Clinical Problem-Solving

Heart or Head?

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A 65-year-old woman was referred to a cardiologist for the evaluation of progressive chest pain. Placement of an aortobifemoral conduit had been performed 14 years earlier for occlusive aortoiliac disease. She had smoked two packs of cigarettes a day for over 40 years. Her history of chest pain was typical of crescendo angina pectoris on exertion, without symptoms that were prolonged or that occurred at rest. Two years earlier, she had had a transient ischemic attack consisting of facial droop and aphasia. She had bilateral carotid bruits, which were greater on the left side than on the right, and a grade 1/6 systolic ejection murmur. The electrocardiogram met the voltage criteria for left ventricular hypertrophy.

There is a high likelihood of coronary artery disease, and cardiac catheterization is a reasonable next step.

Coronary angiography and left-sided cardiac catheterization with left ventriculography were performed through the left femoral graft site. Left ventricular function and end-diastolic pressures were normal, but both intraventricular and intraaortic systolic pressures were elevated (range, 230 to 250 mm Hg). The patient was not known to have hypertension, so brachial pressures were measured with a blood-pressure cuff during catheterization. Systolic brachial pressures were approximately 130 mm Hg bilaterally, representing a pressure gradient of approximately 100 mm Hg as compared with the central aortic pressure. Selective coronary angiography showed mild irregularities throughout the left coronary system, without clinically significant stenosis, and total occlusion of the proximal right coronary artery with bridging collateralization of that vessel as well as substantial left-to-right collateral flow.

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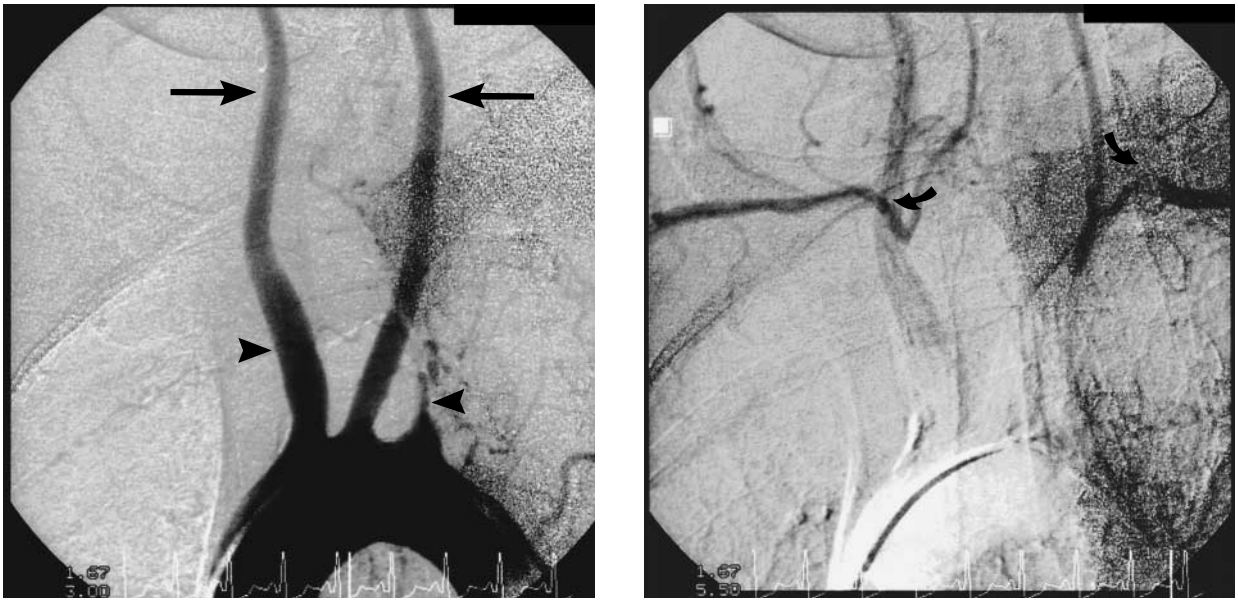
Therapy with beta-blockers, long-acting calcium-channel blockers, or nitrates, singly or in combination, should relieve her symptoms. Lipid-lowering therapy and cessation of smoking would also be helpful. The "mild irregularities" in the left coronary system on angiography, although not flow-limiting, are consistent with the presence of early atherosclerosis.

