Unusual Cause of Acute Stroke in a Young Woman with Patent Foramen Ovale – Duplicated Inferior Vena Cava and May-Thurner Syndrome

The Neurohospitalist
2024, Vol. 14(3) 278–283

DOI: 10.1177/19418744241231314
journals.sagepub.com/home/nho
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Abstract

The etiology of acute ischemic stroke (AIS) may often remain uncertain despite diligent work-up, especially in young people. Although patent foramen ovale (PFO) is a frequent association during such work-up, the actual source of thromboembolism, like deep vein thrombosis (DVT), may not be found. Such associative pathology makes it challenging to prescribe anticoagulation for secondary stroke prevention.

We describe a young woman with a known history of PFO who presented with AIS and underwent endovascular reperfusion therapy. Post-thrombectomy, she developed hypoxic respiratory failure due to pulmonary embolism. Initiation of therapeutic anticoagulation was complicated by a retroperitoneal bleed necessitating imaging studies for etiological work-up. Computed tomographic angiography and venogram showed no active contrast extravasation but demonstrated duplication of the inferior vena cava with DVT in the right iliofemoral vein (RIFV). The proximity of the right common iliac artery compressing RIFV against the pelvic inlet is described as May-Thurner syndrome (MTS). Afterward, the patient was successfully treated with anti-coagulation and PFO closure.

MTS is a rare and underdiagnosed cause of iliofemoral DVT. In patients with known PFO, MTS is a possible cause that needs consideration. Hence, appropriate diagnostic tests are necessary to initiate appropriate management and to prevent AIS recurrence.

Keywords

cryptogenic stroke, deep venous thrombosis, duplicated inferior vena cava, ischemic stroke

Introduction

Acute ischemic stroke (AIS) is a leading cause of physical and cognitive disability among survivors. Besides acute reperfusion therapy, using intravenous thrombolysis and/or endovascular reperfusion therapy (EVT), and work-up for etiology to prevent recurrence are the guiding principles in AIS management. Despite diligent work-up, the cause of stroke may remain elusive, especially in young individuals, and these strokes are categorized as cryptogenic. Such stroke accounts for 15%–35%, depending on the population studied, the extent of diagnostic testing performed, and the definition used.[1] Patent foramen ovale (PFO) is often associated with this subcategory. In this report, we describe an unusual case of embolic stroke in a patient with known PFO. She was found to have acute pelvic deep venous thrombosis (DVT) in the setting of duplicated inferior vena cava (IVC), which is consistent with a variant of May-Thurner syndrome (MTS) pathology.

Case Description

The local institutional review board considers case reports non-research with minimal or no risk to an unidentified

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subject and exempts such studies from a formal review process.

A 37-year-old right-handed woman with a history of hypothyroidism and known PFO presented with altered consciousness and left hemiplegia concerning for AIS. Computed tomographic angiogram (CTA) of the head demonstrated occlusion of the superior division of the right middle cerebral artery (M2). She underwent EVT, achieving thrombolysis in cerebral infarction score of 2A (Figure 1(A)–(D)). Figure 1(E)–(G) depict the extent of the stroke. The right common femoral artery was accessed using ultrasound guidance and an 8Fr vascular sheath followed by Angioseal® closure upon completion of the procedure. No mechanical problem was encountered with the patient's venous anomaly

