An Atypical Presentation of a Thalamic Stroke in a Young Adult with Ankylosing Spondylitis and an Atrial Septal Defect

XIAO C. ZHANG, MD, MS; MATTHEW S. SIKET, MD, MS; BRIAN SILVER, MD

INTRODUCTION

Acute ischemic stroke (AIS) recently declined from the 3rd to the 5th leading cause of death in the United States, due in large part to advances in the prevention of cerebrovascular disease risk factors, such as cigarette smoking, diabetes, hypertension, hypercholesterolemia and better acute treatments, such as IV tPA and the development of stroke centers. However, ischemic stroke remains a leading cause of long-term disability worldwide. The annual incidence for young white and black adult populations (less than 45 years old) is estimated to be 3.4 to 11.3 per 100,000 and 22.8 per 100,000, respectively.1-3 While 40% of strokes in young patients are cryptogenic, common risk factors include untreated microvascular diseases (i.e. hypertension, diabetes), dissection of blood vessels (accounting for about 10–25% of early AIS), and illicit drug use.4-6 A prothrombotic state, characterized by genetic thrombophilia, Protein C deficiency, antiphospholipid antibodies, elevated lipoprotein(a), Factor V Leiden mutation, prothrombin gene mutation, MTHFR TT genotype have been associated with venous thromboembolism, but not clearly with AIS.9-10 Arterial dissection, often precipitated by trauma, is still considered as the most common vascular abnormalities in young adults with AIS; non-traumatic, spontaneous dissection occurs at a reduced frequency and can be associated with connective tissue disorders such as Ehlers-Danlos syndrome and Marfan syndrome.8-11

CASE REPORT

A 23-year-old man was brought to the ED by his elderly grandparents reporting 4 days of profound fatigue, headache, and a subjective sensation of the right corner of his mouth being “pulled to the side” when he talked. The patient reported he recently participated in a body building competition 5 days prior to the ED presentation, with 2 months of rigorous training that involved diet, exercise, weight loss, but without any anabolic steroid use. He reported new-onset memory deficits, occasionally forgetting events that occurred earlier during the day, generalized weakness, and a 5 out-of-10, gradually developing dull frontal headache that began shortly after the competition. The patient’s past medical history was notable for ankylosing spondylitis for which he started taking etanercept (TNFα inhibitor) 5 years earlier.

The patient went to an urgent care center 2 days prior to the ED presentation, where he was diagnosed with dehydration and discharged home after being given 1 liter of IV normal saline. The patient subsequently returned to the ED due to persistent symptoms.

On arrival to the ED, he was afebrile with blood pressure 110/60 mm Hg and pulse rate 64 beats/min. There were no focal neurological deficits; he was alert and oriented x4, and he did not demonstrate any memory deficits. Complete blood count (CBC), comprehensive metabolic panel (CMP), thyroid-stimulating hormone (TSH) reflex, urinalysis, drug

Figure 1. Non-Contrast CT Brain of acute right thalamic infarction. (A) Frontal and (B) coronal views demonstrating an anterior right thalamus infarction (arrow) in a young patient with ankylosing spondylitis, presenting with gradual, intermittent memory loss.

Figure 2. MRI without contrast of acute right thalamic infarction. (A) Axial T2-weighted and (B) diffuse weighted imaging (DWI) confirms a right thalamic infarction (arrow) in the same young patient with ankylosing spondylitis.
of abuse screen were unremarkable; an insidious infectious workup was initiated, including rapid HIV, RPR, and Lyme reflex that were ultimately negative. ECG showed sinus rhythm of 51 beats per minute and the chest X-ray was normal. A non-contrast head CT showed an acute infarction in the anterior aspect of the right thalamus (Figure 1). An MRI of the head and neck confirmed the thalamic infarction (Figure 2); MRA of the head and neck was unremarkable. During hospitalization, a bubble echocardiogram revealed an atrial septal defect (ASD); the blood work, including hypercoagulability studies, lipid panel, and HbA1c were normal. The patient has remained free from recurrent events and maintains a secondary prevention medication regimen including 81mg of aspirin and 80mg of atorvastatin.

DISCUSSION

We report an unusual presentation of a thalamic infarction in a young adult male without cerebrovascular disease risk factors, but with two potentially contributory, but controversial etiologies: ankylosing spondylitis and atrial septal defect.