The marked central hypertension and discordant, but bilaterally equal, brachial pressures are of concern. Coarctation of the aorta that is sufficiently proximal to reduce pressure in both arms and both legs is rare. Although aortic coarctation is occasionally proximal to the origin of the left subclavian artery, arm pressures are unequal in such cases. In any event, there was no difficulty advancing the catheter in the aorta, and a pressure gradient was not reported, making this diagnosis unlikely. Moreover, whatever the form, coarctation in a patient presenting at the age of 65 years would be highly unusual. An atherosclerotic occlusive process, involving both subclavian arteries or a single anomalous subclavian trunk, is more likely. The marked central hypertension could be caused by renal arterial disease involving one or both of the renal arteries and leading to excessive activation of the renin–angiotensin system. The combination of subclavian and renal disease would explain the central-to-peripheral blood-pressure gradient in the arms and the elevated central aortic pressure, respectively.

Abdominal aortography was performed. Both renal arteries were widely patent, and the aortic graft was intact and patent. Arch aortography showed total occlusion of both subclavian arteries, with retrograde flow from both vertebral arteries providing subclavian blood flow (Fig. 1). Selective angiography of the carotid arteries showed moderate bilateral disease of the extracranial internal carotid arteries, which was more extensive in the left artery than in the right. Retrograde filling of the vertebral arteries from the anterior circulation occurred through the posterior communicating arteries, providing flow to the posterior cerebral arteries (Fig. 2). After angiography was completed, intravenous and then oral beta-blockers were administered to lower the elevated blood pressure. Subsequently, an oral dose of nifedipine was given.

As suspected, the patient has bilateral atherosclerotic occlusion of the subclavian arteries, with flow reversal in the vertebral arteries (subclavian "steal") providing the only means of subclavian circulation.



A B

Figure 1. Aortic-Arch Angiogram Showing Normal Antegrade Flow in Both Carotid Arteries (Panel A, Arrows) and Bilateral Occlusion of the Subclavian Arteries at Their Origins (Panel A, Arrowheads), with Retrograde Filling of the Vertebral Arteries Providing Antegrade Blood Flow in the Subclavian Arteries Bilaterally (Panel B, Curved Arrows).

Carotid artery disease is also present, as might have been predicted by the patient's history of a transient ischemic attack and by the finding of carotid bruits on examination. It is surprising that she has not had symptoms of arm claudication or neurologic symptoms. The use of beta-blockers to lower her blood pressure in order to aid vascular closure is reasonable. However, administration of short-acting nifedipine, even orally, for the relief of hypertension has had serious adverse effects. Other agents that can be used for urgent blood-pressure management include short-acting agents such as intravenous nitroprusside, nitroglycerin, beta-blockers, and calcium-channel blockers.

