceptive medication and there was no clinical evidence, for systemic vasculitis or Behçet's disease. Brain magnetic resonance imaging (MRI) showed bilateral, symmetric thalamic lesions compatible with deep-seated venous infarcts (Figure 1). Brain MR- venography revealed a lack of signal at the level of the right lateral and straight sinuses (Figure 2). Lumbar puncture yielded an elevated intracranial pressure with an opening pressure of 260 mmH2O and normal cerebrospinal fluid content. EEG showed a slow background activity (5-6 Hz/cycle). Antiepileptic medication was started in order to control seizures. Laboratory examination showed a markedly decreased serum hemoglobin level (6.8 g/dL) and an increased platelet count (617,000/mm3); thyroid function tests were normal and thyroid antibodies as well as systemic markers for vasculitis were negative. Investigations for hereditary coagulation disorders revealed a decreased protein C activity (50%; 65-140), with normal protein S (88%; 60-130), and antithrombin III (115%; 75-125) activities as well as a heterozygote factor V Leiden mutation. Venous infarct in a setting of dehydration and factor V Leiden mutation was considered in this young patient with seizures and papilledema.

The patient's clinical status started to improve (with a GCS of 11/15 -E4, M5, V2 - on the first day) following intravenous heparin administration and therapy for brain edema. Hemiparesis gradually regressed with complete recovery of mental and motor functions at 10 days follow-up. Treatment with intravenous heparin was continued with warfarin perorally for 6 months.
CASE 2:
A 40-year-old man applied to a psychiatry clinic due to diminished speech and decreased contact with environment of sudden onset 3 weeks ago. This was attributed to major depression and treated as such. However on follow-up, he developed swollen and painful leg, for which Doppler USG revealed thrombosis on the left superficial and popliteal veins. Despite treatment with low molecular weight heparin, he developed pulmonary embolism and treatment was switched to unfractionated heparin. As the patient's mental state deteriorated he was referred to our clinic for neurological evaluation.

On examination he had no spontaneous activity and was totally dependent in his daily activities. He was alert and could obey simple commands but had no verbal response. He could keep the same posture for a long period of time and was unresponsive to any stimulus. Cranial nerve examination was within normal limits and there were no motor deficits, rigidity or spasticity. Deep tendon reflexes were normoactive, there were no pathological reflexes nor any sign of ataxia.

These clinical findings were found to be compatible with akinetic mutism. Brain MRI revealed bilateral lesions compatible with hemorrhagic venous infarcts at the level of globus pallidus (Figure 3). The presence of pulmonary embolism and deep venous thrombosis, both peripheral and cerebral, in a young man within our particular geographical region raised first the suspicion of Behçet's disease and second of systemic vasculitis. The sedimentation rate was 23 mm/h. Antinuclear antibody and Anti-DNA antibody were negative. The level of C3 and C4 were normal. Activities of protein C (80%; N:70-140), protein S (82%; N:60-130) and antithrombin III (37%; N:22-40) were within normal limits and both P-ANCA and C-ANCA were negative. The Pathergy was negative and the patient denied any history of oral aphteous ulcers.

Figure 1: Axial T2-weighted (TE: 86, TR:2900) images showing bilateral thalamic hyperintensities.

Figure 2: Cranial MR-venography obtained at the first day after clinical onset in patient 1 showing an acute thrombosis of the right lateral/transverse sinus.
All laboratory and clinical findings ruled out Behçet's disease, systemic lupus erythematosus and polyarteritis nodosa which were the principal differential diagnosis in this patient with multiple and recurrent venous thrombosis. The only positive finding in this patient was a heterozygous factor V Leiden mutation. The patient was thought to have recurrent thrombotic events in a setting of immobilization secondary to major depression and a hereditary coagulation disorder.

**DISCUSSION**

Both of the presented cases had deep-seated infarcts as the cause of the sudden onset akinetic mutism. This behavioral pathology is believed to be secondary to the disruption of frontal subcortical thalamic connections.

Kumral et al reported 0.6% bi-thalamic infarcts in an ischemic stroke registry of 2750 patients over a period of 7 years\(^4\). Specific clinical presentation namely disorders of consciousness, memory dysfunction, vertical gaze palsy, psychiatric findings as well as bilateral sensory loss have been defined. The most common arterial involvement was found to be in the paramedian thalamic (thalamo-subthalamic) artery territory\(^4,5\). While bilateral thalamic infarcts result from an anatomic variation found in approximately one third of the population with a common arterial origin for both penetrating arteries\(^1-3\), venous occlusions can also result in similar lesions\(^6\).

Differential diagnosis between venous and arterial infarcts can be made according to infarct size, presence of edema and associated other territory infarcts. Venous infarcts are often larger in size, edematous and isolated\(^3,7\). Bilateral thalamic infarcts can also be seen as a result of top of the basilar syndrome; however they generally are associated with occipital, temporal or midbrain lesions. Similar lesion topography can be encountered with posterior cerebral artery main trunk involvement\(^8\). Medullary thalamic and thalamo-striate veins drain into the internal cerebral veins which join the Galen vein to finally constitute the straight sinus together with the inferior sagittal sinus\(^3\). Deep cerebral vein occlusion produces headache, nausea, vomiting, papilledema and sometimes changes in the mental status\(^3\). However, akinetic mutism has been seldom reported\(^3\). Generally cerebral venous thrombosis can present with different signs among which headache,
epilepsy, multiple cranial nerve palsies and neuropsychiatric disorders are more frequent.

Diagnosis of CVT is generally based on MR venography. In case one, cranial MRV revealed occlusion of deep venous drainage confirming the diagnosis. Further investigations showed the presence of a heterozygote mutation for Factor V Leiden and protein C deficiency. Therefore two hereditary coagulation disorders, mild thrombocytosis, and dehydration secondary to diarrhea were thought to be the underlying mechanisms in this particular patient.

The relatively sudden onset psychiatric disorder together with a history of venous thrombotic event seen in case two lead to the suspicion of deep cerebral venous thrombosis. This patient was also found to be heterozygous for factor V Leiden mutation.

Both presented cases emphasize the necessity to search for venous occlusions in the differential diagnosis of patients with acute disorders of consciousness and bilateral thalamic infarcts.

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