Cerebral microemboli detection for monitoring structural cardiac disease

Mohammad Shafie, MD, PhD; Shlee Song, MD; Mani Nezhad, MD; John Lamberti, MD; Mark Cocalis, MD; Michael Cavallaro, RVT; Brenda Rinsky, RVT; Patrick Lyden, MD

Cardiac structural disorders can be detected noninvasively with echocardiography or cardiac MRI. Neither of these techniques, however, visualizes emboli, although thrombi can often be seen on valves or walls. Transcranial Doppler ultrasound (TCD) has been shown to be exquisitely sensitive at detecting microemboli, which may be a harbinger of impending macroembolization resulting in stroke.^{1,2} This report demonstrates the presence of a major valvular thrombus not visualized on echocardiography, but detected by TCD microemboli detection.

Case report

A 15-year-old boy with complex congenital cardiac condition was referred to the stroke clinic at Cedars-Sinai Medical Center (CSMC) for evaluation of persistent headache and visual complaints. Born with a complete atrioventricular canal defect and Shone complex, the patient had required 2 aortic and 3 mitral prosthetic valve replacements, necessitating oral anticoagulation therapy with warfarin and permanent pacemaker placement for sick sinus syndrome. At age 8 years, he began experiencing recurrent episodes of vision changes associated with headaches. In the ensuing years, he had received various diagnoses, from retinal migraine to Susac syndrome, and despite numerous treatments from verapamil to mycophenolate and steroids, he suffered a left branch retinal artery occlusion followed by a right central retinal artery occlusion, leaving him with generalized constriction but preservation of central vision in his left eye, and superior quadrantanopsia in his right eye. Prior to presentation to CSMC, thorough neurologic workup including head and neck CT angiogram and brain MRI and extensive cardiac evaluations with multiple transthoracic echocardiograms (TTEs) and transesophageal echocardiograms (TEEs) were all unremarkable, including no evidence of patent foramen ovale. At presentation to CSMC, he continued to have persistent daily headaches while on daily aspirin 81 mg and warfarin with therapeutic international normalized ratio. The only notable findings on his neurologic examination were his visual field deficits.

To investigate cerebral embolization as a possible source of the patient's vision loss, a complete TCD study detected high-intensity transient signals (HITS) frequently in the entire circle of Willis, in bilateral anterior and posterior circulations, as well as in bilateral ophthalmic arteries (figure 1A). During a 60-minute TCD microemboli detection, HITS were detected at a rate of 156 per hour in bilateral middle cerebral arteries (MCAs). Consequently,

Practical Implications

Consider the potential superiority of transcranial Doppler ultrasound in detection of microemboli-generating cardiac thrombus over multiple cardiac modalities including transthoracic and transesophageal echocardiography.

Department of Neurology (MS), University of California, Irvine; Department of Neurology (SS, MN, M Cavallaro, BR, PL), Cedars-Sinai Medical Center, Los Angeles, CA; Department of Surgery (JL), University of California, San Diego; Children's Heart Institute (JL), Rady Children's Hospital, San Diego, CA; and Benioff Children's Hospital (M Cocalis), University of California, San Francisco.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Correspondence to: patrick.lyden@cshs.org

Figure 1 Complete transcranial Doppler ultrasound (TCD) study and microemboli detection

(A) Complete TCD study on 81 mg aspirin plus warfarin. (B) TCD microemboli detection plus 100% O₂; patient on 162 mg aspirin and warfarin. (All studies with therapeutic international normalized ratio.)

Figure 2 Postoperative transcranial Doppler ultrasound microemboli detection study in bilateral middle cerebral arteries

Postoperative 30 (A) and 60 (B) minutes; patient on 81 mg aspirin and clopidogrel 75 mg.

the patient's dose of aspirin was increased from 81 mg to 162 mg daily in addition to continuation of therapeutic warfarin.

