Case Report

Spinal Cord Infarction in Congenital Afibrinogenemia: A Case Report and Review of the Literature

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A 22-year-old woman with congenital afibrinogenemia presented with acute-onset rapidly progressive quadriparesis as a result of spinal cord infarction caused by vertebral artery dissection. Magnetic resonance imaging scans showed microhemorrhages in addition to edematous swelling suggesting acute ischemia throughout cervical and upper thoracic portions of the spinal cord. Fat-saturated T1-weighted magnetic resonance examination and digital subtraction angiography studies demonstrated cervical vertebral artery dissection on the right. This case provides an example of how a primary bleeding disorder could result in a severe ischemic complication caused by an occlusive vessel wall hematoma. Along with other reports, diagnostic and therapeutic aspects of this paradoxical situation were discussed in the particular setting of acute spinal cord ischemia. **Key Words:** Congenital afibrinogenemia—spinal cord—infarction—stroke—magnetic resonance imaging—dissection—vertebral artery.

Nontraumatic or spontaneous vertebral artery dissection (VAD) is an important but probably underdiagnosed cause of stroke albeit its frequency naturally increased after advent of relatively noninvasive magnetic resonance (MR) and computerized tomography–based angiography techniques into routine clinical practice. The typical clinical presentation mode is an acute ischemic stroke in the posterior circulation in association with neck pain, occipital headache, or both. According to a recently published neurologic case series[1] (the largest so far) of 169 patients with VAD, 77% presented vertebrobasilar ischemia and 71% reported neck/head pain, which was the sole manifestation in 12%. In 8% of the patients, VAD remained clinically silent. The rare manifestations were isolated subarachnoid hemorrhage (2%) and cervical radiculopathy (one case). Occurrence of subarachnoid hemorrhage is much higher in the neurosurgical case series,[2] and might be underestimated in the mentioned report. Indeed, subarachnoid hemorrhage occurs much more frequently with intracranial VAD compared with the extracranial ones.[3] No patient showed symptoms and signs of spinal cord ischemia in these reports.[1,2] Spinal cord involvement is well-recognized manifestation of VAD regardless of the source of the cases, but remained very rare especially in isolation.[4] The spectrum of spinal presentation of VAD encloses cervical radiculopathy,[4-6] spinal cord ischemia,[7-13] and spinal subarachnoid/epidural hemorrhage.[4]

Congenital afibrinogenemia and hypofibrinogenemia are extremely rare disorders of hemostasis with an

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Received April 15, 2008; revision received November 2, 2008; accepted November 3, 2008.

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1052-3057/$—see front matter

doi:10.1016/j.jstrokecerebrovasdis.2008.11.005

estimated incidence of 2 per million births.[14] Congenital afibrinogenemia usually manifests with umbilical cord bleeding, which leads to diagnosis during neonatal period in most cases. Long asymptomatic periods are not uncommon. Major disability without replacement therapy is less likely in congenital afibrinogenemia in comparison with other types of hemorrhagic diathesis. However, later and clinically important hemorrhagic complications are well recognized. Bleedings are often posttraumatic, but sometimes spontaneous.[15,16] These patients seem to be particularly prone to spontaneous spleen rupture in their young adulthood. Spontaneous, and sometimes catastrophic, intracerebral hemorrhages are also reported in patients with congenital afibrinogenemia.[17-20] In addition to hemorrhagic events, arterial and venous thrombotic and thromboembolic complications have been described, but remain exceptionally rare.[21-26] We herein report an afibrinogenemic patient with spinal ischemic stroke caused by VAD.

Case Report

A 22-year-old female university student presented to the emergency department with acute-onset severe neck pain and progressive right-sided weakness predominantly involving her arm. She woke up in a completely normal state in the morning. Around 10 am, she felt numbness in her right arm and very severe right-sided neck pain irradiating into the occiput, which initiated by a head rotation while she was walking. No precipitating factors including trauma were described. Pain and numbness had spontaneously ceased in the subsequent 10 minutes. After a rest for about 2 hours, weakness on the right side appeared.

Neurologic examination by an emergency department physician revealed a right-sided hemiparesis, which was more severe on the arm. Sensory examination was not performed at that time. Computerized tomographic imaging of the head was obtained, and showed no abnormal findings. An ischemic stroke was then diagnosed, and aspirin (300 mg) was administered orally.

On medical history, diagnosis of congenital afibrinogenemia for more than 20 years was elicited. Until the current episode, she had only experienced occasional episodes of minor bleeding and had been using fibrinogen replacement almost regularly around menstruation. No stroke risk factor including hypertension or smoking was present. On admission, blood fibrinogen level was 67 mg/dL (normal range: 144-430). Prothrombin time and activated partial thromboplastin time were immeasurable high (>150 seconds). Apart from slightly low hemoglobin level (10.6 g/dL), complete blood cell count and biochemistry were within normal limits.

The acute stroke team evaluated the patient after progression of her weakness to the left side almost 12 hours after her emergency arrival. Our examination disclosed a quadriparesis sparing her face, which was more severe on the right side and in the upper extremities. The degree of motor weakness, assessed on the Medical Research Council scale, was grade 0 in the right arm, grade 1 in the right leg, grade 2 in the left arm, and 3 negative in the left leg. Babinski's sign was negative bilaterally. Deep tendon reflexes were absent on the right and significantly diminished on the left side. A decreased pain sensation below the level of third cervical (C3) segment was detected bilaterally. In addition, vibration and position sense was diminished below the C4 level on the right side. No loss of temperature sense was elicited. A right-sided Horner's syndrome was noted. The remaining neurologic examination was unremarkable. Of note, cranial nerves were intact.

Spinal MR imaging (MRI), obtained 23 hours after symptom onset, disclosed findings compatible with a spinal cord infarction extending from upper cervical to the midthoracic segments. T2-weighted MRI showed hyperintensity with swelling in the spinal cord predominantly on the right half with some extension to the left reaching from vertebral body C4 to C7. (Fig 1, *A* and *B*). Below this level, this appearance was limited to the central portions of the cord with right dominance, and showed a relative sparing of the periphery. Scattered microhemorrhages within the lesion were noted in an exaggerated manner on T2* gradient-echo (GRE) sequences (Fig 1, *C*). No gadolinium enhancement was observed. Fat-saturated T1-weighted spin-echo imaging showed hyperintense mural hematoma in the right vertebral artery suggestive of dissection (Fig 1, *D*), and occlusion of the vessel was visible on accompanying pulse sequences (Fig 1, *B* and *C*). Cranial MRI was also obtained, and did not reveal any abnormality.

A pulse methylprednisolone (1 g/day) was initiated intravenously for 5 days followed by a rapid taper in 12 days. During the first 4 days, significant improvement of motor deficit in the left side and sensory deficit on the right side was observed. Suggesting an anterior unilateral spinal infarct, her right-sided hemiparesis and left-sided pain sensation deficit persisted. Fifteen days after her admission, standard digital subtraction angiography was performed and disclosed a long segment occlusion of the right vertebral artery compatible with dissection (Fig 2).

In addition to fibrinogen replacement, she was treated conservatively including thromboprophylaxis and extensive rehabilitation program. Of note, we did not use anticoagulants. Her neurologic deficit recovered dramatically over the next few months except for the weakness of her right hand. When discharged after 4 months, she was able to walk and to perform most daily activities without aid.

After that, she continued to improve, and had only significant weakness in the right hand in addition to the mild weakness of the left lower limb. Her bowel and bladder