



# Massive Resting Shunt on c-TCD: A Clue to Pulmonary Arteriovenous Malformation in a Young Stroke Patient

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A 17-year-old female presented with migraine with visual aura. Brain magnetic resonance imaging demonstrated a hyperintense area on diffusion-weighted imaging with corresponding hypointensity on the ADC adjacent to the right cerebral aqueduct [also hyperintense on fluid-attenuated inversion recovery, indicating an acute ischemic infarction (Figure 1a-c)]. No traditional cerebrovascular risk factors were identified. A right-to-left shunt was considered owing to the combination of early-onset cryptogenic stroke, migraine with aura, and a family history of persistent epistaxis affecting her mother, grandfather, and all four maternal aunts.<sup>1,2</sup>

Contrast-enhanced transcranial Doppler (c-TCD) was performed following a standardized protocol.<sup>3</sup> Briefly, an agitated saline contrast agent (9 mL of isotonic saline, 1 mL of air, and a drop of the patient's blood) was administered intravenously. The bilateral middle cerebral arteries were monitored for 25 s after injection, both at rest and during a Valsalva maneuver. The right-to-left shunt was graded based on the maximum microbubble count using a standard four-level classification: small ( $\leq 10$  microbubbles); moderate, (11–20 microbubbles); large, ( $> 20$  microbubbles); and “curtain-like” pattern (uncountable microbubbles).<sup>4</sup> c-TCD examination revealed a “curtain-like” pattern of microbubbles in bilateral middle cerebral arteries immediately and persistently after contrast injection at rest, which was unaffected during the Valsalva maneuver (Figure 1d-i). This finding is highly suggestive of an extracardiac shunt, typically pulmonary arteriovenous malformation (PAVM).<sup>5</sup> Subsequent computed tomography (CT) angiography confirmed a PAVM in the right lower lobe (Figure 1j and k). Genetic testing identified a pathogenic frameshift variant in *ENG* (c.1097\_1100delACGC), confirming the diagnosis of hereditary hemorrhagic telangiectasia (HHT) type 1.<sup>2</sup>

Paradoxical embolism through the PAVM is the most plausible mechanism for cerebral infarction in this young patient. First, her risk of paradoxical embolism score of 9 indicates a high-risk of stroke from paradoxical embolism.<sup>5</sup> c-TCD showed immediate, persistent “curtain-like” microbubbles without Valsalva augmentation, a pattern

characteristic of PAVM, which was confirmed by CT angiography.<sup>6</sup> Second, although she had migraine with aura, the periaqueductal infarct location was atypical for primary migrainous infarction.<sup>7</sup> Third, small vessel disease was highly unlikely given her age and absence of cerebrovascular risk factors or corresponding imaging results.<sup>8</sup>

The confirmation of a pathogenic *ENG* variant and diagnosis of HHT type 1 have direct and profound implications for the patient and her family. Patient management includes treating beyond the symptomatic PAVM to encompass systematic screening for other potential vascular malformations (e.g., cerebral and hepatic) and lifelong multidisciplinary follow-up according to HHT guidelines.<sup>2</sup> Importantly, this genetic diagnosis requires a change in the family care model, allowing for genetic testing for at-risk first-degree relatives. Given the 50% transmission risk of this autosomal dominant disorder, preconception genetic counseling is imperative.<sup>9</sup> This highlights the essential role of genetic testing in shifting HHT management from reactive to preventive.

After diagnostic assessment, the patient underwent embolization of the PAVM in the right lower lobe. After the procedure, her migraine with visual aura disappeared completely, and she did not experience any neurological symptoms. The one-year radiological follow-up confirmed complete occlusion of the malformation.

HHT, an autosomal dominant genetic disorder, affects approximately 1 in 5000 individuals and is defined by vascular malformations that might lead to complications, such as paradoxical embolization.<sup>2</sup> PAVM screening in patients and their first-degree relatives is crucial because untreated PAVMs are associated with risk of stroke and other severe complications.<sup>10</sup> Early detection allows for procedures such as embolization to prevent recurrent paradoxical emboli. This case highlights the significance of using c-TCD for PAVM screening in young patients experiencing a stroke, particularly those with migraines, unexplained neurological symptoms, or a relevant family history.



