

Case Report

Isolated Cortical Vein Thrombosis Associated with Prothrombin Gene Mutation

Elias A. Giraldo, MD, MS,* Rohan Arora, MD,† and Robert A. Koenigsberg, DO*

Isolated cortical vein thrombosis (ICVT) accounts for less than 1% of strokes. We report a 47-year-old female patient who had a frontal hemorrhage with headache associated with contralateral hemiparesis and hemisensory deficit on presentation. This hemorrhagic stroke was localized in a nonarterial territory, and it was caused by ipsilateral and isolated thrombosis of the vein of Labbe found on catheter angiogram that demonstrated a filling defect of the vein of Labbe at its connection with the transverse sinus. There were no filling defects in the superficial middle cerebral veins. Our patient had a family history of cardiovascular disease, stroke, and factor V Leiden mutation and cigarette smoking as stroke risk factors. Complete prothrombotic state laboratory workup revealed a heterozygous prothrombin G20210 A gene mutation. The patient's hospital course was uneventful. Neurologic exam was normal at stroke clinic follow-up 6 weeks later. To our knowledge, this is the first report of an ICVT associated with prothrombin gene mutation.

© 2013 by National Stroke Association

A 47-year-old Caucasian woman was brought to the emergency department 1 hour after sudden onset of headache behind the right eye followed by numbness of her right leg while sitting at her work desk. She tried to get up but was unable to walk because of leg weakness. Subsequently, she complained of paresthesias involving her right arm. She denied nausea or vomiting. She did not have seizures. The patient did not have any medical history. She denied the use of oral contraceptives. Social history was remarkable for a 30 pack-year history of smoking. The patient had a family history of first-degree relatives with stroke, hypertension, diabetes, and factor V Leiden mutation. On presentation, blood pressure was

130/70 mm Hg, pulse was 80 beats per minute, respirations 12 breaths, and temperature 37°C. Neurologic exam demonstrated right hemiparesis with upper extremity 4/5 motor deficit and lower extremity 3/5 motor deficit and right hemisensory loss to light touch. National Institutes of Health Stroke Scale (NIHSS) score = 4 and modified Rankin scale (MRS) score = 3. General exam was normal. A noncontrast head computed tomography scan demonstrated a hemorrhage in the left frontal lobe (Fig 1). A magnetic resonance (MR) imaging scan of the brain revealed an infarct with hemorrhage transformation in the left frontal lobe. Gradient echo showed hemosiderin deposits in the left frontal hemorrhage (Fig 2). An MR angiogram and an MR venogram were both negative. A catheter angiogram revealed near-occlusive thrombus affecting the left vein of Labbe at its junction with the left transverse sinus characterized by abnormal intraluminal filling defects identified on the venous phase (Fig 3). Complete laboratory workup (sedimentation rate, C-reactive protein, homocysteine, rheumatoid factor, antinuclear antibody, antinuclear antigen, anti-double-stranded DNA, lupus anticoagulant, anticardiolipin antibodies [immunoglobulin [Ig] A, IgM, and IgG], protein C, protein S, factor V Leiden mutation, antithrombin III,

From the *Department of Neurology, Drexel University College of Medicine, Philadelphia, Pennsylvania; and †Department of Radiology, Drexel University College of Medicine, Philadelphia, Pennsylvania.

Received November 21, 2012; accepted June 5, 2013.

Address correspondence to Elias A. Giraldo, MD, MS, Department of Neurology, Drexel University College of Medicine, 245 North 15th St, Room 7102, Philadelphia, PA 19102. E-mail: elias.giraldo@drexelmed.edu.

