




Paget-Schroetter Syndrome in a Young Female

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Abstract

Paget-Schroetter syndrome or effort thrombosis is a relatively rare primary spontaneous thrombosis of upper extremity deep veins secondary to entrapment of axillary subclavian veins from an abnormality of the thoracic outlet. It is commonly seen in young adults who lift heavy weights or strenuous use of the upper extremities during athletic activities. Repetitive microtrauma to the subclavian vein secondary to narrow costoclavicular space and strenuous activities leads to intimal layer inflammation, hypertrophy, fibrosis, and coagulation cascade activation. Management of Paget-Schroetter syndrome differs from the venous thrombosis of the lower extremity as treatment includes anticoagulation, thrombolysis, and surgical decompression. Early recognition and timely management are required to prevent significant disability from post-thrombotic syndrome and long-term morbidity from recurrent thromboembolism and pulmonary embolism. Internists and emergency physicians should be aware of the disease's presentation, treatment options, and early referral to vascular surgeons since prompt initiation of appropriate treatment will have better outcomes than delayed treatment. We discussed a case of a 31-year-old female who lifts heavyweight at work, presented with right arm swelling and pain for 2 weeks, and diagnosed with axillary subclavian vein thrombosis secondary to thoracic outlet obstruction. She received a high-dose heparin drip followed by catheter-directed thrombolysis and underwent surgical decompression of axillary subclavian vein via resection of the first rib, subclavius muscle resection, partial anterior scalenectomy, and venolysis. In our review of the literature, randomized controlled studies lack the efficacy and safety of surgical decompression. However, the results are promising based on accumulated experience from vascular surgery experts and small case series. Extensive studies are needed further to delineate the protocol for the management of Paget-Schroetter syndrome.

Keywords

axillary subclavian deep vein thrombosis, thoracic outlet obstruction syndrome, Paget-Schroetter syndrome, upper extremity DVT, catheter-directed thrombolysis, first rib resection, venolysis

Introduction

Upper extremity thrombosis is less common than lower extremity deep vein thrombosis (DVT), but with the increased use of central venous catheters, the incidence of upper extremity DVT has been significantly rising. Upper extremity thrombosis consists of primary and secondary causes. Paget-Schroetter syndrome is an acute presentation of venous thoracic outlet obstruction syndrome with the axillary subclavian vein's compression from an abnormality of the thoracic outlet. It is commonly seen in the dominant arm of the young athletes. Secondary thrombosis in the axillary vein is most commonly caused by catheters, including dialysis catheters, Port-A-Cath, PICC (peripherally inserted central catheter) line, central venous catheters, and pacemakers or defibrillators (automated implantable cardioverter-defibrillator). Treatment of secondary thrombosis

includes mainly anticoagulation, whereas common practicing guidelines for the treatment of effort thrombosis consist of anticoagulation, catheter-directed thrombolytic, and surgical decompression of axillary subclavian vein via resection of the first rib, subclavius muscle resection, partial anterior scalenectomy, and venolysis.

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Case Report

A 31-year-old Caucasian female with a past medical history of asthma, not using any inhalers, and morbid obesity, was initially admitted to an outside hospital 2 weeks ago with right arm swelling and pain, where she was diagnosed with upper extremity DVT. She was evaluated by a vascular surgeon at that time and was discharged home on Eliquis. As her symptoms were persistent, she followed-up with a primary care physician who referred her to vascular surgery. She was admitted again to our facility for further management. She denied shoulder or neck injury and clavicular fracture. She denies any previous history of venous access on the right upper extremity, including Port-A-Cath, a PICC, or central venous catheters. She denies any recent travel, major fracture, major surgery, or previous personal or family history of DVT or pulmonary embolism. The thrombophilia workup was negative. She works at U-Haul, where she lifts heavy-weights. Past surgery history includes wisdom tooth extraction and oral surgery. She denies a history of smoking, alcohol, or drug abuse. She has no known drug allergies. Family history was significant for father with a history of skin cancer and chronic obstructive pulmonary disease in father and a history of cancer in mother, and history of provoked DVT in grandfather.

On examination, temperature 37.3 °C, blood pressure 111/72 mm Hg, heart rate 75 beats per minute, respiratory rate 16 breaths per minute, and saturating 100% on room air. Physical examination revealed pitting edema in the right arm extending from hand to the shoulder, erythema, and tenderness in the arm. Peripheral pulses were palpable. Motor and sensory functions were intact. The rest of the physical examination was unremarkable. Laboratory test results on admission are as reported in Table 1.

