Stroke

ILLUSTRATIVE TEACHING CASES

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Contemporary Challenges of Acute Ischemic Stroke in Takayasu Arteritis

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A 59-year-old woman presented with 5 hours of right-sided weakness and aphasia. She had a history of Takayasu arteritis (TA), managed for 10 years with oral prednisolone. Her right radial pulse was not palpable, and a bruit was audible over the right subclavian artery. Blood pressure in the right and left upper extremities was 85/69 mm Hg and 119/67 mm Hg. National Institutes of Health Stroke Scale score was 12 at admission, and she had no history of cerebrovascular event. Computed tomography showed hypodensity of the left basal ganglia and caudate head with angiography demonstrating left common carotid artery (CCA) and left middle cerebral artery occlusions as well as large ischemic penumbra (Figure 1). tPA (tissue-type plasminogen activator) was not given because she was referred to care 5 hours after symptom onset. As such, she underwent angiography which confirmed numerous steno-occlusive lesions in the supra-aortic branch vessels (Figure 2A through 2C).

A diagnosis of type-I TA (American College of Rheumatology criteria) was made,[1] and it was felt that thrombosis occurred secondary to severe stenosis of the left CCA origin (Figure 2D) with subsequent intracranial vessel emboli. The patient underwent endovascular recanalization of the left CCA origin, followed by intracranial stent-retrieval, and extracranial stent reconstruction. Angiography demonstrated a Thrombolysis in Cerebral Infarction score of 3/3 (Figure 3A). Puncture-to-reperfusion time was 62 minutes. The retrieved emboli resembled typical arterial clot (Figure 3B). Intravenous infusion of platelet glycoprotein IIb/IIIa inhibitors (tirofiban,0.1 μg/kg per minute) for 8 hours and dual antiplatelet therapy (aspirin 100 mg plus clopidogrel 75 mg) was initiated. The following day, her neurological function improved. Noncontrast computed tomography showed evolving infarction (Figure 3C) without hemorrhage. Rheumatological screening showed an elevated erythrocyte sedimentation rate of 60 mm/h and a CRP (C-reactive protein) level of 76.10 mg/L. Her autoimmune profile and echocardiogram were normal. By postoperative day 14, she had recovered to National Institutes of Health Stroke Scale and modified Rankin Scale scores of 3 and 1. She was discharged on dual antiplatelet therapy, high-dose prednisolone (60 mg), and methotrexate (10 mg) therapy. Three months later, she returned without recurrent symptoms and a normal erythrocyte sedimentation rate (5 mm/h) and CRP (<1 mg/L). Follow-up angiography demonstrated patency of the extracranial and intracranial vessels (Figure 3D) and neither further nor recurrent lesions.

Transparency and Openness Promotion (TOP)

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DISCUSSION

TA is an idiopathic large vessel vasculitis which is heterogeneous in geographic distribution and clinical presentation. The incidence of TA is variable, ranging from 2.6 per million in Europe and North America to 40 per million in Asia. Young women account for 80% to 90% of TA cases, with age of onset usually ranging between 10 and 40 years.[2] The inflammatory process in TA may be limited

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Nonstandard Abbreviation and Acronyms

CCA	common carotid artery
CRP	C-reactive protein
TA	Takayasu arteritis
tPA	tissue-type plasminogen activator

or involve multiple vessels, including the aorta and renal, brachiocephalic, common carotid, and subclavian arteries. Angiography is considered the gold standard for diagnosis and used to classify TA into phenotypes according to the distribution of inflammation.[3] As the disease progresses, inflammation can lead to narrowing, occlusion, or dilation, which cause a wide range of symptoms. The onset of symptoms, which include constitutional symptoms (weight loss and fever), arthralgias, absent or weak peripheral pulses, limb claudication, arterial bruits, hypertension, angina, and gastrointestinal symptoms, tends to be chronic or subacute. Measurement of brachial blood pressure alone is inaccurate, and a decreased value obtained in one arm might be expected when the subclavian arteries are affected in TA. Therefore, it is advisable to perform additional and bilateral measurements to avoid misdiagnosis.[4]