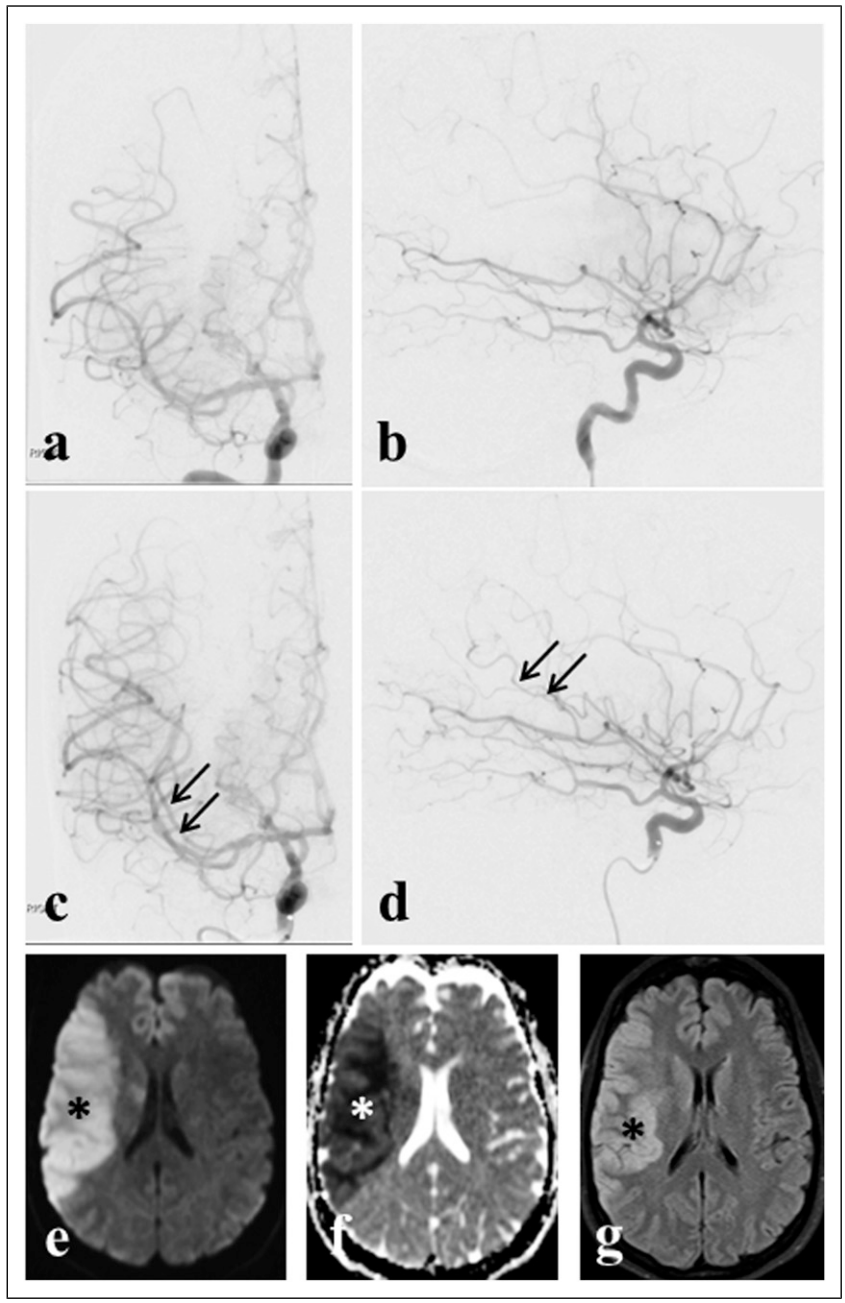

Figure 1. Cerebral angiogram performed during endovascular reperfusion therapy prior to (A: antero-posterior view; B: lateral view) and after (C: antero-posterior view; D: lateral view) thrombectomy. Arrows indicate the superior division of right middle cerebral artery recanalization. Magnetic resonance imaging of the brain obtained after intervention shows extent of the acute stroke (D: DWI; E: ADC; F: FLAIR sequences respectively and extent of stroke indicated with *).

overlying the large conducting (elastic) artery. Of note, the patient had a history of two spontaneous abortions and subsequently underwent in vitro fertilization treatments a year prior to the current hospitalization. Furthermore, the patient was also known to have a "heart murmur." Two years prior to the current hospitalization, the patient had a spontaneous abortion at 15 weeks of pregnancy in the setting of COVID-19 infection. This prompted a hypercoagulable workup and a transesophageal echocardiogram to delineate cardiac pathology better, and thus, PFO was diagnosed. Patient was on progestin-only oral contraceptive pills.

On hospital day (HD)-1, she had a worsening neurological status and progressive hypoxic respiratory failure requiring intubation. CT/CTA of the head demonstrated cerebral infarct progression with re-occlusion of the right M2. CTA of the chest showed a right lower lobe subsegmental pulmonary embolism (PE) and left lower lobe pneumonia (Figure 2(A) and (B)). Bilateral upper and lower extremity (LE) venous Doppler studies showed no evidence of DVT. A heparin infusion was started for the management of PE. On HD-2, a four-point hemoglobin drop necessitated investigation with CTA of the abdomen and pelvis that showed large, mixed-density retroperitoneal and intraperitoneal space hematomas (Figure 2(E)) extending into the right groin without active extravasation. Further imaging review also demonstrated a duplicated IVC (Figure 3(A)–(D)) with MTS pathology and associated extensive right iliofemoral vein (RIFV) DVT (Figure 2(C)–(E)). Transthoracic echocardiogram redemonstrated the PFO with right-to-left shunt. On HD-3 a heparin infusion was restarted as repeat imaging did not show any worsening of hemorrhagic transformation of the cerebral infarction. The patient was extubated on HD-5 and underwent inpatient rehabilitation. She was transitioned to enoxaparin until PFO closure which was performed six weeks after AIS with the Amplatzer™ Talisman™ PFO Occluder. She is being treated with apixaban for at least three months. Hypercoagulable work-up did not show any predisposing genetic mutations, including negative Factor V Leiden and Prothrombin 20 210 G/A mutation, and normal levels of functional Antithrombin III and Protein S. Lupus anticoagulant screen and cardiolipin antibody levels were unremarkable.

