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Case Reports

Trousseau Syndrome in a 25-Year-Old Woman with Occult Colon Malignancy, Lynch Syndrome, and Chronic Thromboembolic Pulmonary Hypertension

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We present a rare case of thrombosis associated with an occult colon malignancy (Trousseau syndrome) in a 25-year-old woman who also presented with previously unidentified Lynch syndrome and acute-on-chronic thromboembolic pulmonary hypertension. Staged treatment included bilateral pulmonary endarterectomy under deep hypothermic circulatory arrest, followed 11 days later by laparoscopic subtotal colectomy and creation of a primary anastomosis. The patient tolerated both procedures well and recovered normal functional status. Final pathologic analysis of the resected colon mass revealed a pT3N0, stage IIA adenocarcinoma; no adjuvant therapy was administered. At her one-year follow-up visit, the patient was cancer-free, remained on lifelong apixaban anticoagulation, and was undergoing routine monitoring and genetic counseling. This case highlights the need for multidisciplinary management of a patient with severe chronic thromboembolic pulmonary hypertension and a concomitant malignancy. ***(Tex Heart Inst J 2022;49(3):e207419)***

Cancer-associated thrombosis, a syndrome first described by Trousseau in 1865,[1] is well documented.[2,3] It is the second-leading cause of death in cancer patients, after disease progression.[4] National guidelines recommend that patients with cancer-related venous thromboembolism undergo prolonged anticoagulation for 3 and 6 months, which indicates the long-standing risk.[2] Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare but severe manifestation of cancer-associated thrombosis that is not amenable to medical treatment or, in many cases, to surgical correction after permanent structural changes to the pulmonary artery (PA) have occurred.[5,6] We present a rare case of Trousseau syndrome associated with an occult colonic malignancy in a young woman who also presented with previously unidentified Lynch syndrome and acute-on-chronic CTEPH.

Case Report

A 25-year-old African American woman weighing 92 kg (body mass index, 34.6) presented at another hospital with shortness of breath at rest (New York Heart Association [NYHA] functional class IV), hypoxia, and pleuritic chest pain after an extended period of travel. Her medical history included sickle cell trait, iron deficiency anemia with talc pica (a possible cocarcinogen),[7] and multiple upper respiratory infections refractory to both antibiotic and steroid therapy. Her familial history included hypertension, and she had a 50-year-old second-degree relative with thyroid cancer who had no identifiable genetic syndromes. At presentation, the patient was hemodynamically stable, was receiving supplemental oxygen through a nasal cannula, and had a hemoglobin

level of 6.9 g/dL. A chest radiograph revealed consolidation of the mid left lung. A duplex ultrasonogram of the lower extremities showed no deep venous thrombosis. A computed tomogram revealed multiple pulmonary emboli throughout the PA tree, especially in the left PA. The patient was then transferred to our tertiary center for further clinical management.

When the patient arrived, we requested an interventional radiology consultation. A pulmonary angiogram revealed a filling defect in the central left PA and a complete lack of perfusion to the left lung and right upper lobe that was associated with moderate-to-severe pulmonary hypertension (Fig. 1). Catheter-based thrombolysis was attempted, but failed because of the patient's chronic thromboembolic disease burden. Examination of a biopsy specimen revealed only an organizing thrombus. Right-sided heart catheterization revealed an elevated right ventricular (RV) pressure of approximately 45 mmHg. A transthoracic echocardiogram showed mild tricuspid regurgitation, no regional wall-motion abnormalities, and septal flattening and leftward bowing of the intra-atrial septum. The septal findings indicated RV pressure and volume overload.

To determine the cause of the PA obstruction, a full-body scan was obtained with use of positron emission tomography and computed tomography. The scan revealed a near-occlusive, hypermetabolic mass (maximum standardized uptake value, 17.5) in the transverse colon (Fig. 2). Endoscopic biopsy of the mass and stenting of the transverse colon were performed. Subsequent pathologic analysis of the biopsy specimen resulted in a diagnosis of adenocarcinoma associated with tubulovillous adenoma, but no locoregional nodal or distant metastases. Genetic analysis of a specimen from the tumor identified a germline mutation in the *MLH1* gene, p.D63H variant, consistent with hereditary nonpolyposis colorectal cancer (Lynch syndrome). After consultation with our center's colorectal surgery service and the cardiothoracic surgery team, we recommended and the patient chose, after giving informed consent, to proceed with staged surgical procedures: bilateral pulmonary endarterectomy first, followed by laparoscopic subtotal colectomy days later.