The differential diagnosis for TA includes other causes of large vessel vasculitis including syphilis, tuberculosis, lupus, rheumatoid arthritis, spondyloarthropathies, Behçet's disease, Kawasaki disease, and giant cell arteritis. Distinction may be challenging, and close attention epidemiological and demographic characteristics complements the clinical and imaging findings. Approximately 10% to 20% patients with TA exhibit neurological manifestations. Nearly 48% with vertebral artery involvement experience visual disturbance, while 80% with carotid and vertebral artery involvement exhibited transient ischemic attacks or cerebrovascular accidents.[5] The cause of stroke in TA is either occlusive or embolic. Common carotid and vertebral artery involvement cause progressive ischemia, leading to ischemic symptoms such as visual disturbance, headache, vertigo, syncope, convulsion, and stroke. By contrast, acute stroke with true large vessel occlusion secondary to TA is rare and reported only in isolated cases. Approximately 80% of these showed involvement of the anterior circulation, most commonly embolic.[6]

The treatment of TA includes pharmacological therapy or carefully selected vascular intervention. Pharmacological therapy aims to control disease progression and prevent recurrent ischemic symptoms. Glucocorticoids are the most effective agent for patients with active TA. The addition of immunosuppressive agents, such as methotrexate, may be used in refractory cases or to minimize morbidity associated with long-term exposure. Inflammatory markers are commonly used to monitor disease progression during remission stages. Current guidelines on anticoagulation in TA remain unclear and practical results are conflicting. In one case of TA, aspirin was concomitantly used with warfarin effectively.[6] Thrombus formation can be presumed to be provoked by the inflammatory milieu in TA; however, the risk of further clot formation from ongoing inflammation appears dependent on disease control and requires individualization.[6] Immunosuppressive agents such as azathioprine, leflunomide, mycophenolate mofetil, and cyclophosphamide have been in a supplementary role during corticosteroid tapering.

High restenosis rates following vascular intervention ranging from 37% to 62% usually obviates prophylactic intervention.[7] Patients who undergo emergent extracranial reconstruction with stenting should be carefully followed to ensure long-term patency. However, thrombolysis alone may fail acutely due to presence of extracranial and intracranial lesions and high clot burden.[6,8,9] The collateral circulation in this case of advanced TA facilitated mapping for thrombectomy eligibility as

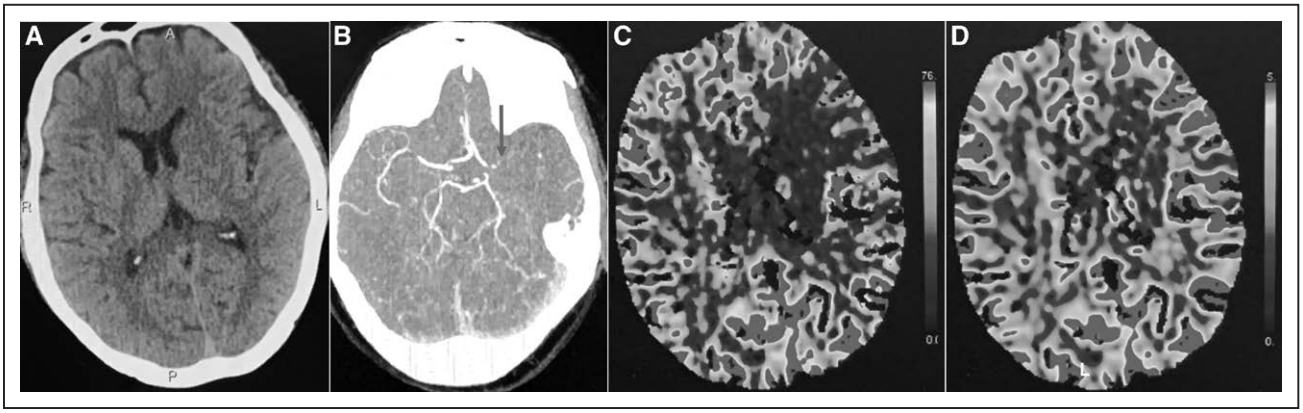

Figure 1. A, Initial noncontrast head computed tomography (CT) showed hypodensity of the left basal ganglia and caudate head.
B, CT angiography revealed a filling defect involving the left middle cerebral artery. Perfusion data showed mismatch between cerebral blood flow (**C**) and cerebral blood volume (**D**) in the affected middle cerebral artery territory.

