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The difficulties of differentiating vasculitis from its mimics

ABSTRACT

The signs and symptoms of vasculitis are not specific, and tests for confirming the diagnosis can be misleading. Thus, when considering a diagnosis of vasculitis, physicians need to keep an open mind. With a case vignette, the author illustrates some of the difficulties in diagnosing "vasculitis."

INFLAMMATION IS ONLY one of the many causes of vascular injury. For this reason, and because the treatment of vasculitis often involves the use of potentially toxic agents, the clinician should keep an open mind when evaluating patients with organ ischemia.

Even biopsy findings can be misleading

IS IT VASCULITIS— OR SOME OTHER VESSEL INJURY?

Numerous conditions can injure or occlude blood vessels and mimic the clinical picture of vasculitis.[1] In fact, the clinical manifestations of vascular injury depend more on the size and location of the affected vessel than on the cause of the injury.

For example, damage to small vessels can cause a variety of cutaneous changes, including palpable purpura, urticaria, livedo reticularis, papulovesicular lesions, and nodules. Likewise, such involvement of small vessels can lead to dysfunction of the heart, kidney, gastrointestinal tract, and nerves. When medium-sized arteries are affected, cutaneous nodules or ulcerations, peripheral gangrene, or organ infarction can evolve. Disease of large vessels can result in claudication or major organ dysfunction.

Tests used to diagnose vasculitis lack specificity

Lack of specificity of angiographic, biopsy, and laboratory findings may create further difficulty in diagnosing vasculitis.

Angiography. Irregularities of vessel walls, segmental arterial occlusions, and vascular dilatations—angiographic findings considered characteristic of vasculitis—may appear in a variety of nonvasculitic conditions (TABLE 1).

Biopsy findings. The histopathology of vascular tissues can also be misleading. For example, fibrinoid changes in a vessel wall may result from acute arterial hypertension rather than from vasculitis. Vascular hypertrophy is common in the lower leg of normal individuals, as is cellular infiltration of perivascular tissues.[2] And vascular inflammation can result not only from immunologic events but also from such processes as infection,[3] embolic phenomena,[4] and cold-induced injury.[5]

Laboratory tests may likewise lead the clinician astray. The appearance of an anti-DNA antibody or an antineutrophilic cytoplasmic antibody (ANCA), which are deemed fairly specific for systemic lupus erythematosus (SLE) and Wegener's granulomatosis, respectively, may actually reflect an infectious or neoplastic process.[6,7]

Clinical findings. Finally, cutaneous lesions of a nonvascular nature (eg, neutrophilic dermatoses,[8] pyoderma gangrenosum,[9] erythema nodosum,[10] insect bites[11]) may be mistaken for those caused by vasculitis.

The following vignette illustrates some of the difficulties in diagnosing "vasculitis."

CASE PRESENTATION

A 69-year-old woman presented with worsening hypertension, a cyanotic toe, and renal insufficiency. Two years previously, biopsy of a

skin rash had shown "leukocytoclastic angiitis." At that time, laboratory studies disclosed a mild anemia, an erythrocyte sedimentation rate (ESR) of 85 mm/hour, a serum creatinine value of 2.2 mg/dL, a urine protein concentration of 30 mg/dL, and a negative test for antinuclear antibodies (ANA). The patient declined to undergo renal biopsy. She received prednisone in doses as high as 60 mg per day, but ischemic necrosis of the left hip necessitated stopping this treatment.

Four months before admission, the patient developed cyanosis of her left third toe. She also complained of fatigue, weakness, depression, and mild weight loss. The finding of severe stenoses of the carotid arteries led to bilateral carotid endarterectomies. Over the ensuing months, her hypertension and renal failure worsened.

At admission to the hospital, the patient's blood pressure was 200/126 mm Hg. She had several small purpuric lesions on her extremities and a faint erythematous eruption on her back. The left third toe was cyanotic, and pulses in the left leg were diminished. Cardiac examination was unremarkable, and there were no abdominal bruits. A radiograph showed aneurysmal dilatation of the thoracic aorta.

Laboratory studies were as follows:

- Hematocrit 24.6%
- White blood cell count 12.8×10^9/L
- ESR 72 mm/hour
- Urine protein 1+ with a normal urine sediment
- Serum creatinine concentration 3 mg/dL
- Serum cholesterol concentration 228 mg/dL
- Serum triglyceride concentration 192 mg/dL
- Antinuclear antibodies positive at a 1:80 dilution (homogeneous pattern)
- Anti-DNA antibody present in a low titer
- Serum cryoglobulins were absent.

Initial diagnostic considerations included SLE and polyarteritis nodosa. However, the combination of progressive renal failure, ischemia of a digit, and asymmetric pulses in a patient with known atherosclerosis made atheromatous embolic disease a more likely diagnosis.

The patient was ultimately discharged and died at home. At autopsy, histologic examination of the kidneys showed intravascular clefts typical of cholesterol deposits in small renal arteries. There was no evidence of vasculitis.

TABLE 1

Angiographic mimics of vasculitis

- Amyloidosis
- Atrial myxoma
- Drug abuse (eg, ergot derivatives and sympathomimetic agents)
- Ehlers-Danlos syndrome
- Exposure to cold or radiation
- Fibromuscular dysplasia
- Infection (eg, bacterial, fungal, rickettsial, spirochetal, viral)
- Injection of contrast material
- Migraine
- Moyamoya disease
- Neoplasm (eg, pheochromocytoma, vascular lymphoma, vascular encasement by solid tumor)
- Neurofibromatosis
- Pseudoxanthoma elasticum
- Systemic hypertension
- Thrombotic thrombocytopenic purpura
- Trauma

SOURCE: ADAPTED FROM SACK KE. MIMICKERS OF VASCULITIS, IN: KOOPMAN WJ, EDITOR. ARTHRITIS AND ALLIED CONDITIONS, 13TH EDITION. BALTIMORE: WILLIAMS AND WILKINS, 1997:1525–1546.

Anti-DNA and ANCA may reflect infection or neoplasms

COMMENT: THE TREACHEROUS DIAGNOSTIC PATH

This case illustrates some of the ways atheromatous emboli can produce a picture of "vasculitis." Skin lesions accompanied by digital cyanosis, accelerated hypertension, and renal insufficiency certainly bring to mind polyarteritis nodosa. And positive tests for ANA and anti-DNA antibodies as well as elevated ESRs also suggest connective tissue disease. Indeed, many patients with atheroembolic disease have a low

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serum complement level,[12] a finding typical of active SLE. This case also illustrates the nonspecificity of vascular inflammation in a biopsy specimen. Although this patient's rash (deemed leukocytoclastic vasculitis) could have reflected another disease process, similar rashes can occur in atheroembolic disease.[13]

This case illustrates how the pathway to the diagnosis of vasculitis can indeed be treacherous; and seldom in medicine is the admonition *primum non nocere*—first, do no harm—more applicable.

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