Discussion

The cause of AIS, especially in young individuals, often remains elusive despite extensive etiological work-up and is classified as cryptogenic stroke. Even in our patient, a routine search for DVT using LE vascular dopplers could not identify a thromboembolic source. Only after contrast-administered imaging studies could incidental duplicated IVC and iliofemoral DVT be identified in the presence of MTS pathology. Although our patient had PE and needed therapeutic anticoagulation to prevent pulmonary hypertension, imaging to evaluate for pelvic DVT may not be applicable. However, the decision on long-term anticoagulation beyond 3-6 months

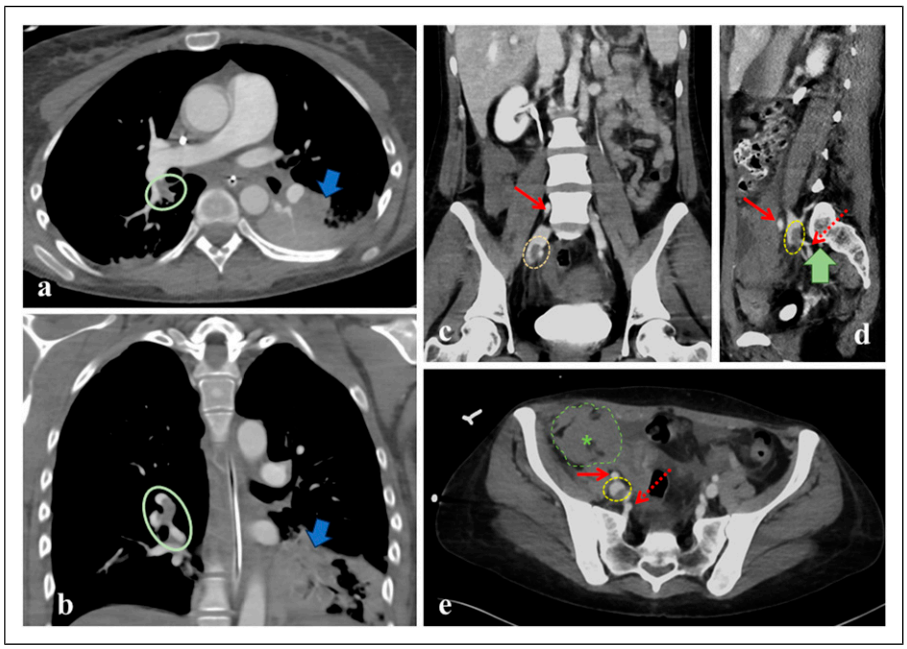

Figure 2. CT angiogram of the chest (a) axial and (b) coronal view shows right lower lobe subsegmental pulmonary embolism demonstrated as filling defect in the arteries (encircled in green) and left lower lobe consolidation (blue solid arrow). CT angiogram with venous follow through of the abdomen and pelvis (c: coronal; d: sagittal; e: axial, respectively) shows thrombus in the right iliofemoral vein (yellow dotted circle) in close relation to right common iliac artery (red arrow), right internal iliac artery (red dotted arrow) and bony prominence of ala of the sacrum (green solid arrow). Extravasated retro- and intra-peritoneal blood shown in the enclosed area depicted with green *.