Follow-up TCD microemboli detection demonstrated 178 and 107 HITS, in the left and right MCAs, respectively. To delineate the composition of these microbubbles, i.e., gas vs solid, 100% oxygen was administered during TCD microemboli detection. While on oxygen, TCD detected 128 and 167 HITS in the left and right MCAs, respectively (figure 1B). Subsequently, repeat cardiac imaging including TTE and TEE studies to detect a microemboli source were unremarkable. Given the patient's persistent microemboli despite aggressive antithrombotic therapy, the patient underwent open heart surgery and was found to have an organized thrombus on his mitral mechanical heart valve (MHV). He received replacement of his aortic and mitral mechanical valves with bioprosthetic valves. On a follow-up visit to CSMC, approximately a month after his surgery, while remaining on daily aspirin 81 mg and clopidogrel 75 mg, the patient's headache episodes had resolved, and his repeat 60-minute TCD microemboli detection did not reveal any HITS (figure 2, A and B).

DISCUSSION

Cerebral microembolization, a commonly recognized phenomenon after cardiac procedures, and its detection as HITS on TCD has been widely reported in patients with prosthetic MHVs.^{1,3} Most HITS in these patients are thought to be gaseous microbubbles produced through cavitation, during which the MHV closure creates a region of low pressure near the valve, resulting in formation of microscopic gas bubbles.⁴ However, an unknown fraction of HITS detected by TCD may represent solid microemboli.⁵ The distinction between gaseous and solid microemboli is clinically relevant since previous studies suggested that gaseous emboli appear to have minimal effect on neurologic outcome,⁵ while solid microemboli are thought to be thromboembolic and believed to be associated with stroke and cognitive

deficits.⁶ To distinguish solid thromboembolic from benign gaseous microparticles in patients with MHVs, inhalation of 100% oxygen has been used to suppress cavitation and transiently decrease the counts of HITS detected by TCD due to gaseous compared to no effect on solid microemboli.⁷

This case highlights the utility of TCD with microemboli detection to identify continuous generation of microemboli despite 100% oxygen administration in a patient with prosthetic MHVs, necessitating urgent surgical intervention and detection of a thrombus adhered to the mechanical mitral valve. Furthermore, this case reflects the potential superiority of TCD in detection of microemboli-generating cardiac thrombus over multiple cardiac modalities including TTE and TEE.

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Received May 17, 2016. Accepted in final form November 28, 2016.

AUTHOR CONTRIBUTIONS

M. Shafie: concept, data collection and analysis, manuscript draft, revisions, and finalization. S. Song: concept, data collection and analysis, manuscript revisions, and finalization. M. Nezhad: concept, data collection and analysis, manuscript revisions. J. Lamberti: concept, data collection and analysis, manuscript revisions. M. Cocalis: concept, data collection and analysis, manuscript revisions. M. Cavallaro: concept, data collection and analysis, manuscript revisions. B. Rinsky: concept, data collection and analysis, manuscript revisions. P. Lyden: concept, data collection and analysis, manuscript revisions and finalization.

STUDY FUNDING

No targeted funding reported.

DISCLOSURES

M. Shafie reports no disclosures. S. Song serves on scientific advisory boards for Portola and Boehringer Ingelheim; serves as a consultant for Stryker; and receives research support from Genentech, NIH, and California Community Foundation. M. Nezhad, J. Lamberti, M. Cocalis, and M. Cavallaro report no disclosures. B. Rinsky performs transcranial Doppler ultrasound studies at Cedars-Sinai Medical Center. P. Lyden serves on Data Safety Monitoring Boards for St. Jude Medical, ZOLL, and The Netherlands Government; serves as an Associate Editor of *International Journal of Stroke* and on the editorial boards of *Stroke* and *Journal of Stroke and Cerebrovascular Disorders*; receives publishing royalties for *Thrombolytic Therapy for Acute Ischemic Stroke, Third Edition* (Humana Press, 2015); and receives research support from NIH/National Institute of Neurological Disorders and Stroke. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.