Clinical Reasoning: A 50-year-old man with “elephantiasis” and headache

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SECTION 1

A 50-year-old man with a medical history of “elephantiasis” of the legs, status post left above the knee amputation with prosthetic limb, and hypothyroidism presented with 1 week of headache and nausea. The headache was continuous, with gradual worsening over the 7 days prior to admission, and he had minimal relief with ibuprofen. On the second day, he developed nausea. He denied any history of headaches, blurred or double vision, numbness, weakness, tingling, loss of balance, vertigo, chest pain, palpitations, or shortness of breath. In the emergency room, he was afebrile with a heart rate of 78 beats

per minute and regular, and a blood pressure of 132/78 mm Hg. General physical examination revealed right leg hypertrophy with hyperpigmentation, and edema more prominent distally (tree-barking) (figure 1). A comprehensive neurologic examination had normal results. Basic laboratory tests including complete blood count, basic metabolic panel, and thyroid tests were within normal limits. Head CT showed a hypodensity in the left cerebellar hemisphere (figure 1).

Question for consideration:

1. What is your differential diagnosis?

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Figure 1 Patient photograph and CT

(A) Right leg hypertrophy with hyperpigmentation and tree-barking. (B) Noncontrast brain CT shows a hypodensity in left cerebellum.

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SECTION 2

The patient has a subacute headache with a CT scan showing a hypodensity in the left cerebellar hemisphere. The most likely etiology of the patient's findings is a cerebellar stroke, which typically presents acutely and is more likely to be associated with headache at onset than strokes in other locations.¹ Other possible causes of cerebellar hypodensity on CT scan include an inflammatory cerebellitis or a cerebellar tumor. The normal neurologic examination does not exclude a vascular etiology since the absence of

cerebellar findings on examination is not uncommon in patients with cerebellar stroke.²

The patient had a brain MRI that showed an acute left cerebellar infarction and another small acute infarct in the left corona radiata (figure 2). Magnetic resonance angiography head and neck were within normal limits.

Question for consideration:

1. What is your next step in the management of this patient?

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Figure 2 MRI diffusion-weighted sequence

MRI shows an acute left cerebellar infarct and a small infarct in the left corona radiata.

SECTION 3

The brain MRI showed infarcts in multiple vascular territories in both the posterior and anterior circulation (left posterior inferior cerebellar artery and left middle cerebral artery), which is a pattern typically considered suggestive of a proximal cardio-aortic embolic source, but that may also be seen with other etiologies such as vasculitis and multifocal atherosclerosis.³ Given that his vessel imaging did not demonstrate a stenosis, a cardiac source was highly suspected. Electrocardiogram and inpatient telemetry showed no evidence of atrial fibrillation. A transthoracic echocardiogram with agitated saline injection was performed, demonstrating right to left shunting consistent with a patent foramen ovale (PFO) without an associated atrial septal aneurysm, and this was confirmed by a transesophageal echocardiogram. Given the association between lower extremity and pelvic thrombi and cryptogenic stroke in patients

with a PFO,⁴ the patient underwent lower extremity Doppler imaging and magnetic resonance venography (MRV) of the pelvis that showed no definite evidence of venous thrombi. The pelvic MRV, however, showed extensive pelvic varices (figure 3). The patient was started on aspirin that was later held due to hemorrhoidal bleeding requiring blood transfusion.

Consideration of deep vein thrombosis as a potential source of paradoxical embolism led to a re-evaluation of the patient's diagnosis of elephantiasis. A more thorough dermatologic examination revealed extensive purplish discoloration of the skin of the hypertrophied leg as well as of the abdomen and back (figure 3).

Questions for consideration:

1. What is the likely diagnosis?
2. How would you manage the patient now?

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Figure 3 Patient photographs and magnetic resonance venography

(A) Extensive purplish discoloration of skin on abdomen and back. (B) Magnetic resonance venography of the pelvis shows extensive pelvic varices (arrows).

SECTION 4

The patient had evidence of diffuse capillary malformations, lower extremity hypertrophy, widespread varicosities, and possible paradoxical embolism suggestive of Klippel-Trenaunay syndrome (KTS).

The prevalence of KTS is 1/20,000 to 1/100,000. It consists of diffuse capillary, venous, and lymphatic malformations and abnormal bone or soft tissue growth (e.g., leg hypertrophy).⁵ It is strongly associated with risk of venous thromboembolism or pulmonary embolism (~50%), which likely occurs in the setting of stasis in enlarged distorted venous malformations.⁶ It may also be associated with ischemic strokes⁷ and intracranial aneurysms.⁸ No gene has been identified as a cause of this syndrome although it is thought to be related to a factor involved in embryogenic angiogenesis.⁵

Given the increased risk of deep venous thrombosis in patients with KTS, the embolic pattern of the patient's infarcts on MRI, and the presence of a PFO, paradoxical embolism was thought the most likely stroke mechanism. Obtaining an MRI helped identify another clinically silent infarct in a different vascular territory, which raised the suspicion for a cardio-aortic embolic source.

While the use of chronic anticoagulation may be a reasonable stroke prevention strategy given the high risk of thrombotic complications with this disease, in patients with KTS and gastrointestinal involvement there is a significant competing risk of life-threatening gastrointestinal bleeding.⁹ PFO is found in about 25% of the normal population and is more common in patients with cryptogenic stroke than other stroke subtypes. The medical and surgical treatment of PFO is controversial.³ Although there is lack of evidence to support the routine closure of a PFO in patients with cryptogenic stroke pending results of ongoing trials,¹⁰ it was performed in this patient given the risk of recurrent paradoxical embolism and the relative contraindication to long-term anticoagulation.

DISCUSSION In patients with cryptogenic stroke, a careful skin and musculoskeletal examination may help determine the stroke mechanism. While evidence-based medicine suggests no benefit of PFO closure over medical therapy in general, in this patient with substantial bleeding risk in the context of chronic anticoagulation, PFO closure may be a reasonable stroke prevention strategy to prevent recurrent paradoxical embolism.

AUTHOR CONTRIBUTIONS

Shadi Yaghi: manuscript preparation and editing. Tomoko Kitago: manuscript revision. Mitchell S.V. Elkind: manuscript editing and obtaining figures.

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