1052-3057/\$ - see front matter

© 2013 by National Stroke Association

<http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.06.004>



Figure 1. Noncontrast head computed tomography showed hematoma in the left frontal lobe (arrow).

methylenetetrahydrofolate reductase [MTHFR] gene, thrombomodulin gene, coagulation factor VII, and coagulation factor VIII) was negative except for a heterozygous trait (1 copy) for prothrombin G20210 A gene mutation. Long-term oral anticoagulation was started with warfarin. Bridge anticoagulation with intravenous unfractionated heparin was discontinued once the patient's

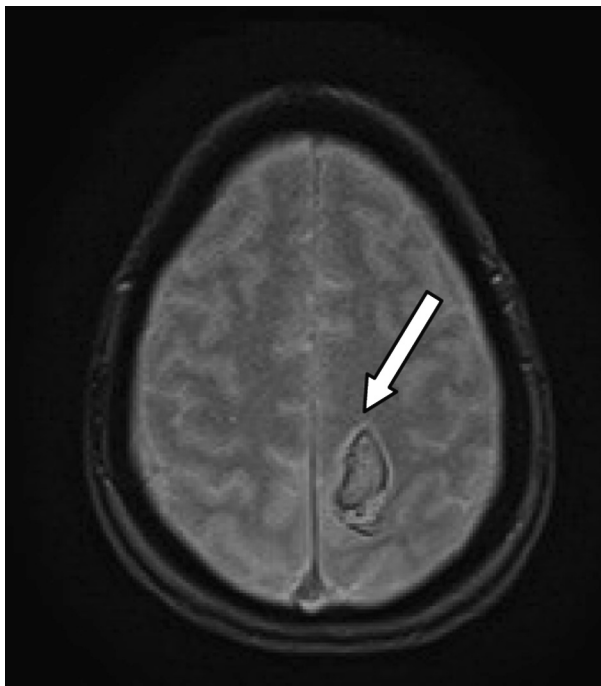


Figure 2. Gradient echo brain magnetic resonance imaging demonstrated hemosiderin deposits in frontal hematoma (arrow).

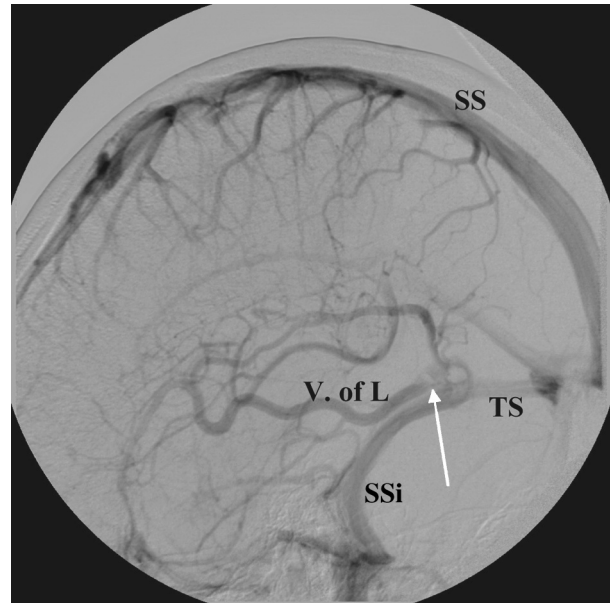


Figure 3. Filling defect (arrow) in the V. of L draining into the TS (venous phase of left carotid injection). Abbreviations: SS, sagittal sinus; SSi, sigmoid sinus; TS, transverse sinus; V. of L, vein of Labbe.

international normalized ratio = 2-3. Four-day hospital course was uneventful and the patient improved from neurologic deficits with NIHSS score = 1 (right lower extremity 4+ /5 motor deficit) and MRS score = 2. The patient was discharged home with physical and occupational therapy. On stroke clinic follow-up 6 weeks later, the patient's neurologic exam was back to normal with NIHSS score = 0 and MRS score = 0.

Discussion

We report a patient with a hemorrhagic cerebral infarction caused by isolated thrombosis of the left vein of Labbe associated with prothrombin G20210 A gene mutation. The veins of Labbe are part of the superficial venous system of the brain. They are also called the inferior anastomotic veins, and they connect the superficial middle cerebral veins and the transverse sinuses.¹ Isolated cortical vein thrombosis (ICVT) in the absence of cerebral sinus thrombosis is rare and represents less than 1% of patients with stroke.² The vascular territory of the vein of Labbe's drainage usually overlaps with the vascular territory of the middle cerebral artery temporal branches. Thrombosis of this vein typically results in a characteristic pattern of hemorrhagic infarction in the lateral aspect of the underlying temporal lobe.³ Our patient's left frontal hemorrhage (Fig 1) did not follow any arterial territory. The patient's hemorrhagic venous infarct location might have been a consequence of venous hypertension caused by the abrupt occlusion of the left vein of Labbe at its junction with the ipsilateral superficial middle cerebral veins and the ipsilateral transverse sinus. The catheter cerebral angiogram might have shown cerebral vein thrombosis