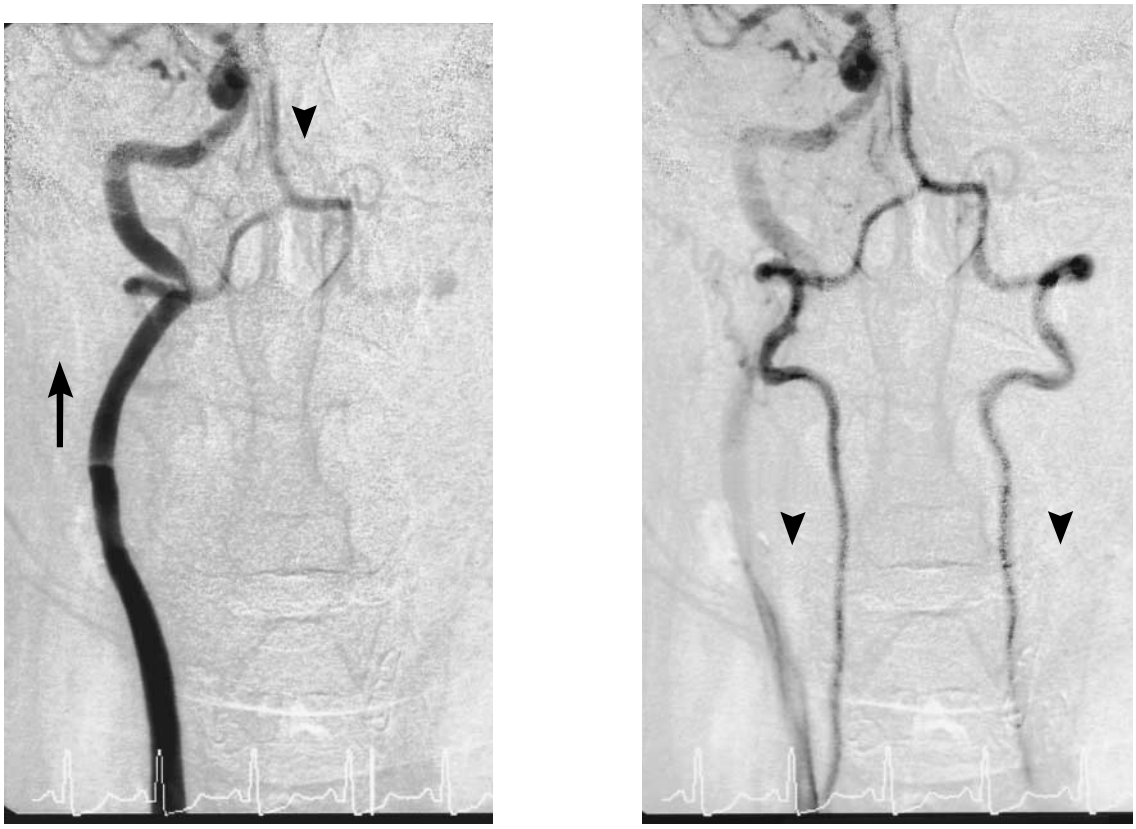
While the sheath was being removed, the brachial cuff systolic pressures fell to 50 to 60 mm Hg. The patient presumably had central pressures that were at least 90 to 100 mm Hg higher. Aphasia developed, with weakness in the right arm and right leg. Brachial cuff pressure was restored to approximately 120 mm Hg with atropine, a continuous infusion of dopamine, and an intermittent and then continuous infusion of phenylephrine. The patient's neurologic symptoms resolved, although they returned during occasional drops in blood pressure.

Although most neurologic complications after catheterization are the result of embolic phenomena, this patient's symptoms seem to be the result of the sudden reduction in cerebral perfusion pressure that is related to severe, multivessel cerebrovascular disease. The combination of flow reversal in both vertebral arteries with cerebral steal, along with prominent stenosis of the left internal carotid artery, caused ischemia of the watershed area in the left hemisphere at presumably near-normal aortic pressures.

The patient's blood pressure stabilized over the next several hours. Dopamine and phenylephrine were discontinued. Cranial computed tomography without the administration of contrast material revealed no hemorrhage or infarction. Later that evening, approximately 10 hours after the neurologic symptoms had resolved, the patient had an episode of angina. Coincident cuff pressure was approximately 120 to 130 mm Hg, and the heart rate was 80 to 90 beats per minute. She was treated with the judicious use of intravenous nitrates and oral beta-blockers.

The patient has a narrow range of blood pressure that will allow for adequate cerebral perfusion but not provoke coronary ischemia. It is possible that the recent onset of her anginal syndrome was related to the closure of the second subclavian artery. This may have resulted in a centrally mediated increase in blood pressure to satisfy the requirements of cerebral perfusion, thus causing angina without a concomitant change in the coronary circulation.

