# Spontaneous Bilateral Vertebral Artery Dissection Secondary to PAI-1, MTHFR C677T and ACE Gene Mutations in a Young Man

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Vertebral artery dissections (VAD) present with posterior neck pain, suboccipital headache and posterior circulation ische-mia [1]. The annual incidence is 1-1.5 per 100,000 [1]. Causes include trauma, respiratory infection, hypertension, oral contraceptive drugs, inherited connective tissue disorders [2] and genetic mutations. We report bilateral spontaneous VAD in a healthy young man in association with MTHFR C677T, PAI-1 and ACE gene mutations.

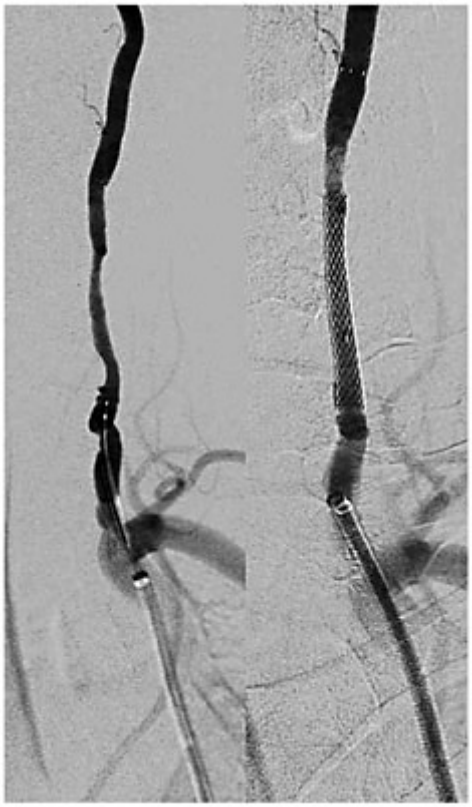
## Case Report

A 42-year-old healthy man with no history of hypertension, diabetes mellitus, headaches or smoking presented with acute severe posterior neck pain with occipital headache, vertigo and vomiting. The patient had not sustained any trauma recently and had not undergone any unusual physical activity or neck manipulation. He has no personal or family history of systemic illnesses, connective tissue diseases, myocardial infarctions or cerebrovascular insults. Physical examination revealed a weight of 77 kg and systolic blood pressure of 170 mm Hg. He was afebrile with no neck stiffness, and no carotid bruits or cardiac murmurs. He had a normal neurologic examination except for an unsteady gait with persistent tendency to fall to the left side and an abnormal tandem walking.

MRI of the brain revealed an acute infarct involving the inferior aspect of the left cerebellum. Four-vessel angiography revealed focal dissection of both vertebral arteries. The dissection of the left vertebral artery extended over 1.1 cm with a narrowing of 60%. The patient was started on intravenous heparin and underwent sequential stenting of both vertebral arteries (fig. 1).

**Fig. 1**

Angiography of the left vertebral artery revealing the dissection and stenosis corrected by insertion of a metallic stent.



Investigation revealed normal protein C, protein S, anti-thrombin III, fibrinogen level, p-ANCA, c-ANCA, ANA and negative anti-cardiolipin antibody.

Screening for genetic mutations revealed homozygous MTHFR C677T, homozygous 4G allele of the PAI-1 gene, homozygous D-allele of the ACE gene, heterozygous factor V Leiden and heterozygous factor II G20210A.

## Discussion

Stroke in young adults is no longer a rare phenomenon. One third occur in patients younger than 65 years [3]. Etiologies include atrial fibrillation with embolization [3], hypertension, diabetes mellitus, cervicocerebral stenosis [1,2,4], cerebral venous thrombosis [5] and a hypercoaguable state [4,5,6,7,8,9].

Carotid stenosis and strokes are associated with PAI-1 mutation [4]. Venous thrombosis has been associated with factor V Leiden, prothrombin II G20210A and MTHFR C677T gene mutations [5,6]. The prothrombin II G20210A mutant gene is associated with a 5.1-fold increase in ischemia [7].

The most frequent candidate polymorphism associated with the risk of cerebral stroke include ACE, factor V Leiden, MTHFR, prothrombin G20210A and apolipoprotein E [8]. The thrombogenic risk factor increases with the cumulative existence of the variant mutations: the gene-dose effect [6,9].

Our patient suffered from VAD associated with MTHFR C677T, ACE and PAI-1 gene mutations. These specific mutations have been reported to be associated with cerebral venous thrombosis and cerebral stokes [4,5,10] but not with VAD. The genetic variants support the gene-dose effect theory.

## Conclusion

We suggest that patients who present with spontaneous unilateral or bilateral VAD without any recognizable

cause should be studied for MTHFR C677T, ACE and PAI-1 gene mutations.

Carriers of these gene mutations need to control further risk factors for cerebral strokes and should screen their vertebral arteries in case they experience unexplainable headache and neck pain.


1. **External Resources**
2. **External Resources**
3. **External Resources**
4. Streifler JY, Rosenberg N, Chetrit A, Eskaraev R, Sela BA, Dardik R, Zivelin A, Ravid B, Davidson J, Seligsohn U, Inbal A: Cerebrovascular events in patients with significant stenosis of the carotid artery are associated with hyperhomocysteinemia and platelet antigen-1 (Leu33Pro) polymorphism. Stroke 2001;32:2753-2758.
   **External Resources**
5. **External Resources**
6. **External Resources**
7. **External Resources**
8. **External Resources**
9. Pezzini A, Grassi M, Del Zotto E, Archetti S, Spezi R, Vergani V, Assanelli D, Caimi L, Padovani A: Cumulative effect of predisposing ge-notypes and their interaction with modifiable factors on the risk of ischemic stroke in young adults. Stroke 2005;36:533-539.
   **External Resources**
10. **External Resources**