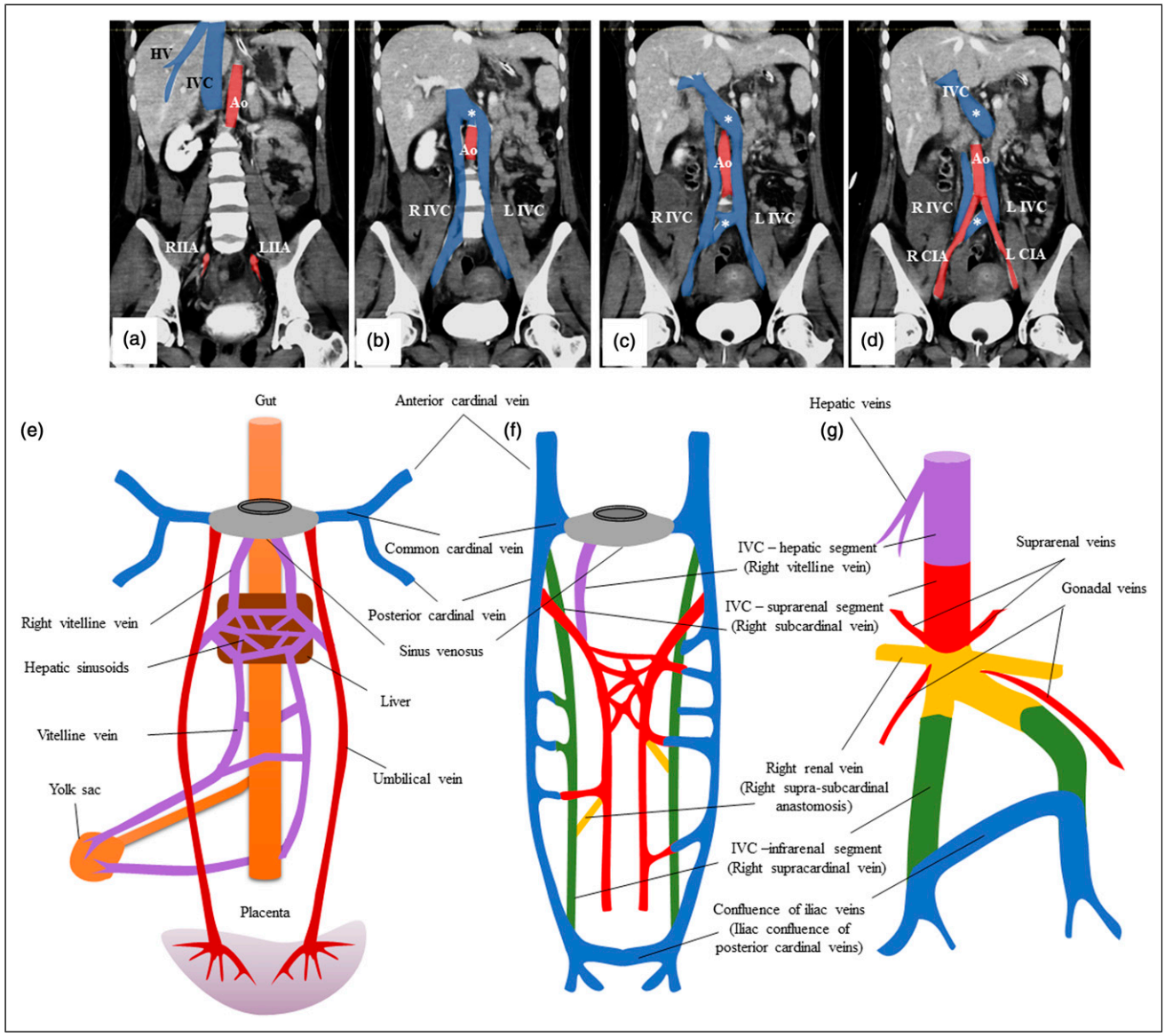

Figure 3. (a-d) CT angiogram of the abdomen and pelvis with venous follow through imaging protocol shows vascular anomaly that are color coded to represent the major arteries (red) and venous (blue) structures. Coronal images represent postero-anterior orientation left to right. Ao – abdominal aorta; HV – hepatic vein; IVC – inferior vena cava; L CIA – left common iliac artery; LIIA – left internal iliac artery; L IVC – left inferior vena; R CIA – right common iliac artery; RIIA – right internal iliac artery; R IVC – right inferior vena cava. * bridging vein. (e-f) Schematic diagram shows progressive development of IVC during the first 4-8 weeks and final anatomical variant in the index patient. Embryonic portions evolving in adult IVC are correspondingly color-coded.

would need an etiological work-up to prevent recurrent PE due to local/anatomical variants like MTS and systemic hypercoagulability.