The medical options appear to be quite limited. Surgical carotid–subclavian bypass or transposition,



A B

Figure 2. Angiographic Studies after the Selective Injection of Contrast Material in the Right Carotid Artery.
Panel A shows antegrade filling of the right carotid artery (arrow) through the circle of Willis to the posterior cerebral artery, with subsequent retrograde basilar-artery filling (arrowhead). The late-phase angiogram in Panel B shows continued retrograde vertebral filling (arrowheads).

with accompanying carotid endarterectomy, would normalize flow in both the carotid and subclavian arteries and would obviate the steal from the vertebral circulation. However, simple left carotid endarterectomy would not be likely to improve the cerebral perfusion adequately in the presence of continued bilateral flow reversal in the vertebral arteries and contralateral carotid-artery stenosis.

Alternatively, percutaneous transluminal angioplasty, with adjunctive stent implantation, of either subclavian artery would provide antegrade flow to the posterior circulation and relieve the steal from the vertebral circulation. The need for surgical or percutaneous revascularization of the left carotid artery, which has only moderate stenosis but causes symptoms because of the posterior-circulation steal, could be determined later.

Percutaneous transluminal angioplasty with stenting of the left subclavian artery was performed successfully, with the restoration of antegrade flow in the left subclavian and vertebral arteries (Fig. 3). The blood pressure fell markedly after subclavian revascularization but did not become normal. The patient was treated medically thereafter, without further neurologic or anginal symptoms.

COMMENTARY

Although the constellation of anatomical and clinical abnormalities in this patient is unusual, the abnormalities illustrate several important, and more common, diagnostic and therapeutic issues. The risk of associated coronary disease in patients with peripheral vascular disease is well established. Patients with abnormal ankle–brachial pressure indexes are more likely to die from a cardiovascular cause within 5 to 10 years than those with normal indexes.[1-3] Recent data also show a correlation between the thickness of the intima and media of the carotid artery, as determined by ultrasonography, and subsequent cardiovascular events.[4] Not only is peripheral vascular

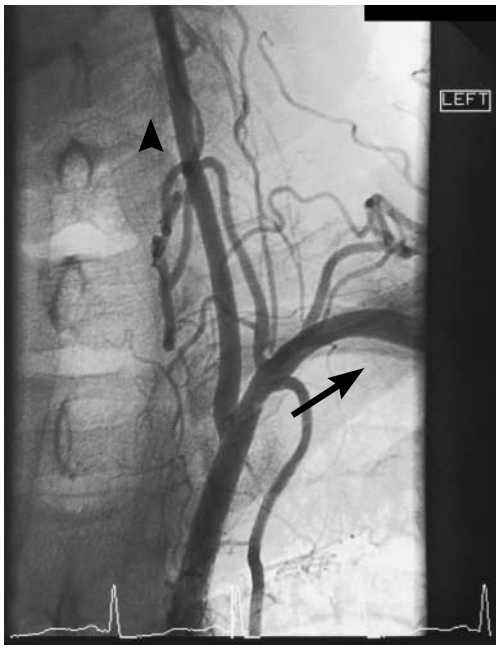


Figure 3. Left Subclavian Angiogram Obtained after Percutaneous Revascularization with Balloon Angioplasty and Intravascular Stent Placement.

Antegrade flow has been reestablished in both the subclavian artery (arrow) and the vertebral artery (arrowhead).

disease a marker of coronary disease, but the converse relation is also known to exist. The incidence of renal-artery stenosis is greater in patients with coronary artery disease, especially if they have renal insufficiency, than in those without coronary artery disease, and the incidence increases with the extent of coronary involvement.[5,6]

This patient's angina appears to have been related to occult, severe systemic hypertension. The hypertension imposed a substantial myocardial workload in the presence of a right coronary occlusion subserving viable myocardium, thereby causing ischemic symptoms. The resolution of her angina after the relief of hypertension lends support to this proposed mechanism.