Hospital Course

Initial venogram showed patent proximal brachial and basilic veins, thrombosis of proximal right axillary vein, subclavian vein, right brachiocephalic vein, and patent superior vena cava as shown in Figure 1. Diagnosis of venous thoracic outlet obstruction syndrome or Paget-Schroetter syndrome was made and initiated on a heparin drip and catheter-directed thrombolytic therapy to decrease the clot's burden before surgical decompression of the axillary subclavian vein. Twenty-four hours after thrombolysis, a venogram was performed again, which showed improved flow, 50% residual clot in the right axillary and subclavian vein, and patent superior vena cava and jugular veins. Thrombolysis and heparin drip resumed after the venogram and continued for 3 days with a repeat venogram every day. She had multiple rechecks and venograms by vascular surgery. Overall, clot burden is much improved 3 days after thrombolysis, as shown in Figure 2, but there is occlusion of the vein at the pinch point between the clavicle and first rib.

Table 1. Laboratory Test Results on Admission.

Laboratory findings	Result	Normal range
WBC	8.6	4-10 × 10 ³ /μL
Hemoglobin	12	11.2-15.7 g/dL
Platelets	290	163-369 × 10 ³ /μL
Sodium	136	136-144 mEq/L
Potassium	4.3	3.5-5.1 mEq/L
Chloride	106	98-110 mEq/L
Bicarbonate	23	20-30 mEq/L
BUN	18	7-23 mg/dL
Creatinine	0.91	0.57-1.11 mg/dL
Glucose	97	70-99 mg/dL
Calcium	9.1	8.5-10.3 mg/dL
AST	76 (high)	5-42 units/L
ALT	54 (high)	5-49 units/L
Total bilirubin	0.5	0.1-1.2 mg/dL
Alkaline phosphatase	49	35-141 units/L
Phosphorus	4.2	2.3-4.7 mg/dL
Total protein	5.7 (low)	6.1-8.3 g/dL

Abbreviations: WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine transaminase.

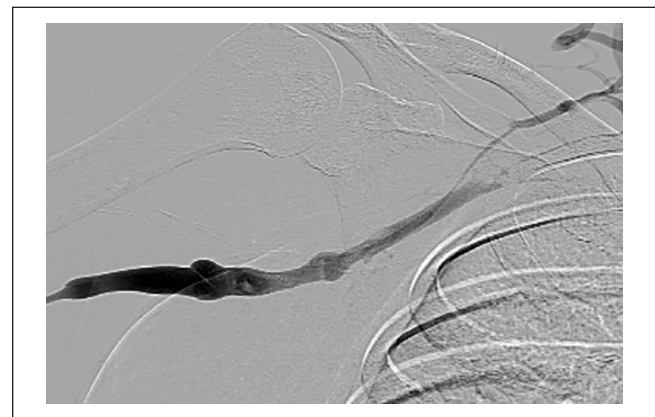


Figure 1. Venogram before thrombolysis.

She continued on low-dose heparin for 3 more days, and thrombolytics were stopped. As there is increased risk for recurrence of clot until the first rib resection is done, a decision was made to perform open surgical decompression of the axillary subclavian vein via resection of first rib subclavian muscle resection, partial anterior scalenectomy, and venolysis. Subsequently, she was discharged on Eliquis.

Discussion

Deep venous thrombosis primarily develops in the lower extremity venous system and less commonly in the upper extremities. However, with the increased use of central venous catheters, pacemakers, defibrillators incidence of upper extremity DVT has been increased. Upper extremity



Figure 2. Venogram after thrombolysis.

thrombosis predominantly involves brachial, axillary, and subclavian veins, less commonly in internal jugular veins, radial, and ulnar veins. Upper extremity DVT accounts for 1% to 4% of all venous thrombosis cases.^{1,2} Annual incidence of upper extremity DVT is 3 to 4 cases per 1 00 000 population.^{2,3} Primary thrombosis in the upper extremity can be spontaneous, secondary to venous thoracic outlet obstruction, and effort related. It occurs most frequently in the dominant arm of young athletes. Secondary thrombosis is substantially caused by catheters, including dialysis catheters, Port-A-Cath, PICC line, central venous catheters, pacemakers, or automated implantable cardioverter-defibrillator, followed by malignancies and less commonly by surgery, trauma to arm, and shoulder, pregnancy, and hormonal therapy.⁴ Although DVT is predominantly caused by acquired and inherited thrombophilias, it is less commonly contributed to upper extremity thrombosis than lower extremity DVT.^{5,6} Paget-Schroetter syndrome, also referred to as effort thrombosis of the axillary subclavian vein, is a rare primary spontaneous thrombosis of upper extremity deep veins secondary to compression of axillary subclavian vein from the abnormality of the thoracic outlet, which can be acquired and congenital anomalies. Main causes of thoracic outlet obstruction include congenital bony and muscular anomalies such as cervical ribs, abnormal scalene muscle attachment, and cervical fibro cartilaginous bands; acquired causes include trauma and scalene muscle hypertrophy from repeated upper extremity activities.

