CASE REPORT

Spontaneously developed paraplegia in a patient with Factor V Leiden mutation

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Factor V Leiden (FVL) mutation is the one-point mutation in G1691A in the tenth exon of the gene for Factor V, caused by the substitution of glutamine for arginine at codon 506. We present here a patient with a mutation of the Factor V gene and taking anticoagulant therapy, who became paraplegic following surgery for dural hematoma and spontaneous spinal intramedullary hematoma. His physical examination revealed T5 ASIA A, complete paraplegia. Our case is important in the literature, as being the first case with spinal intramedullary hematoma that developed due to anticoagulant use.

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Prothrombotic pathologies may be acquired or hereditary, or may exist due to more than one cause. Disorders defined as the causes of hereditary thrombophilia include dysfibrinogenemia, and those due to mutations in the genes coding for antithrombin III, protein C, protein S, prothrombin (prothrombin G20210A) and Factor V, and due to deficiencies of these factors.^{1,2} The most frequent cause of hereditary thrombophilia is the resistance for activated protein C (APC). The most frequent mutation that causes resistance for APC is the mutation in the gene for Factor V.³ Factor V Leiden (FVL) mutation is the one-point mutation in G1691A in the tenth exon of the gene for Factor V, caused by the substitution of glutamine for arginine at codon 506. The prevalence of FVL mutation changes between 2 and 15%.⁴

We present here a patient with a mutation of the Factor V gene and taking anticoagulant therapy, who became paraplegic aftermath surgery for dural hematoma and spontaneous spinal intramedullary hematoma.

A 46-year-old male patient attended the cardiovascular surgery clinic 14 months ago with complaints of suddenly existing pain and swelling below his knee. The diameter of the cruris below the right knee was found to be 3 cm larger compared with the left side, and the Homan's test was determined to be positive. Doppler USG revealed hypoechoic thrombus in the right CFV and PV, permitting partial blood flow; this sign was interpreted as acute DVT, and acute medical therapy was applied. He was recommended to take coumadin 1 × 1, and was then discharged from the hospital. On 21 July 2014, the patient again attended the cardiovascular surgery clinic with complaints of pain and swelling in the right thigh. Doppler USG revealed subacute thrombus in the right femoral vein and posterior tibial vein. The genetic analysis revealed homozygous missense mutation in the gene G1691A (R560Q and Arg506Gln), and he was diagnosed with FVL mutation. Prothrombin gene, FV Cambridge, MTHFR C667T and MTHFR A1298C mutations were not determined, and protein C, protein S and Antithrombin 3 activities, and homocysteine level were in the normal ranges. Family history did not reveal the diagnosis of a similar disease. The patient was evaluated by the rheumatologist on 8th August 2014, and Lupus anticoagulant antibody (LAC) was

determined to be positive, and the beta 2 glycoprotein level was normal; with these findings, the patient was diagnosed as antiphospholipid syndrome, and chloroquine treatment was started. In his subsequent follow-ups at the rheumatology clinic, it was considered that the LAC positivity (false-positivity) was related to the anticoagulant use, and the chloroquine therapy was stopped; his echocardiogram and the tests for the detection of an inflammatory disease were found to be normal at those dates. The patient attended the emergency clinic on 4 June 2015, with the complaint of a sudden feeling of heat in the left foot; he had been experiencing backache for 1 week, but the physicians did not take this into account. No anamnesis of trauma was present, and he had been taking his drugs regularly. During his follow-up in the emergency clinic, over two days a rapidly progressing weakness developed in his lower extremities. Cranial, cervical and lumbar magnetic resonance images were found to be normal; however, his thoracic MRI revealed a lesion of approximately 22 × 6 mm in size, in the right anterior of medulla spinalis at T4–5 level, that was visualized hyperintense in the T2A series, and isointense in the T1A series (Figure 1). Brain surgeons operated emergently on the patient; a hemorrhage located in the dura and spinal intramedullary area was evacuated, and decompression was carried by a T3–4 laminectomy. Intramedullary hematoma was determined during the operation. He was referred to the physical therapy and rehabilitation clinic after the surgery. His physical examination revealed T5 ASIA A complete paraplegia.

Factor V (Leiden) gene locus is located in chromosome 1 (1q24.2). Factor V gene mutation is the substitution of A nucleotide for the G nucleotide at position 1691 (G1691A), and the replacement of a single amino acid (Arg506Gln) in one of the three different APC cleavage sites of the Factor Va molecule. FVL mutation shows autosomal dominant inheritance, and accounts for most of the cases existing with APC resistance. In the cases with FVL mutation, APC cannot normally inactivate the Factor V. Frequency of the FVL mutation is reported to exist in 20–25% of the patients with the first venous thrombosis attack, and in 20–50% of the patients with repeated venous thrombosis attacks.⁵ The risk of thromboembolism increases nearly sevenfold with the heterozygous mutation, and nearly eightyfold with the

Figure 1. Thoracic MRI images of the patient.

homozygous mutation, compared with the normal population. The incidence of venous thromboembolism is about 1/1000 in the normal population, and homozygous mutation exists in about 1% of the cases with venous thromboembolism.¹

In various studies, FVL frequency has been reported to vary between 3.5 and 15% in Turkey; however, the frequency of carriers was found to be about 7.9% in adults and about 10.9% in neonates.⁶ Gürgey *et al.*⁷ investigated 146 cases with thrombosis in Turkey, and FVL mutation was detected in 45 patients; seven of these existed with a homozygous mutation and 38 had heterozygous mutation. Genetic analysis of our patient revealed homozygous mutation.

Jackson⁸ first defined nontraumatic, spontaneous spinal hematoma, and the clinical onset is a sudden backache generally occurs with radicular spread in more than 50% of cases. Following the spread of severe, local pain over all vertebral area, complete paralysis can develop, generally within minutes or hours. Cases with spinal epidural hematoma related to oral anticoagulant use have been reported in the literature. Most of the cases existed with spinal epidural hematoma in the posterior region; one case was determined to have spinal epidural hematoma in the anterior region, and was treated using conservative measures.⁹ Our case existed with a spontaneous back pain lasting for one week, and his analysis, using visualization techniques, revealed anterior spinal subdural hematoma and spinal intramedullary hematoma.

Surgical treatment may not be preferred for epidural hematomas if the symptoms are not clinically progressive or if signs of early recovery exist. If there are signs of progressive spinal cord compression, surgical treatment must generally be performed, whatever may be the cause of hematoma.¹⁰ Success rates in surgical treatment depend on the time between the onset of the symptoms and surgical intervention. The surgical outcome is also better in those cases where the hematomas are localized in the lumbosacral region, compared with hematomas in the thoracic area and hematomas localized at the level of a single vertebra. Clinical neurological impairment was thought to be better explained by arterial hemorrhage, originating from the blood-rich area supplied by the epidural arteries.^{11,12} Surgical treatment was performed in our case due to the progressive existence of complete paralysis that developed after the existing hematoma; the postoperative examination of the patient was in accordance with complete spinal cord damage.

Our case is important in the literature, as being the first case with spinal intramedullary hematoma that developed due to anticoagulant use. We have also stressed that a sudden pain in the spine has to be considered very seriously in cases with FVL mutation, and these cases need a careful neurological examination and must be analyzed by visualization techniques like MRI, if necessary, to avoid missing any disease.

COMPETING INTERESTS

The authors declare no conflict of interest.

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