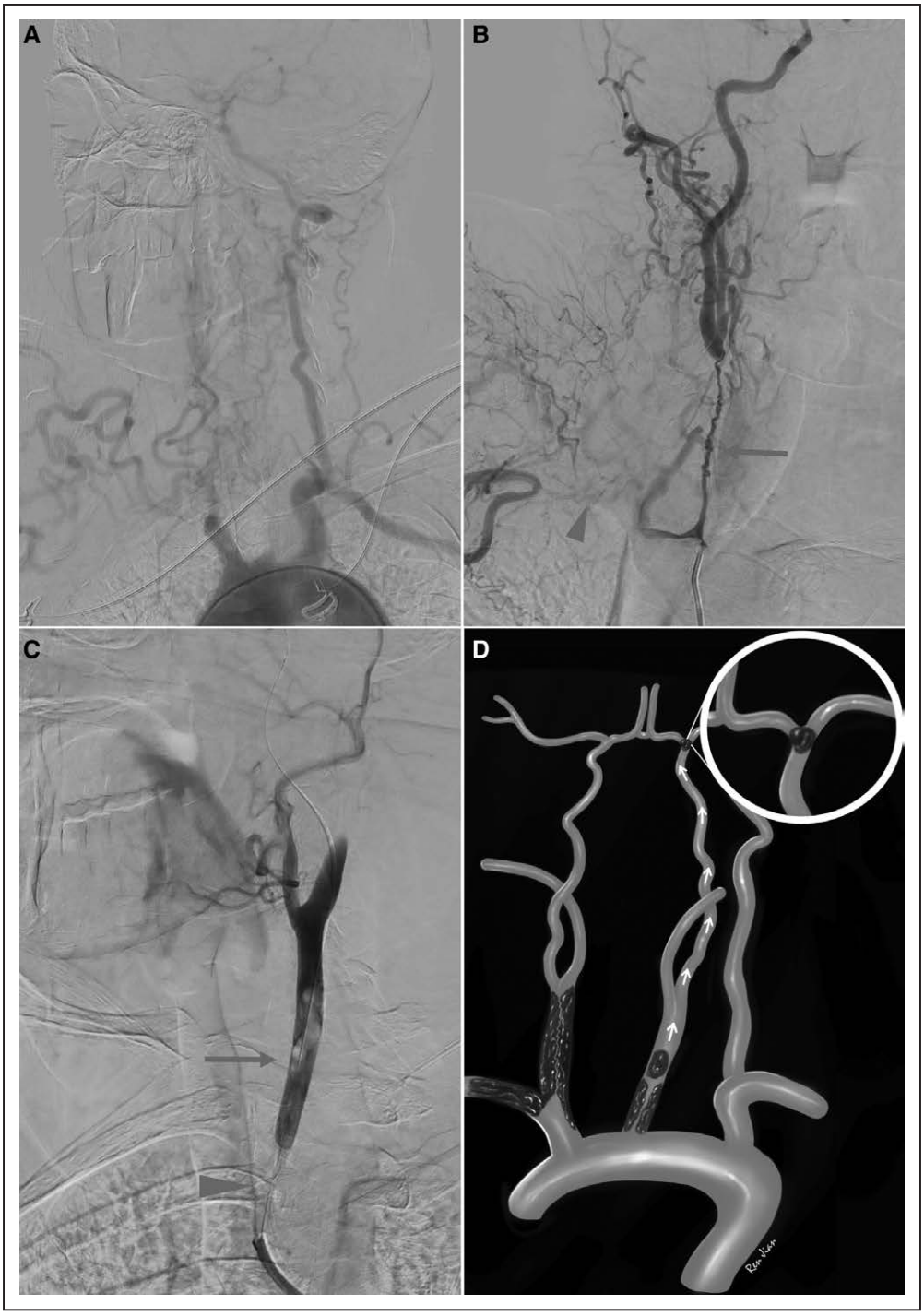

Figure 2. Initial diagnostic catheter angiography.
A, Digital subtraction angiography (DSA) of the aortic arch showed multiple supra-aortic branch vessel stenoocclusive segments including (**B**) the occluded subclavian artery (arrowhead), and common carotid artery (CCA; arrow), with beaded string sign indicated further severe stenoses. **C**, During endovascular recanalization of the left CCA/innominate (arrowhead) a large intraluminal clot (arrow) secondary to the left CCA origin was seen, likely the source of the distal emboli. **D**, Tandem occlusive embolus resulted in complete occlusion of the left internal carotid artery terminus, schematically illustrated.

multimodality computed tomography imaging allowed precise depiction and access evaluation.

