CASE

The utility of histopathologic characteristics of thrombi in large vessel occlusions

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Neurology: Clinical Practice December 2019 vol. 9 no. 6 481-483 doi:10.1212/CPJ.0000000000000630

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A 53-year-old woman presented to the emergency department 40 minutes after the sudden onset of right facial droop and inability to speak. She had a history of controlled hypertension, hypothyroidism after resected thyroid cancer, and dermatofibrosarcoma protuberans. Her initial NIH Stroke Scale (NIHSS) was 4 (mild dysarthria, severe aphasia, and mild facial palsy). A CT angiogram demonstrated a left superior division M2 occlusion. She was treated with IV-tissue plasminogen activator (tPA) 1 hour after witnessed symptom onset. During repeat examinations within the first 30 minutes after initiation of tPA, she had no early improvement.

PRACTICAL IMPLICATIONS

Consider reviewing the histopathology of retrieved thrombi from patients treated with mechanical thrombectomy. Histopathologic features of thrombi have the potential to provide a large array of information in the identification of stroke mechanism and subsequent treatment.

An endovascular thrombectomy was performed with successful recanalization. On gross examination, the retrieved thrombus was white and well-circumscribed (figure). The sample was sent to pathology for histologic characterization. Subsequent to reperfusion, the patient's NIHSS was 0, illustrating an immediate and profound resolution of her deficits.

Based on the gross appearance of the clot, the source of embolism was hypothesized to be cardiac. A brain MRI identified several areas of restricted diffusion consistent with acute infarcts in multiple cerebrovascular territories. Transthoracic and transesophageal echocardiogram revealed a mobile echodensity of the aortic valve. Cardiothoracic surgery was consulted, and the patient underwent an aortic valve replacement.

Histopathology from the thrombectomy specimen and the resected aortic valve vegetation were identical: both demonstrated fibrinous exudate without infectious organisms or calcium deposition. The surrounding valvular tissue showed fibroelastosis and inflammation. The thrombus was identified as white-clot predominated by fibrin and degenerative debris with rare interspersed macrophages and a rim of neutrophils at the edge. Von Kossa staining was performed on the thrombus, which did not show calcification within the sample. The patient was diagnosed with nonbacterial thrombotic (marantic) endocarditis. A CT of the chest, abdomen, and pelvis revealed no malignancy. The patient was discharged on antiplatelet and statin therapy with follow-up scheduled for additional testing for malignant, autoimmune, and hypercoagulable conditions.

Discussion

There is no doubt that the surge of endovascular therapy has revolutionized acute stroke care. Current guidelines recommend endovascular therapy in patients with occlusion of the internal carotid artery or proximal middle cerebral artery.[1] For those with more distal occlusions (such as the M2 segment), the guidelines and available evidence from randomized controlled trials are

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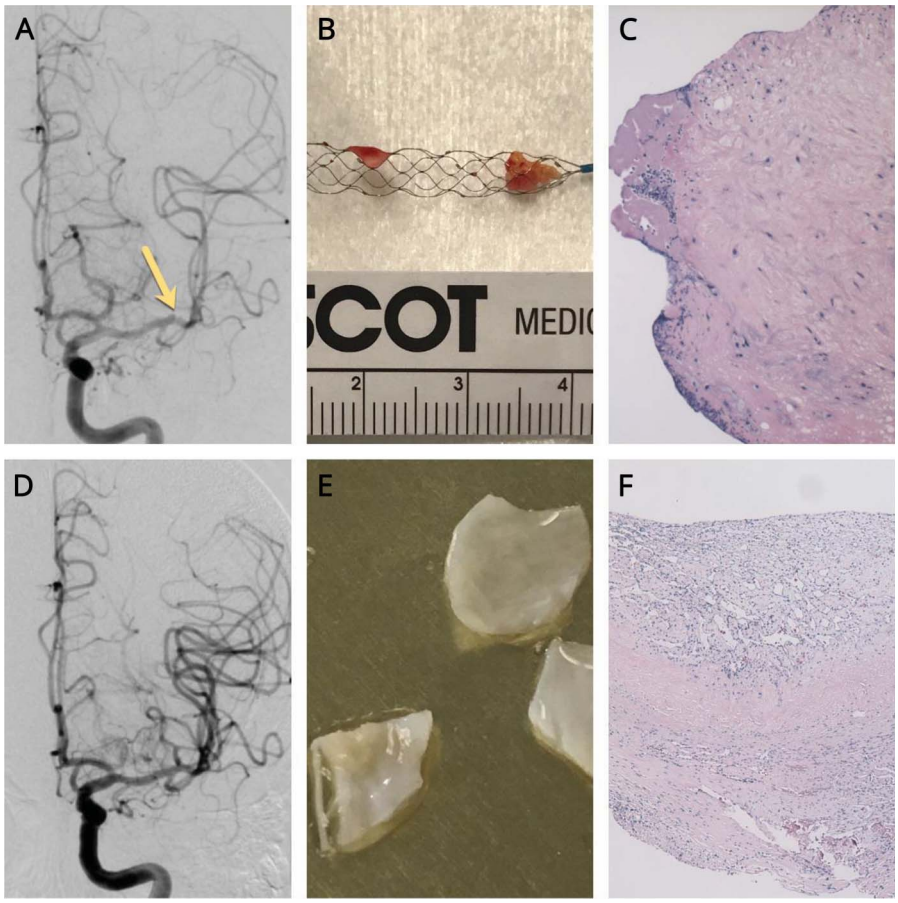
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Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