Since the subclavian vein passes through costoclavicular space at the anterior part of the first rib and clavicular junction, it is more susceptible to external compression from repetitive movements of the arm and shoulder due to overhead activities and exercises. Intima is more vulnerable to repetitive microtrauma leading to proliferation, fibrosis, and hyperplasia of the vein wall, which subsequently triggers a coagulation cascade resulting in thrombosis.⁷ Pathogenetic

factors for effort thrombosis are costoclavicular narrowing from bony/muscular abnormalities and endothelial microtrauma from repetitive arm activities.

Paget-Schroetter syndrome presents with sudden onset of severe arm swelling, heaviness, and pain. Other symptoms include discoloration, paresthesias, and weakness in the arms. In severe cases with superior vena cava syndrome, collaterals can be seen on the arms and chest. The test of choice to diagnose upper extremity thrombosis is compression ultrasonography with a sensitivity and specificity of 97% and 96%, respectively.⁸ Computed tomography (CT) venography and magnetic resonance (MR) venography is more sensitive (100%) than compression ultrasonography. Given that compression ultrasonography is widely available, cost-effective, and less invasive, it is more commonly used than CT and MR venography. If compression ultrasonography is inconclusive or equivocal, CT or MR venography can be used for high clinical suspicion cases.

Complications from venous thrombosis include pulmonary embolism, post-thrombotic syndrome, and recurrence of thrombosis. Nevertheless, these complications are less common in upper extremity DVT compared with lower extremity thrombosis. The incidence of pulmonary embolism (PE) in upper extremity thrombosis is 5.6%. On the other hand, the rate of PE from lower extremity DVT is 25%.⁹ PEs are 4 to 5 times more likely to originate from lower extremity DVT than upper extremity DVT. The mortality rate from PE that arises from upper extremity DVT is 0.7%. Post-thrombotic syndrome is a chronic debilitating and disabling complication of DVT of extremities, reducing the quality of life, especially when the dominant limb is involved. It mainly presents with chronic pain, swelling, varicose veins, and, in severe cases, with ulcers. It is less common in the upper extremity compared with the lower extremity. The risk of developing post-thrombotic syndrome (primary and secondary together) and recurrent thromboembolism in upper extremity DVT is 19.4% and 7.5%, respectively.¹⁰

In the early 1970s, treatment involved arm elevation, rest, and anticoagulation. Ten years later, thrombolysis was included in the treatment plan since there was an increased recurrence of thrombosis with anticoagulation alone. Thrombolysis relieves symptoms by decreasing the clot burden. As effort thrombosis involves external compression of the axillary subclavian vein from bony abnormality at thoracic outlet, underlying mechanical obstruction needs to be relieved with surgical intervention. Prevention of long-term morbidity with recurrence of thrombosis, symptom relief, and overall outcomes are better achieved with first rib resection after thrombolysis.^{11,12} If no first rib resection is done at the first event, 40% of patients will require resection eventually secondary to recurrent thrombosis and persistent symptoms. Functional outcomes, including an early return to the

activities and work, are better with thrombolysis with early surgical intervention groups.¹³ Complications associated with early surgery after thrombolysis include increased risk of bleeding and hemothorax. In Paget-Schroetter syndrome, the duration of symptoms plays a crucial role in the treatment. Thrombolysis is more likely to be successful in patients whose symptoms started in less than 14 days.¹⁴ Guidelines currently practicing are based on the small case series, single institutional case studies, and vascular surgery expert opinions with promising results.¹⁵ No randomized controlled trials are available to assess surgical and catheter-directed thrombolysis' efficacy and safety, and further prospective large multicenter studies are needed. There is no statistically significant difference in the symptom resolution in the groups with first rib resection in less or more than 6 weeks.¹⁶ CHEST Guideline and expert panel report recommend 3 months of anticoagulation therapy for upper extremity DVT involving axillary and more proximal veins irrespective of thrombolytic therapy.¹⁷ Still, there are no specific guidelines on the duration of anticoagulation for Paget-Schroetter syndrome. More studies are required on the duration of anticoagulation in these patients.

Conclusion

Internist, primary care physicians, and emergency room physicians can easily miss Paget-Schroetter syndrome. Increased awareness about the disease and timely referral to vascular surgeons is of paramount importance among physicians to prevent complications and worst outcomes with a delay of care. Prompt diagnosis and early initiation of treatment are imperative for better results. Since the management of effort thrombosis differs from the regular DVT, physicians need to be familiar with treatment options, including thrombolysis and surgical intervention. A multidisciplinary team approach with an internist, vascular surgeon, and hematologist is required to manage the Paget-Schroetter syndrome as it includes both medical and surgical options. Randomized controlled studies are needed to evaluate the efficacy of thrombolysis and surgical options.

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Author Contributions

VS conducted the chart review. VS, MP, MB, VG, and VMK contributed to writing the introduction, discussion, and conclusion. VS drafted the manuscript. All authors contributed substantially to its revision.

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Ethical Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal consent was obtained

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