The patient was taken to the operating room, intubated endotracheally, and placed under general anesthesia. Vital signs were monitored by invasive hemodynamic means and cerebral oximetry. An intraoperative transesophageal echocardiogram confirmed the presence of extensive thrombi in the PA tree and normal RV function. A median sternotomy was performed, and the anterior pericardium was widely opened. After the patient was fully heparinized, central aortic and bicaval venous cannulae were placed, and cardiopulmonary bypass was initiated. The patient was cooled to a temperature of 15 °C, and deep hypothermic circulatory arrest was established. Continuous electroencephalographic monitoring was started. Circulation was reestablished at 15-min intervals with use of intermittent cardioplegia. The right PA was opened and endarterectomized; the intimal layers were preserved as far into the segmental branches as possible. A similar technique was performed on the left PA. The PAs were closed with use of 5-0 Prolene sutures as the patient was rewarmed. Bronchoscopic evaluation revealed minimal airway hemorrhage. Cardiopulmonary bypass was discontinued without complications. The estimated blood loss was 750 mL. The patient was transferred to the cardiac intensive care unit (ICU) with minimal need for pressor support and was extubated within 6 hours. She was transferred from the ICU the next day and promptly scheduled for her second-stage laparoscopic abdominal procedure. The only complication, Dressler syndrome on postoperative day 12, was managed with pericardial drainage and administration of prednisone and colchicine.

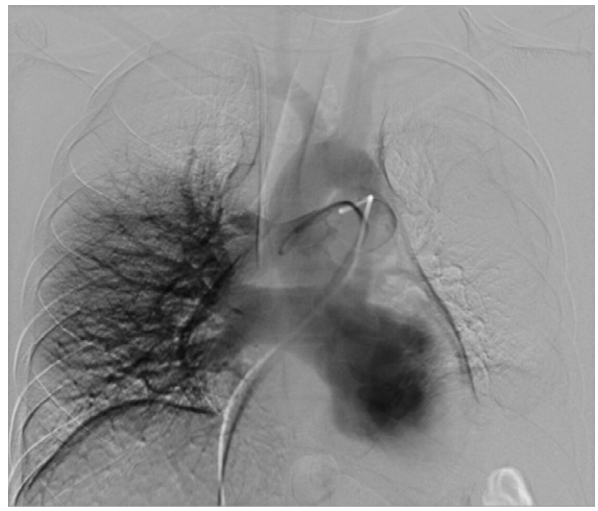

Fig. 1 *Pulmonary angiogram reveals a complete lack of perfusion in the left lung and the right upper lobe.*

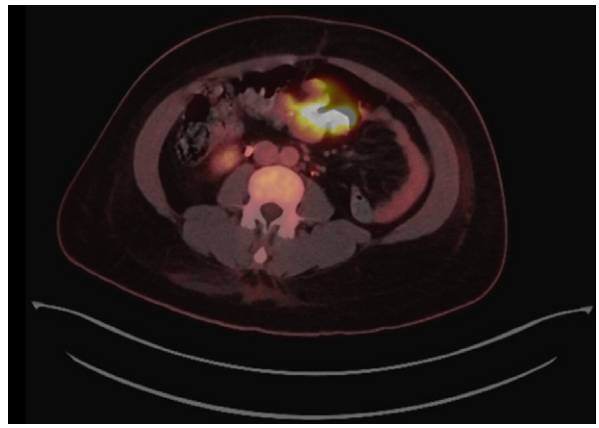

Fig. 2 *Positron emission tomographic/computed tomographic scan shows a hypermetabolic mass in the mid transverse colon, representing a primary colon malignancy.*