The thalamus is a midline symmetrical structure within the vertebrate brain, situated between the cerebral cortex and the midbrain, responsible for relaying sensory and motor signals to the cerebral cortex. The anterior nucleus of the thalamus (ANT) contains 13 nuclei, all of which have very different roles in memory processing and emotional and executive functions. Clinical and experimental studies have shown that unilateral damage to the ANT in the paramedian artery territory produces neuropsychological disturbances, including episodic memory deficits, as observed in Wernicke-Korsakoff syndrome. Early stages of unilateral ischemic involvement include impairment of arousal with decreased level of consciousness, lasting from hours to days, with potential persistent features such as confusion, agitation, aggression. Hypophonia (soft speech), dysprosody (disordered melody, intonation, or accents), reduced verbal fluency, and frequent perseveration may also be observed, but syntactic structure is generally preserved.

Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial spine, characterized by chronic back pain and progressive stiffness of the spine with extraarticular comorbidities including uveitis, inflammatory bowel disease, cardiovascular disease and restrictive pulmonary diseases. While observational studies have shown an increased risk for cardiovascular complications, such as increased aortic regurgitation with patients with AS, the risk for stroke in patients with AS remains controversial. A prospective, Taiwanese population-based longitudinal follow-up study showed an increased risk of developing ischemic stroke in young patients with AS; meanwhile, a meta-analysis comparing the occurrence of stroke in AS patients [1004/9791] and healthy controls [22,899/1,239,041] showed a significantly increased occurrence of strokes in AS patients as compared to healthy controls, 3.6% vs. 1.78% respectively [OR = 1.5, 95% CI]. Another source of controversy lies within the role of TNF-α and its inhibitor, such as etanercept in ischemic stroke. While the reported risk of stroke of 3% with etanercept led to the initial diagnosis of our patient’s thalamic stroke, a recent multivariate meta-analysis revealed that certain TNF-α polymorphisms, such as the TNF-α -238G/A was associated with increased ischemic stroke risk in Asian adults. Furthermore, etanercept used in rat studies showed significantly protection against ischemic strokes, and when it is used in conjunction with α-lipoic acid, they promoted improved stroke recovery rates.

Finally, the role of common cardiac abnormalities such as patent foramen ovale (PFO), atrial septal defect (ASD), atrial septal aneurysm (ASA) remain controversial in the implication of embolic causes for AIS, with studies suggesting an increased prevalence of PFO and ASA in patients with cryptogenic stroke, without sufficient data to implicate causality. Meta-analyses of RCTs and observational studies on patients with cryptogenic stroke with confirmed PFO or ASD failed to show any significant benefit from percutaneous catheter-based closure of PFO as compared with antiplatelet or anticoagulant therapies in reduction of recurrent strokes. Our patient was found to have an ASD, in which it is biologically plausible that he may have had a transient hypercoagulability due to the weight-loss regimen with dehydration that bodybuilders undergo; a large right-to-left shunt coupled with a Valsalva maneuver during vigorous lifting of weights could have caused a clot ejection, resulting in AIS.

CONCLUSION

Three current controversies in stroke are simultaneously explored in this case: the diagnosis of stroke in a young patient without focal neurologic deficits, the risk of stroke in ankylosing spondylitis, and the optimal management of atrial septal defects in the stroke population. Acute injury to the anterior thalamus may result in memory deficits similar to Wernicke-Korsakoff syndrome and recent meta-analysis suggests an increase in occurrence of AIS in AS patients. Etanercept, a TNF-α inhibitor, has been shown to prevent and even promote recovery rates in ischemic strokes in animal models, despite pharmaceutical warnings of potential AIS. Finally, while right to left shunt coupled with valsalva maneuver [i.e. weightlifting] in patients with ASD may lead to a clot ejection causing AIS, percutaneous catheter-based closure of PFO has not been shown to provide significant benefit as compared with antiplatelet or anticoagulant therapies in reduction of recurrent strokes. Patients diagnosed with thalamic strokes should undergo inpatient studies, including hypercoagulopathy studies, advanced imaging, and echocardiograms, with close outpatient follow-up.
References


Authors
Xiao C. Zhang, MD, MS; Department of Emergency Medicine, Alpert Medical School of Brown University, Providence, RI.
Matthew S. Siket, MD, MS; Department of Emergency Medicine, Alpert Medical School of Brown University, Providence, RI.
Brian Silver, MD; Department of Neurology, Comprehensive Stroke Center, Rhode Island Hospital, Providence, RI.

Funding and Support
No disclosures.

Correspondence
Xiao Chi Zhang, MD, MS
Rhode Island Hospital
593 Eddy Street, Claverick 100
Providence, RI 02903
xzhang1@lifespan.org