Sublingual nifedipine has been widely used to lower blood pressure rapidly in hypertensive emergencies, although this indication has not been approved by the Food and Drug Administration. There are multiple reports of serious adverse events associated with this practice. Specifically, severe hypotension, acute myocardial infarction, unstable angina, transient ischemic neurologic events, stroke, and death have all been reported after the use of sublingual nifedipine to lower blood pressure, and they have led to a call for a moratorium on such use.[7]

In this patient, there appeared to be a relation between cerebral ischemia and systemic hypertension, given the observed reduction in blood pressure once cerebral perfusion improved with the restoration of antegrade flow in the vertebral arteries. In animal models, global cerebral ischemia has been shown to increase systemic arterial pressure.[8] Specifically, medullary ischemia induced by intracisternal administration of endothelin-1 increased plasma norepinephrine and adrenaline levels and raised the mean arterial blood pressure in rats.[9] The hypertensive response to cerebral ischemia is probably related to elevations of intracellular calcium-ion concentrations in the regulatory sympathetic neurons, and the response can be attenuated with calcium-channel blockade.[10] The marked hypotensive effects of nifedipine observed in this patient may have been due, at least in part, to the blocking of this central mechanism of her hypertension.

The reversal of blood flow in the vertebral arteries resulting from proximal subclavian-artery occlusion was first postulated by Harrison in 1829[11] but was not angiographically confirmed until 1960, by Contorni.[12] In 1961, the term "subclavian steal" syndrome was coined to describe the syndrome of accompanying clinical manifestations.[13] These include arm claudication and nonhemispheric neurologic symptoms such as episodic syncope, vertigo, diplopia, and ataxia, but hemispheric symptoms are also common.[14] The classic combination of neurologic symptoms that occurs with exercise in an ischemic arm is distinctly unusual.[14] Previous reports have not included angina as a symptom.

To cause a reversal of flow in the vertebral arteries, a pressure gradient of 20 to 40 mm Hg is required between the vertebral–basilar and vertebral–subclavian junction.[15] Even in the presence of flow reversal, symptoms are unusual except in patients with multivessel cerebrovascular disease. Inadequate collateral contribution from the circle of Willis, the result of concomitant carotid artery disease or, less frequently, an inadequate posterior communicating arterial conduit, reduces the ability of the anterior cerebral circulation to compensate for the deficit in posterior circulatory flow.[16] Symptoms of watershed cerebral ischemia can result, as they did in this patient.

Occlusion of the subclavian artery is usually due to atherosclerotic disease but is occasionally caused by tumor,[17] embolism,[18] trauma,[19] or Takayasu's arteritis.[17] In addition to the classic subclavian steal syndrome, coronary subclavian steal is increasingly recognized as a clinical syndrome. Use of the internal thoracic artery as a conduit in coronary-artery bypass surgery, in a patient who also has subclavian occlusive disease, can result in coronary ischemia due to the reversal of flow in the thoracic and anastomosed coronary arteries.[20] Revascularization in patients with subclavian disease is usually reserved for patients with exercise-limiting angina pectoris due to coronary–subclavian steal and those with neuro-

logic or arm symptoms of the subclavian steal syndrome.

Stenosis or occlusion of the subclavian artery is often managed with percutaneous techniques rather than surgery. Surgery, with the use of either carotid–subclavian bypass or subclavian–carotid transposition, has a mortality rate of 1 to 2 percent.[21-23] Long-term patency rates are higher for transposition than for bypass.[22]

Percutaneous revascularization for the treatment of subclavian disease has been performed for almost two decades[24]; adjunctive stenting has been used in the past five years.[25,26] A recent meta-analysis by Hadjipetrou et al. showed that the rates of technical success, stroke, and death were similar for surgery and percutaneous revascularization.[27] However, in that analysis, stenting was associated with a 3 percent recurrence rate after a mean follow-up of 20 months, as compared with a 16 percent recurrence rate for surgery after a mean follow-up of 51 months.

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