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Figure Imaging and pathology



AP view of cerebral angiogram before recanalization of the superior division of MCA with arrow pointing to occluded vessel stump (A); angiography after restoration of flow by proximal balloon-guide catheter with stent retriever thrombectomy using a Medtronic 4 × 40 mm Solitaire device (D); retrieved thrombus within stent (B); gross pathology of the removed aortic valve with sterile vegetation (E); hematoxylin and eosin stain at ×100 magnification of thrombus showing degenerating debris and neutrophils at edge of tissue (C); hematoxylin and eosin stain at ×40 magnification of valve tissue with vegetation and neovascularization (F). AP = anterior-posterior; MCA = middle cerebral artery.

less certain and recommend careful selection of patients to be referred for endovascular therapy. Although M2 occlusions tend to respond moderately well to tPA, clot dissolution with fibrinolysis may also depend on the composition of the clot, not just the site of occlusion.

Clots have traditionally been classified as "red-clot" (erythrocyte-predominant), "white-clot" (platelet and fibrin predominant), or mixed. Red-clots are theorized to form under conditions of turbulent or slow flow states with the classic example being atrial fibrillation. White-clots form in the setting of inflammatory conditions or in situ plaque rupture. The composition of clots may influence response to fibrinolysis and ease of extraction with mechanical thrombectomy, in addition to informing the etiologic diagnosis of the stroke. For example, the presence of atheromatous gruel (a mixture of extracellular matrix, macrophages, and lipid) is associated with lower rates of recanalization.[2] Conversely, thrombi that are erythrocyte-predominant are theorized to be more amenable to recanalization. In one animal model study, the middle cerebral artery of rabbits was embolized with either red or white autologous clot and subsequently injected with intra-arterial-tPA. The results found that clot lysis and return of cerebral perfusion occurred only with red-clots.[3]

The etiology of our patient's stroke was marantic endocarditis, a pathology distinct from more conventional sources of embolism. The characteristic white thrombus associated with marantic endocarditis is platelet and fibrin predominant. The most commonly affected valves are the aortic and mitral valves with characteristically negative cultures. Malignancy is the most commonly implicated etiology followed by systemic lupus erythematosus. Specifically, adenocarcinoma of the lung and pancreas have the strongest association.[4]

To date, available studies on the histopathology of thrombi from endovascular retrieval have not yet been shown to correlate with stroke severity, outcome, or mechanism, but these studies have several limitations.[5] Furthermore, the histopathologic data are only available to clinicians retrospectively; further study will need to be directed toward identifying predictors of clot composition in the acute treatment phase. Nonetheless, an increase in the availability of retrieved thrombi from mechanical thrombectomy will open the doors for further study on clot composition and how best to use this information.

Study funding

No targeted funding reported.

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Disclosure

The authors report no disclosures. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

Publication history

Received by *Neurology: Clinical Practice* October 4, 2018. Accepted in final form January 25, 2019.

References

1. Powers WJ, Rabinstein AA, Ackerson T, et al. American Heart Association Stroke Council. 2018 Guidelines for the early Management of patients with Acute ischemic Stroke: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke 2018;49:e46–e110.
2. Hashimoto T, Hayakawa M, Funatsu N, et al. Histopathologic analysis of retrieved thrombi associated with successful reperfusion after acute stroke thrombectomy. Stroke 2016;47:3035–3037.
3. Kirchhof K, Sikinger M, Welzel T, Zoubaa S, Sartor K. Does the result of thrombolysis with recombinant tissue-type plasminogen activator (rt-PA) in rabbits depend on the erythrocyte- and fibrin-content of a thrombus? [in German]. Rofo 2004;176:98–105.
4. Ogata J, Yutani C, Otsubo R, et al. Heart and vessel pathology underlying brain infarction in 142 stroke patients. Ann Neurol 2008;63:770–781.
5. Marder VJ, Chute DJ, Starkman S, et al. Analysis of thrombi retrieved from cerebral arteries of patients with acute ischemic stroke. Stroke 2006;37:2086–2093.

Appendix Authors

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Lester Y. Leung, MD, Msc	Tufts Medical Center, Boston	Author	Designed and conceptualized manuscript, revision for intellectual content

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