Stroke Risk in Patients with DVT

A higher incidence of LE DVT in patients with presumed paradoxical embolism is noted, especially in younger patients (<55 years old) with cryptogenic stroke.[2] Other studies, however, report that failure to identify the source of venous thrombi is common, possibly due to delayed timing in obtaining imaging studies.[3] It is accepted that DVT risk increases with age as risk factors for clot formation rise. However, the degree to which DVT is responsible for stroke remains unclear other than disease processes such as hypercoagulable states and cancer. The risk factors in our patient to develop DVT include her use of progesterone-only contraceptive pills (hypercoagulability) and anatomical venous anomaly (structural predisposition).

CT venogram was used to diagnose pelvic DVT in our patient. Pooled analysis of CT venogram studies reports a

96% sensitivity and 95% specificity in diagnosing proximal DVT.[4] Similarly, magnetic resonance (MR) venogram has 92% sensitivity and 95% specificity in diagnosing DVT.[5] Since both modalities have similar DVT detection rates, either imaging can be chosen depending on local availability, expertise, imaging and patient factors (eg, contrast administration, radiation exposure in CT imaging, and claustrophobia, presence of metallic objects for MR imaging).

Stroke Risk in Patients with PFO

The prevalence of PFO in the general population is 25%–30%, but incidence in patients with cryptogenic stroke is reported as higher, 40%–50%.[6] Several studies report an association between PFO and cryptogenic stroke. For example, younger patients with PFO have a higher probability of stroke, as do patients with larger PFO.[7] However, the causal relationship remains unclear as approximately 30% of PFOs in cryptogenic stroke were found incidentally, making the estimation of stroke risk and the treatment challenging.[8] Atrial septal aneurysm (ASA) in the presence of PFO is strongly linked to increased stroke risk; however, ASA is only present in approximately 1% of PFO patients.[7] Of note, our patient was treated with a PFO closure device to prevent recurrent AIS, and ASA was noted during the procedure.

MTS as a Cause for DVT

In 1957, Dr. May and Dr. Thurner first described MTS as a compression of the left iliofemoral vein by the right common iliac artery (RCIA) against the vertebral body. They reported intraluminal fibrous bands in the left iliofemoral vein secondary to compression from the RCIA in 22% of the 430 cadavers they dissected.[9] Among all causes for DVT, MTS accounts for 2%–5%.[9,10] However, retrospective pathological studies and radiographic studies, especially those with left LE DVT, report MTS incidence as high as 22%–76%.[9] Of note, men have a higher incidence of pain and swelling in the left leg, and women tend to be younger and more often present with a pulmonary embolism.[11] Our patient fits into these described profile except for having a RIFV DVT due to duplication IVC and its proximity to RCIA and the pelvic inlet (Figure 2(D) and (E)). The RIFV DVT noted in our case is likely formed both from compression against the pelvic inlet (resulting in stasis) and transmitted pulsation from the neighboring common and internal iliac arteries (thus irritating the endothelium, forming bands, and referred to as spurs).[12]

Endovascular stenting is often used for vessel-on-vessel compression and sequelae of MTS. Acute thrombosis may warrant anticoagulation for up to a year, but long-term anticoagulation is not warranted, with 99% patency rates in non-thrombotic occlusions.[13] However, a position statement from the Society of Interventional Radiology recommends anticoagulation for "at least several months" in patients with DVT or post-thrombotic syndrome.[14]

Ontology of Duplicated IVC

The incidence of duplicated IVC is estimated at ~.3%–.4%. The IVC development is a sequential process of fusion and regression of embryological veins, namely the posterior cardinal, subcardinal, supracardinal, and vitelline veins.[15] In the fourth week of embryological development, the right and left horns of the sinus venosus receive paired common cardinal, umbilical, and vitelline veins (Figure 3(E)). In the subsequent two weeks, paired subcardinal and supracardinal veins emerge as dominant tributaries, forming multiple channels draining into the posterior cardinal veins (Figure 3(F)). The adult derivatives of the duplicated IVC seen in our patient are color-coded in Figure 3(G). The anastomosis between the duplicated IVC at the iliac and renal veins level rendered them to compression and venous stasis. This anatomical variation possibly predisposed the patient to develop DVT in conjunction with her hormonal contraceptive intake.

Conclusion

In a young woman presenting with AIS with PFO, pelvic vascular imaging in additional to femoral venous screening is recommended. If DVT is noted and/or other high risk anatomical variant like duplicated IVC is found, anticoagulation is recommended for stroke and PE prevention. In addition, PFO closure needs to be considered to further reduce the chances of paradoxical embolism.