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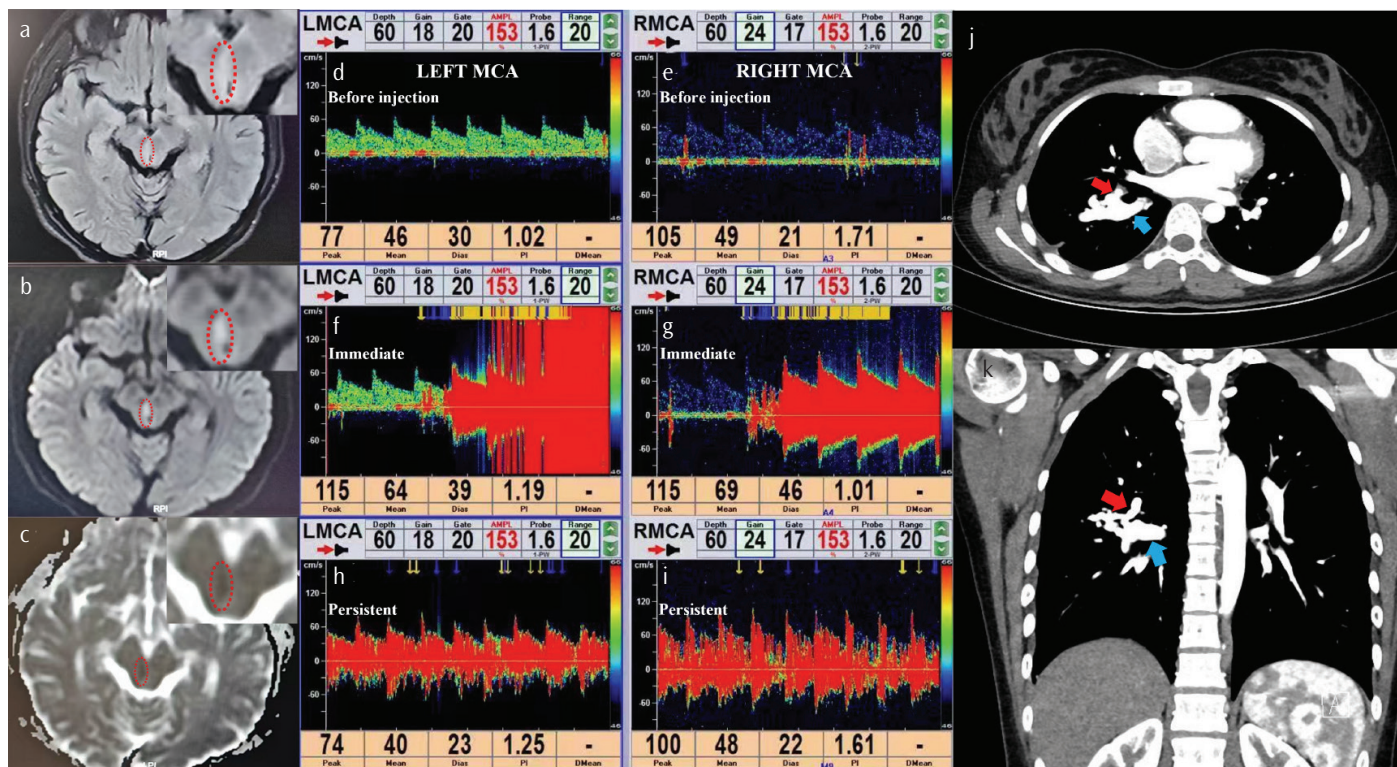
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**FIG. 1.** Brain MRI, c-TCD, and CT angiography. (a-c) Brain MRI of a right periaqueductal acute infarct (outlined by red dashed lines; magnified views in insets). Signal characteristics: subtle hyperintensity on fluid-attenuated inversion recovery (a), hyperintensity on diffusion-weighted imaging (b), and hypointensity on ADC (c). (d-i). Bilateral MCA c-TCD waveforms at baseline (d, e), immediately after (f, g), and persistently after contrast injection at rest (h, i), showing an immediate and persistent “curtain-like” microbubble pattern. (j, k) CT angiography confirms a right lower lobe pulmonary arteriovenous malformation, showing early contrast filling within the malformation (red arrow) and dilated draining pulmonary veins (blue arrow). MRI, magnetic resonance imaging; CT, computed tomography; c-TCD, contrast-enhanced transcranial Doppler.

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