Eleven days after the first surgery, the patient underwent laparoscopic subtotal colectomy and creation of a primary anastomosis. A small, contained intramesenteric perforation was noted intraoperatively, along with an associated intra-abdominal abscess (not associated with the tumor) extending from the proximal aspect of the previously placed colonic stent adherent to the small bowel and requiring resection. The adenocarcinoma removed from the resected colon tract was 7.5 cm in diameter, was moderately differentiated, and had invaded through the muscularis propria to the fibroadipose tissue. No lymphovascular or perineural invasion and no peritoneal tumor deposits were seen. Thirty-one lymph nodes were sampled; all were negative for carcinoma. Histopathologic analysis of a specimen taken from the resected colonic adenocarcinoma revealed mucin residues (Fig. 3). Final pathologic staging of the primary tumor, according to the American Joint Committee on Cancer (8th edition) system, was pT3N0, stage IIA. Our center's oncology service recommended no further adjuvant therapy, because it is not indicated for low-risk stage IIA colon cancer in the presence of Lynch syndrome. The patient was discharged from the hospital and placed on a lifelong regimen of anticoagulation with apixaban. She was also referred for genetic counseling and for continued monitoring. At her 1-year follow-up visit, she was cancer-free, had recovered normal functional status, and had resumed activities of daily living.

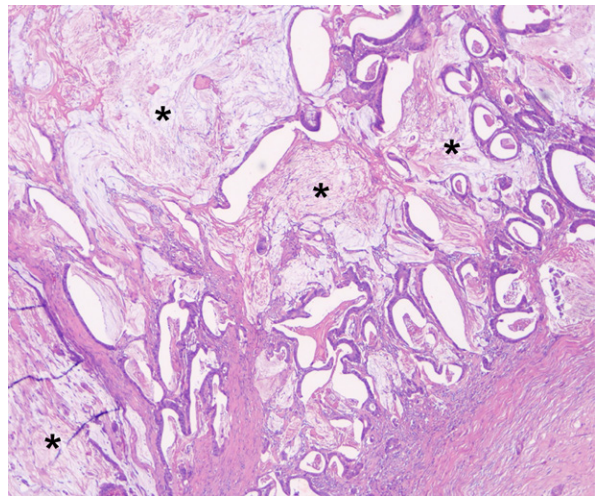

Fig. 3 *Photomicrograph of a specimen from the patient's resected colonic adenocarcinoma shows mucin residues (asterisks) (H & E, orig. ×40).*

Discussion

In this rare case of Trousseau syndrome,[1] a young woman with previously unidentified Lynch syndrome had cancer-induced thrombosis and consequent CTEPH. Chronic thromboembolic pulmonary hypertension is itself rare (approximately 15,000 cases reported annually in the United States).[6,8] It is often treated surgically, resulting in improved quality of life and survival, especially in carefully selected patients and at experienced centers.[6,9] Although cancer-associated thrombosis is multifactorial, the most notable contributing factor in this case was the malignancy type. Cancers can activate the coagulation cascade through various pathways, but adenocarcinomas in particular use mucin to directly cause nonenzymatic activation of factor X.[3] Adenocarcinomas also activate selectins independent of the coagulation cascade.[2] Other less specific factors range from aberrations in tissue factor expression among different cells to differences in ethnic backgrounds.[10] The combination of these factors is responsible for the prothrombotic milieu.

This case had several notable features. The thrombus formation associated with a previously asymptomatic primary adenocarcinoma of the colon in our patient was likely long-standing. Her daily ingestion of talc may have been cocarcinogenic.[7] Her young age and disease chronicity enabled her to be well compensated, despite the minimal perfusion of her left lung. Initial pulmonary endarterectomy, an effective treatment for CTEPH,[6,9] enabled the safe and timely curative resection of her abdominal malignancy days later. Although the severity of our patient's CTEPH necessitated lifelong anticoagulation with apixaban postoperatively,[2,11] she was eventually able to resume activities of daily living at her previous level. In this case, coordinated multidisciplinary surgical treatment resulted in the acute relief of central ventilation and perfusion defects, resection of a malignant colon mass, a return to NYHA functional class I, and freedom from cancer at 1-year follow-up.

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Contributions: Drs. Matthews and Garcia contributed equally to this report.

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