Appendix

Abbreviations

AIS	Acute ischemic stroke
ASA	Atrial septal aneurysm
CTA	Computed tomography angiogram
DVT	Deep venous thrombosis
EVT	Endovascular reperfusion therapy
IVC	Inferior vena cava
LE	Lower extremity
MR	Magnetic resonance
MTS	May-Thurner syndrome
PE	Pulmonary embolism
PFO	Patent foramen ovale
RCIA	Right common iliac artery
RIFV	Right iliofemoral vein

Author Contributions

SL – Initial draft, literature review
JWR – Initial draft, critical review
SHS – review of final draft
BR – Study design, conception, critical review of final version

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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References

1. Ibeh C, Elkind MSV. Stroke prevention after cryptogenic stroke. *Curr Cardiol Rep*. 2021;23:174-20211016. doi:10.1007/s11886-021-01604-1
2. Cramer SC, Rordorf G, Maki JH, et al. Increased pelvic vein thrombi in cryptogenic stroke: results of the paradoxical emboli from large veins in ischemic stroke (PELVIS) study. *Stroke Vasc Interv Neurol* 2004; 35: 46-50. 20031204. doi:10.1161/01.Str.0000106137.42649.Ab.
3. Ioannidis SG, Mitsias PD. Patent foramen ovale in cryptogenic ischemic stroke: direct cause, risk factor, or incidental Finding? *Front Neurol*. 2020;11:567-625. doi:10.3389/fneur.2020.00567
4. Thomas SM, Goodacre SW, Sampson FC, van Beek EJR. Diagnostic value of CT for deep vein thrombosis: results of a systematic review and meta-analysis. *Clin Radiol*. 2008;63:299-304. doi:10.1016/j.crad.2007.09.010
5. Silickas J, Black SA, Phinikaridou A, Gwozdz AM, Smith A, Saha P. Use of computed tomography and magnetic resonance imaging in central venous disease. *Methodist Debakey Cardiovasc J*. 2018;14:188-195. doi:10.14797/mdcj-14-3-188
6. Hara H, Virmani R, Ladich E, et al. Patent foramen ovale: current pathology, pathophysiology, and clinical status. *J Am Coll Cardiol*. 2005;46:1768-1776. doi:10.1016/j.jacc.2005.08.038
7. Greer DM, Aparicio HJ, Siddiqi OK, et al. 32 - cardiac diseases. In: JC Grotta, GW Albers, JP Broderick, et al., eds. *Stroke*. 7th ed. Philadelphia: Elsevier; 2022:477-487. e476.
8. Alsheikh-Ali AA, Thaler DE, Kent DM. Patent foramen ovale in cryptogenic stroke: incidental or pathogenic? *Stroke Vasc Interv Neurol*. 2009;40:2349-2355. doi:10.1161/strokeaha.109.547828
9. Harbin MM, Lutsey PL. May-Thurner syndrome: history of understanding and need for defining population prevalence. *J Thromb Haemost*. 2020;18:534-542. doi:10.1111/jth.14707
10. Mousa AY, AbuRahma AF. May-Thurner syndrome: update and review. *Ann Vasc Surg* 2013;27:984-995. 20130710. doi:10.1016/j.avsg.2013.05.001
11. Kaltenmeier CT, Erben Y, Indes J, et al. Systematic review of May-Thurner syndrome with emphasis on gender differences. *J Vasc Surg Venous Lymphat Disord*. 2018;6:399-407. doi:10.1016/j.jvsv.2017.11.006
12. Mangla A, Hamad H. *May-Thurner Syndrome. [Updated 2022 Nov 30]*. Treasure Island (FL): StatPearls Publishing; 2023.
13. Xiao N, Genet M, Khaja M, Desai KR. Antithrombotic therapy after deep venous intervention. *Semin Intervent Radiol*. 2022;39:357-363. 20221117. doi:10.1055/s-0042-1757340
14. Vedantham S, Weinberg I, Desai KR, et al. Society of interventional radiology position statement on the management of chronic iliofemoral venous obstruction with endovascular placement of metallic Stents. *J Vasc Interv Radiol*. 2023;34:1643-1657. e6. 20230616. doi:10.1016/j.jvir.2023.06.013.
15. Li SJ, Lee J, Hall J, Sutherland TR. The inferior vena cava: anatomical variants and acquired pathologies. *Insights Imaging*. 2021;12:123. doi:10.1186/s13244-021-01066-7