Considering the often-poor arterial access related to multiple occlusive lesions in the supra-aortic vessels and vessel friability in the setting of severe inflammation, medical management has more often been employed.[6,8,9] Historically, management included standard treatment, intravenous tPA administration, oral anticoagulation, antiplatelet therapy, or a combination of these. However, reports of efficacy are conflicting with some patients

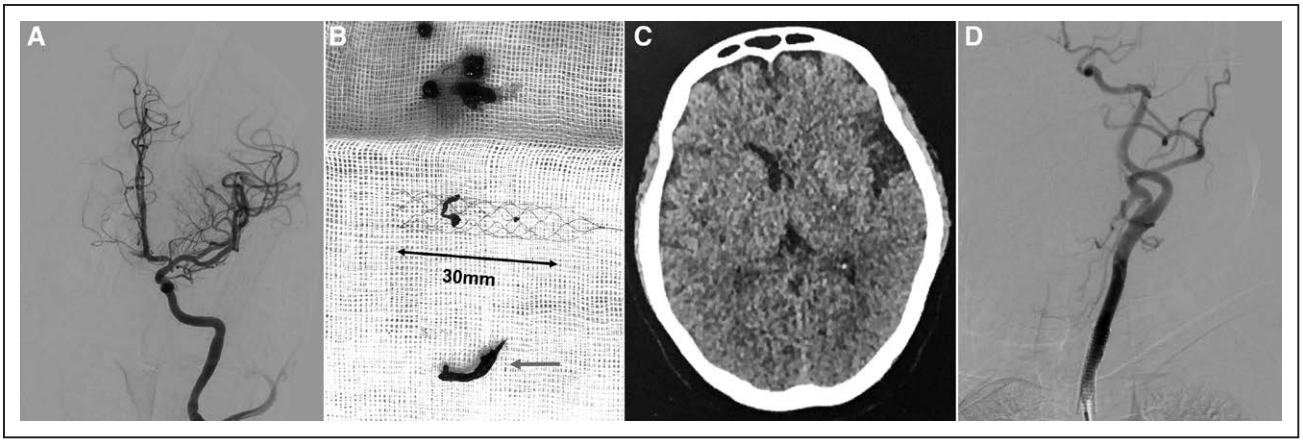

Figure 3. Completion catheter angiography.
A, Complete middle cerebral artery (MCA) recanalization was achieved, and (**B**) gross appearance of the retrieved embolus was unremarkable.**C**, Postprocedural head computed tomography showed evolving infarction involving the left basal ganglia and head of the caudate nucleus. **D**, Three-month follow-up angiography demonstrated patency of the left common carotid artery origin stent reconstruction as well as the previously affected MCA.

TAKE HOME POINTS

- Takayasu arteritis (TA) is a rare cause of stroke often involving younger patients. Involvement of proximal arch great vessels with extension into the carotid system in patients with TA can act as source of embolic large vessel occlusion.
- Mechanical thrombectomy may be considered for eligible patients with large vessel occlusion stroke secondary to TA based on clot burden and medical futility.
- Supra-aortic vessel stenoses or occlusions are common in patients with advanced TA. Angiographic mapping is critical for endovascular treatment and subtyping.
- Pharmacological therapy is the mainstay of TA. Careful optimization of neurological and rheumatologic regimens is paramount to the long-term management of chronic disease.

exhibiting improvement and others developing recurrent stroke due to extracranial clots following initial tPA administration requiring warfarin, or developing recurrent stroke following warfarin therapy and requiring antiplatelet therapy.[6,8,9] With improved endovascular technique, clot burden may invite revascularization as in this case. In the setting of tandem embolism, angioplasty and stenting is routinely undertaken to recanalize the extracranial access and facilitate subsequent intracranial clot retrieval.[10] To avoid thrombosis or reocclusion, antiplatelet therapy was empirically used for this patient in keeping with standard interventional practice. Notably, efficacy and optimal dosing is not established in TA. Given concern for bleeding, a decreased dose of glycoprotein IIb/IIIa inhibitor was used compared with routine interventional practice with transition to oral dual antiplatelet therapy.

Restenosis/reocclusion is the most common late complication after stent placement, as frequently as 62%.[7] Corticosteroid dose and active disease at the time of intervention are important risk factors for restenosis or reocclusion after revascularization procedure.[7] If restenosis occurs, the treatment strategy depends on disease activity, collaterals, onset of neurological manifestations, and their severity. Symptomatic restenosis with active disease is a precarious situation, and invasive measures should be reserved for an inactive period whenever possible.

When considered for retreatment, a drug-coated balloon or stent may be considered. Occlusion may be treated with carotid endarterectomy, excising both the restenotic lesion and previously implanted stent, but this requires open surgery and even cardiopulmonary bypass if arch reconstruction is entertained. Thus, subclavian-CCA bypass grafting or CCA interposition may also be considered. There is no current consensus regarding choice of intervention for extracranial carotid stenosis or occlusion.

This case demonstrates the multifarious challenges in the management of acute ischemic stroke secondary to advanced TA. An approach to medical and interventional management is illustrated, which can be considered based on individual patient factors and clinical judgement.

ARTICLE INFORMATION

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