A CASE OF PHLEGMASIA CERULEA DOLENS AND MAY-THURNER SYNDROME IN A YOUNG MALE WITH TRIPLE-POSITIVE ANTIPHOSPHOLIPID ANTIBODY SYNDROME

C. Siu, DO, P. Patel, DO, R. Decker, MD; S. Li, DO; W. Adeel, MD

Department of Internal Medicine, Lehigh Valley Health Network, Allentown, PA

INTRODUCTION

Phlegmasia cerulea dolens (PCD) is an uncommon form of deep vein thrombosis (DVT) typically presenting with acute limb swelling, pain, and cyanosis. Diagnosis of PCD should be made promptly as these patients may develop limb-threatening complications such as gangrene and compartment syndrome.

CASE REPORT

A 37-year-old obese male with type 2 diabetes, hypertension, and hyperlipidemia was directly admitted to the medicine floor with extensive left lower extremity DVT found on outpatient duplex ultrasonography.

- Former smoker with 14pack-year history. Quit 5 years ago
- Recent 15-hour long car ride. No past history of DVT
- Family history positive for SLE in two cousins and grandmother
- Vital Signs:
  - Patient's BMI 40 kg/m2
  - Afebrile, hemodynamically stable
  - HR 94-109
  - SpO2 in high 90s on Room Air
- Lower Extremity Physical Exam:
  - Extremities: **Left lower extremity was tender and edematous with cyanosis.**
  - Vascular: 2+ dorsal pedis pulses and 2+ posterior tibial pulses bilaterally

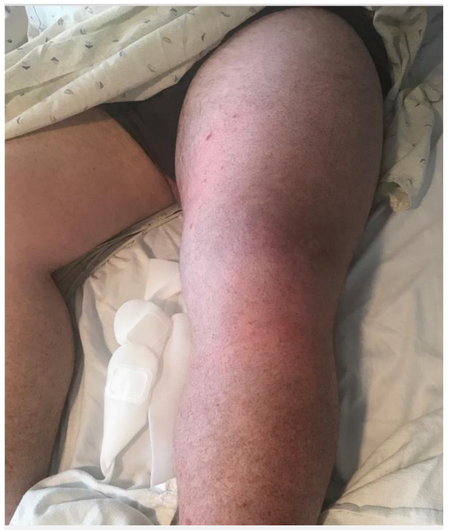

Image1: Cyanosis and diffuse swelling of the left lower extremity

Initial Labs included:

- Unremarkable CMP
- Troponin x2 negative
- NT pro-BNP WNL
- PT 15, INR 1.2, and PTT 88.5 (confirmed with repeat labs)

Bilateral Venous Duplex Lower Extremity

Report Impressions: Occlusive clot is seen within the left posterior tibial, peroneal, popliteal, femoral, proximal profunda femoral and common femoral veins which are dilated, hypoechoic, when applicable non-compressible and without color duplex flow.

Diagnosis:

Phlegmasia Cerulea Dolens

Hospital Treatment

- Initiated subcutaneous enoxaparin
- IR performed catheter-directed thrombolysis. Continuous heparin (500 units/hr) and tPA (1mg/hr) infusion with daily PTT and daily venogram by IR
- Repeat venogram noted resolution of thrombus in common femoral vein after ~46 hours of continuous infusions.
- Suspected May-Thurner Syndrome (MTS) by IR. Patient underwent stent placement of left common iliac vein, external iliac vein, and common femoral vein
- Patient received bridging to warfarin with enoxaparin and was discharged home two days after stent placement.

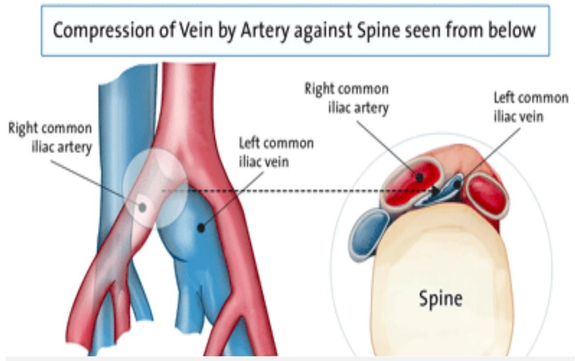

Image2: Compression of left common iliac vein by right common iliac artery. From Judy Holdstock. The Whiteley Clinic ©2001-2020

Additional testing during hospitalization

- Hematology was consulted and ordered testing for antiphospholipid syndrome
- Testing revealed positivity for:
  - Anti-cardiolipin IgG, IgA
  - Anti-beta-2 glycoprotein IgG
  - dRVVT

Positivity confirmed with repeat testing of anti-cardiolipin and dRVVT at 15 weeks after hospitalization

Revised classification criteria for the antiphospholipid syndrome[8]

Antiphospholipid syndrome is present if at least one of the clinical criteria and one of the laboratory criteria that follow are met*
Clinical criteria
1. Vascular thrombosis[¶] One or more clinical episodes[Δ] of arterial, venous, or small vessel thrombosis[◇], in any tissue or organ. Thrombosis must be confirmed by objective validated criteria (ie, unequivocal findings of appropriate imaging studies or histopathology). For histopathologic confirmation, thrombosis should be present without significant evidence of inflammation in the vessel wall.
2. Pregnancy morbidity a. One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal fetal morphology documented by ultrasound or by direct examination of the fetus; or b. One or more premature births of a morphologically normal neonate before the 34th week of gestation because of: (i) eclampsia or severe preeclampsia defined according to standard definitions, or (ii) recognized features of placental insufficiency[§]; or c. Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded. In studies of populations of patients who have more than one type of pregnancy morbidity, investigators are strongly encouraged to stratify groups of subjects according to a, b, or c above.
Laboratory criteria[¥]
1. LA present in plasma, on two or more occasions at least 12 weeks apart, detected according to the guidelines of the International Society on Thrombosis and Haemostasis (Scientific Subcommittee on LAs/phospholipid-dependent antibodies).
2. aCL of IgG and/or IgM isotype in serum or plasma, present in medium or high titer (ie, >40 GPL or MPL, or >the 99th percentile), on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA.
3. Anti-beta-2 glycoprotein-I antibody of IgG and/or IgM isotype in serum or plasma (in titer >the 99th percentile), present on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA, according to recommended procedures.

Causes of Thrombosis:

- **Antiphospholipid Syndrome**
- **May-Thurner Syndrome**

CONCLUSIONS

- Treatment of PCD is anticoagulation therapy with adjunctive catheter-directed thrombolysis.
  - Outcomes comparing additional catheter-directed thrombolysis versus anticoagulation alone have shown that combination treatment reduces the incidence of post-thrombotic syndrome in patients with acute iliofemoral DVT.
- Recognition of DVT associated with MTS is important as treatment includes stent placement to maintain venous outflow.
- Recognition of triple-positive antiphospholipid syndrome is an indication for extended anticoagulation as this portends a high risk of recurrent VTE.
  - The choice of therapy for secondary prevention is warfarin with INR goal of 2-3.
  - The use of direct oral anticoagulation in patients with APS remains controversial - with recent studies showing increased risk of recurrent thrombosis, particularly in patients with triple-positive APS.

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