CLINICAL VIGNETTE

The Blue Hand

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The patient is a 47-year-old female who presented to our office with left suprascapular pain radiating to her posterior neck and asthma. She also had seasonal allergies and hypothyroidism. Family history included atrial fibrillation in her mother and CAD in her father. She is a nonsmoker and does not drink alcohol. She reported onset of similar symptoms two years ago. At that time, she also had blurring of vision with daily headaches for a few weeks. She subsequently developed chest and upper back pains which prompted an urgent care visit. She was told she had ‘’inflammation in the lungs” and was sent home with asthma treatment. One month later, her right hand “turned blue”. Doppler ultrasound of her right upper extremity showed “chronic arterial occlusion of the radial artery (mid and distal) as well as suggestion of mid-ulnar artery occlusion”. Doppler ultrasound of left upper extremity and both lower extremities showed no occlusion. Chest x-ray showed no active disease. She had hematologic evaluation that was negative for a clotting disorder. Vascular surgery performed a right upper extremity thrombectomy. This did not provide relief of her pain, weakness and loss of sensation on this arm. Due to persistent ischemic symptoms, a brachial to ulnar graft was performed but did not provide relief of symptoms. Doppler of this arm one year later showed “hemodynamically significant arterial disease with moderate insufficiency at rest, evidence of digit ischemia in second and fourth digits. The third and fifth digits showed occlusion at the proximal phalanges.

Amputation was recommended and she sought a second opinion at a university hospital. CT- CTA of the right upper extremity showed extreme arteritis of the vessels serving the right upper extremity with extensive inflammation surrounding the distal brachial artery and its branches. The radial and ulnar arteries were occluded. Differential considerations included Takayasu’s arteritis, and Buerger’s disease. CT- CTA of left upper extremity was “non-diagnostic”, without evidence of significant vascular abnormality elsewhere in the chest, abdomen or lower extremities. Specifically, there are no areas of vascular wall thickening to suggest active vasculitis.

Rheumatology consult was obtained and the diagnosis of Takayasu arteritis (TA) was made. She was started on prednisone, infliximab and methotrexate for six months.

At initial presentation in our clinic, she complained of supraclavicular pain radiating to her posterior neck.

Physical exam showed normotensive BP on left arm. She deferred BP reading on the right arm. There was no palpable radial pulse on the right, normal radial pulse on the left. Her hands were equally warm and not discolored. The rest of the PE was normal. She had no carotid, subclavian, renal, or abdominal bruits.

Previous laboratory findings showed normal CBC, CMP, CRP and urinalysis; ESR was slightly elevated at 23. Further testing showed positive ANA at 1:40 with speckled pattern. ANCA panel, rheumatoid factor, HLA B27 were negative. C3 and C4 complement levels were adequate; Vitamin D was slightly low at 26.

CT angiogram of upper extremities showed “patent right subclavian artery with distal occlusion of the brachial artery and ulnar artery distal to the graft. The right radial artery was occluded beyond the level of the mid right forearm”. CT angiogram of the chest demonstrated “focal dilatation and intraluminal webs within right subclavian artery with no associated arterial wall thickening. The thoracic aorta and great vessels are normal in caliber, with no focal thickening. Imaging of the abdomen and pelvis showed normal iliac vessels.

On patient’s follow up visit, she had complaints of chest pain. Cardiology evaluation and testing showed negative stress ECHO.

Patient is currently stable and is off methotrexate due to nausea. She is maintained on adalimumab, leflunomide and prednisone. She reports continued impairment in her ability to perform her job adequately as phlebotomist because of fatigue and pain in her arm.

Discussion

TA is a rare disease, affecting mostly Asian women, but has been described in different parts of the world. The annual incidence of TA in different countries generally ranges from 0.4 to 2.6 cases per million. Japan has the highest prevalence of 40 cases/million. In other countries, the prevalence rate ranges from 4.7 to 8 cases per million.[1]

The pathogenesis of TA is thought to be through cell-mediated mechanisms, mainly cytotoxic lymphocytes causing vascular injury by releasing large amounts of cytolytic protein perforin.[2] The inflammation may be local or may involve the entire vessel. The majority of the lesions are stenotic, however aneurysms can be found in one third of patients.[1] The initial symptoms can be nonspecific including weight loss, low grade fever, fatigue, arthralgias or myalgias, vertigo, lightheadedness, syncope, orthostasis, HA. Signs and symptoms such as carotidynia, weak or absent pulses, limb claudication, arterial bruits, may provide more clues. Associated medical conditions may include HTN, angina, post-prandial pain, skin lesions similar to erythema nodosum and pyoderma gangrenosum, and strokes.[2] In one study, the median delay in diagnosis was 17.5 months.[3] Because of delayed diagnosis, irreversible vascular damage can occur.

Biopsy is not routine in the diagnosis of TA. Arteriography, the current gold standard, shows morphology and extent of vascular lesions.[4] MRI is also useful because it can provide clear images of the artery wall without contrast or radiation exposure. This is especially important in patients who will require serial studies for many years.[5]

The mainstay of treatment of TA is glucocorticoids. Those with active disease for which glucocorticoid therapy does not provide sustained remission may be treated with methotrexate, azathioprine, leflunomide, mycophenolate mofetil and tocilizumab. Angioplasty, bypass grafts, or other forms of surgery may be performed for large aneurysms or for irreversible stenosis.[6]

It is challenging to treat and monitor disease in patients with TA as markers of inflammation do not reliably correlate with disease activity and imaging results are neither sensitive nor specific. At present, the only reliable means of assessing disease activity is serial imaging, but this has limitations because often by the time a new lesion is detected, there has already been vascular damage.

Conclusion

TA diagnosis requires a high index of suspicion and management is a challenge. TA has to be in the differential diagnosis of patients who present with constitutional symptoms if the diagnosis is to be made in a timely fashion. Collaboration with radiology can be key in establishing the proper diagnosis. Even after the diagnosis has been made and the patient is on maintenance therapy, continued symptom vigilance is needed because of lack of laboratory parameters that reflect disease activity.

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