with partial spontaneous recanalization because this study showed only thrombosis of the vein of Labbe at its connection with the transverse sinus without filling defects in the superficial middle cerebral veins. This might be explained by the fact that the catheter angiogram was obtained 24 hours after stroke symptom onset. We started anticoagulation after the catheter angiogram.

The incidence of cerebral venous thrombosis (CVT) including ICVT is unknown because of the lack of epidemiological information. Most cases of CVT have been found in the young as demonstrated in the largest observational study on CVT ($n = 465$) in which it was found that the patients' median age was 37 years.⁴ In addition, the International Study on Cerebral Vein and Dural Sinus Thrombosis showed that the prognosis of CVT is good in terms of mortality and disability (MRS score ≤ 2) for most adult patients with early and appropriate treatment except for a group of patients (13%) who had bad outcomes (MRS score ≥ 3).⁴ Our patient was 47 years old and had an excellent functional outcome (MRS score = 0) in accordance with prior literature.

Prothrombin G20210A gene mutation is a point mutation in the 3'-untranslated region of the prothrombin gene (G20210 G to A) that is associated with increased plasma levels of this clotting zymogen and has been identified as an independent risk factor for deep venous thrombosis.⁵ Prothrombin G20210 A mutation is found in 2% of Caucasians with a pooled odds ratio of CVT = 9.27 (95% confidence interval: 5.85-14.67) that is stronger than its association with venous thromboembolism in general.⁵ Our patient was a Caucasian and had a prothrombin G20210 A heterozygous mutation that is associated with a 2-3 times higher risk to develop a first venous thrombotic event (2-3 in 1000 people per year).⁶ Of 6 genes and their 6 respective polymorphisms associated with CVT, factor V Leiden G1619 A gene mutation and prothrombin G20210 A gene mutation appear to contribute to about one third of the cases of CVT occurring

every year in the United States. These gene mutations confer a greater genetic susceptibility for venous rather than arterial thrombosis.⁷ Our patient's thrombophilia might have been enhanced by predisposing factors such as cigarette smoking and family history of factor V Leiden mutation.

We report the first case of isolated thrombosis of the vein of Labbe associated with a heterozygous prothrombin G20210 A gene mutation. Our case demonstrates the usefulness of obtaining a gold standard catheter angiogram for the evaluation of a hemorrhagic stroke and how important is to obtain a complete prothrombotic state laboratory workup in patients with thrombophilia that require long-term anticoagulation for secondary stroke prevention.

References

1. Carpenter MB. Core text of neuroanatomy. Baltimore, MD: Williams & Wilkins, 1991:458.
2. Rathakrishnan R, Sharma VJ, Luen TH, et al. The clinico-radiological spectrum of isolated cortical vein thrombosis. *J Clin Neurosci* 2011;18:1408-1411.
3. Osborne AG. Diagnostic cerebral angiography. Philadelphia, PA: Lippincott Williams & Wilkins, 1999:217-227.
4. Ferro JM, Canhão P, Stam J, et al. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004;35:664-670.
5. Poort SR, Rosendaal FR, Reitsma PH, et al. A common genetic variation in the 3' untranslated region of the prothrombin gene is associated with elevated prothrombin plasma levels and an increase in venous thrombosis. *Blood* 1996;88:3698-3703.
6. Dentali F, Crowther M, Ageno W. Thrombophilic abnormalities, oral contraceptives, and risk of cerebral vein thrombosis: a meta-analysis. *Blood* 2006;107:2766-2773.
7. Saposnik G, Barinagarrementeria F, Brown RD Jr, et al. Diagnosis and management of cerebral venous thrombosis. A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011;42:1158-1192.