Woman with Sickle Cell Disease with Current Sigmoid Sinus Thrombosis and History of Inadequate Warfarin Use during a Past Thrombotic Event

Asuman Çelikkbilek^a Mehmet Çelikkbilek^b Alper Bozkurt^c
Başak Karakurum Göksel^d Meliha Tan^d Hakan Özdoğu^e

Departments of ^aNeurology, ^bInternal Medicine, and ^cRadiology, Başkent University, Medical School, Ankara, and the Departments of ^dNeurology and ^eHematology, Başkent University, Medical School, Adana, Turkey

Key Words

Venous sinus thrombosis · Sickle cell disease · Inadequate warfarin use · Magnetic resonance venography

Abstract

We report a 20-year-old woman with sickle cell disease (SCD) who presented with a severe pulsating headache, nausea, and vomiting. Her history was significant for a past thrombotic event during which she had not used anticoagulation therapy as prescribed. Her mental status was mildly confused. On funduscopic examination, papilledema and retinal hemorrhages were found. Results of a computed tomogram were normal. A lumbar puncture demonstrated increased intracranial pressure (60 cm H₂O). Magnetic resonance venography demonstrated a right sigmoid sinus thrombosis. Although SCD has been reported as a cause of thrombotic dural venous sinus events, this case increases the knowledge about neurological complications of SCD. The patient was treated with low molecular weight heparin, blood transfusions, acetazolamide, and methylprednisolone, and her symptoms and signs resolved.

Introduction

Sickle cell disease (SCD) is a well-known hereditary hematologic disorder of hemoglobin. Although SCD has been reported as a cause of dural venous sinus thrombosis (DVST) events, this case increases the knowledge about neurological complications of SCD [1]. Clinical manifestation of DVST can be life-threatening and

cause long-term neurologic deficits [2]. Here, we report a patient with SCD with a current sigmoid DVST and a medical history significant for a thrombotic event. She had been offered warfarin for the prior event but did not use the correct dosage.

Case Report

A 20-year-old woman with homozygous SCD was admitted to the Neurology Department at Başkent University in Adana, Turkey, for evaluation of a severe pulsating headache, nausea, and vomiting of 1 week duration. She had no fever, head trauma, or signs suggesting a respiratory tract infection. She complained of photophobia and phonophobia. On examination, her mental status was assessed as mildly confused; she subsequently became agitated. Her vital signs were within normal ranges. Results of a physical examination were normal. Funduscopic examination revealed papilledema and retinal hemorrhages (fig. 1). Her bilateral visual acuity was 3/10 with normal pupillary responses. She did not cooperate on vision field test.

She did not use alcohol or tobacco. Her medical history was significant for a thrombotic event 6 months earlier that had been treated with a right external iliac venous stent. She had been given warfarin, but she did not use it as prescribed. Along with inadequate warfarin use, she also had not attended the scheduled follow-ups.

Remarkable laboratory values (table 1) were: hemoglobin, 6.8 g/dl; hematocrit, 18%; white blood cell count, 23,200/mm³; and International Normalized Ratio (INR), 1.3. The hemoglobin S content was 76%. Hypercoagulation tests (i.e., antiphospholipid antibodies, antithrombin-3, and homocysteine levels) were negative, but her protein C and S levels were low. A lumbar puncture revealed an opening pressure of 60 cm H₂O. The cerebrospinal fluid analysis showed: glucose, 60 mg/dl (serum, 87 mg/dl); protein, 18 mg/dl; no white blood cells; no organisms on Gram staining, and no growth on bacterial cultures. After treatment a control lumbar puncture revealed a pressure of 17 cm H₂O.

Results of a brain computed tomogram were normal. Magnetic resonance imaging (MRI) and MR venography (MRV) showed a complete thrombosis of the right sigmoid dural venous sinus (fig. 2). She was treated with erythrocyte suspension transfusions and low-molecular-weight heparin (LMWH) (5,000 U s.c. two times daily; which was subsequently changed to warfarin during hospitalization), with methylprednisolone (48 mg daily) and acetazolamide (250 mg three times daily) to decrease the high intracranial pressure. Her symptoms resolved 15 days after the beginning of the treatment. During hospitalization her photophobia and phonophobia resolved. Her mental status became normal. A decision was made to continue therapy with warfarin after discharge lifelong. The patient was followed up closely with her parents' help and INR controls applied.

Control MRI and MRV examinations performed 3 weeks after the beginning of anticoagulation therapy showed an insoluble thrombosis that was still visible but had not progressed. In the 3rd month, control MRV was performed and partial flow obtained at the right sigmoid dural venous sinus. Visual tests were normal. MRV was repeated six months after discharge and chronic thrombus was seen at the right sigmoid dural venous sinus.

Discussion

Aseptic DVST is an important complication of SCD with high morbidity and mortality [2]. The current case increases the knowledge about neurological complications of SCD. It demonstrates the importance of effective anticoagulation therapy in an SCD patient with a medical history of a thrombotic event.

The alteration in mental status and the increased intracranial pressure together with headache, vomiting, and visual deficit should lead the physicians to suspect DVST. The symptoms and signs of DVST can vary from headache to coma [3]. Headache is the most frequently occurring symptom of DVST [4], as was the case in our patient. MRI and MRV are crucial for confirming DVST [5]. The sagittal sinus is most commonly involved in DVST [4]; however, in our patient, a right sigmoid sinus thrombosis was found.

DVST has been associated with infections, dehydration, renal failure, trauma, cancer, and hematologic disorders [6, 7]. Increased adherence of sickle cells to the vascular endothelia [8], abnormal platelet activation [9], endothelial cell damage and activation of cell adhesion molecules [10], low levels of proteins C and S, and increased antiphospholipids [11] contribute to thrombogenesis and vascular occlusion in SCD. The results of our patient's tests for hypercoagulation were negative, except for the low levels of protein C and S, which SCD patients usually have [12].

Unfractionated heparin and LMWH have been reported to be effective in treating DVST [13]. We treated our patient with LMWH because of easy administration to agitated and mentally confused patients.

In conclusion, in patients with SCD, careful medical histories should be taken, and physicians should be alert to any neurologic signs and symptoms that might be indicative of DVST. SCD patients with a history of a thrombotic event should be followed up closely to ensure adequate use of anticoagulation therapy.

Table 1. Patient's laboratory values

	Patient's value	Normal range
Hb, g/dl	6.8	12–17.5
Htc, %	18	36–53
WBC, /mm ³	23,200	4,500–11,000
INR	1.3	0.85–1.20
Hb S, %	76	negative
Antiphospholipid antibodies	negative	negative
Antithrombin 3, %	95	75–125
Homocysteine, μmol/l	15	5–15
Protein C, IU/dl	61	70–140
Protein S, IU/l	58	72–130
Serum glucose, mg/dl	87	60–105
Cerebrospinal fluid (CSF) glucose, mg/dl	60	40–70
CSF protein, mg/dl	18	15–45
CSF WBC	negative	
CSF gram stain	no bacteria	
CSF bacterial cultures	negative	

Fig. 1. Fundusoscopic examination revealed papilledema and retinal hemorrhages.

Fig. 2. Complete thrombosis of the right sigmoid dural venous sinus.

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