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# Pulmonary Infarction due to Paget-Schroetter Syndrome and Nephrotic Syndrome

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
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**Conflict of interest:** None declared

**Patient:** Male, 23  
**Final Diagnosis:** Minimal change disease  
**Symptoms:** Right arm and neck swelling  
**Medication:** —  
**Clinical Procedure:** Catheter-directed thrombolysis  
**Specialty:** Cardiology





**Objective:** Rare co-existence of disease or pathology  
**Background:** Risk factors for venous thromboembolism can include a combination of genetic, anatomic, and physiologic factors, some of which are modifiable. Patients presenting to the hospital with venous thromboembolism may have multiple risk factors that require testing beyond the initial admission labs and hypercoagulability screening panel.

**Case Report:** We describe a right-handed patient who lifts weights for exercise, who presented with pulmonary infarcts and clot in the right superior vena cava/subclavian vein. These were due to a combination of 1) an acquired hypercoagulability from minimal change disease and 2) dynamic anatomic narrowing of the subclavian vein, which is known as Paget-Schroetter syndrome. Despite normal serum levels of antithrombin, protein C and S, his serum albumin was low, which prompted workup for proteinuria. Testing revealed nephrotic range proteinuria as well as dynamic occlusion of the right subclavian vein on magnetic resonance venography only when the patient lifted and externally rotated his arms.

**Conclusions:** This case report highlights the need for a thorough history and physical examination, as well as additional testing in some patients beyond the initial admission laboratory tests and screening panel for hypercoagulability. Tests could include diagnostic imaging testing with provoking maneuvers, which can help elucidate dynamic physiology. Such testing, when appropriate, can help to inform the treatment plan and prevent recurrent thromboses.

**MeSH Keywords:** Nephrotic Syndrome • Pulmonary Embolism • Thrombophilia • Upper Extremity Deep Vein Thrombosis

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/919141>

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## Background

The Centers for Disease Control and Prevention estimate that there are over 500 000 hospitalizations in the United States for venous thromboembolism per year [1]. The risk factors for venous thromboembolism are well studied [2]. They include factors that are genetic, physiologic, and anatomic [3]. Given how common an admission is for venous thromboembolism, many hospitals have implemented a standardized panel to test the blood for suspected hypercoagulability. These panels can be abnormal in up to 50% of those tested [4]. However, not all risk factors can be identified through laboratory testing. A thorough history and physical examination is needed to determine if additional laboratory and radiographic testing is needed beyond the typical admission labs and hypercoagulability screening panel.

We present a case of a young, active, right-handed patient with a large obstructing clot in the superior vena cava and right subclavian vein, as well as pulmonary infarcts. Workup revealed that he had a combination of 2 rare predisposing factors for venous thromboembolism, including nephrotic range proteinuria due to minimal change disease and dynamic anatomic occlusion of the subclavian vein due to Paget-Schroetter syndrome [5]. This syndrome develops most commonly in patients who do repetitive overhead movements for exercise or their job. In this particular case, multiple tests beyond typical admission laboratory tests and the screening panel for hypercoagulability were required to make the diagnoses, including a urine protein level and magnetic resonance venography with dynamic provoking maneuvers.

This case highlights the need for practicing physicians to 1) formulate a broad differential diagnosis for venous thromboembolism after taking a thorough history and 2) consider obtaining additional tests, including tests with dynamic provoking maneuvers, in order to elicit dynamic pathology that would otherwise remain elusive.

## Case Report

The patient was a 23-year-old male who presented with several days of right arm and neck swelling, scapular discomfort that was worse with inspiration and new onset exertional dyspnea. He denied recent immobilization, air travel, smoking or a personal or family history of vascular thrombosis. He lifted weights regularly for exercise but did not do repeated overhead lifting for his job. He is right-handed. Physical examination was notable for generalized swelling of the right arm and neck but the superficial veins in the area were not noted to be engorged. Computed tomographic angiography showed a filling defect in the superior vena cava with right arm/chest wall

edema, suggestive of upstream thrombosis (Figure 1A) as well as multiple pulmonary emboli with infarcts (Figure 1B). Upper extremity ultrasound confirmed occlusive right axillosubclavian thrombosis. Ultrasound did not reveal thrombosis in the veins of the lower extremities. Transthoracic echocardiogram showed no right heart strain. He was treated with a standard dose intravenous heparin drip.

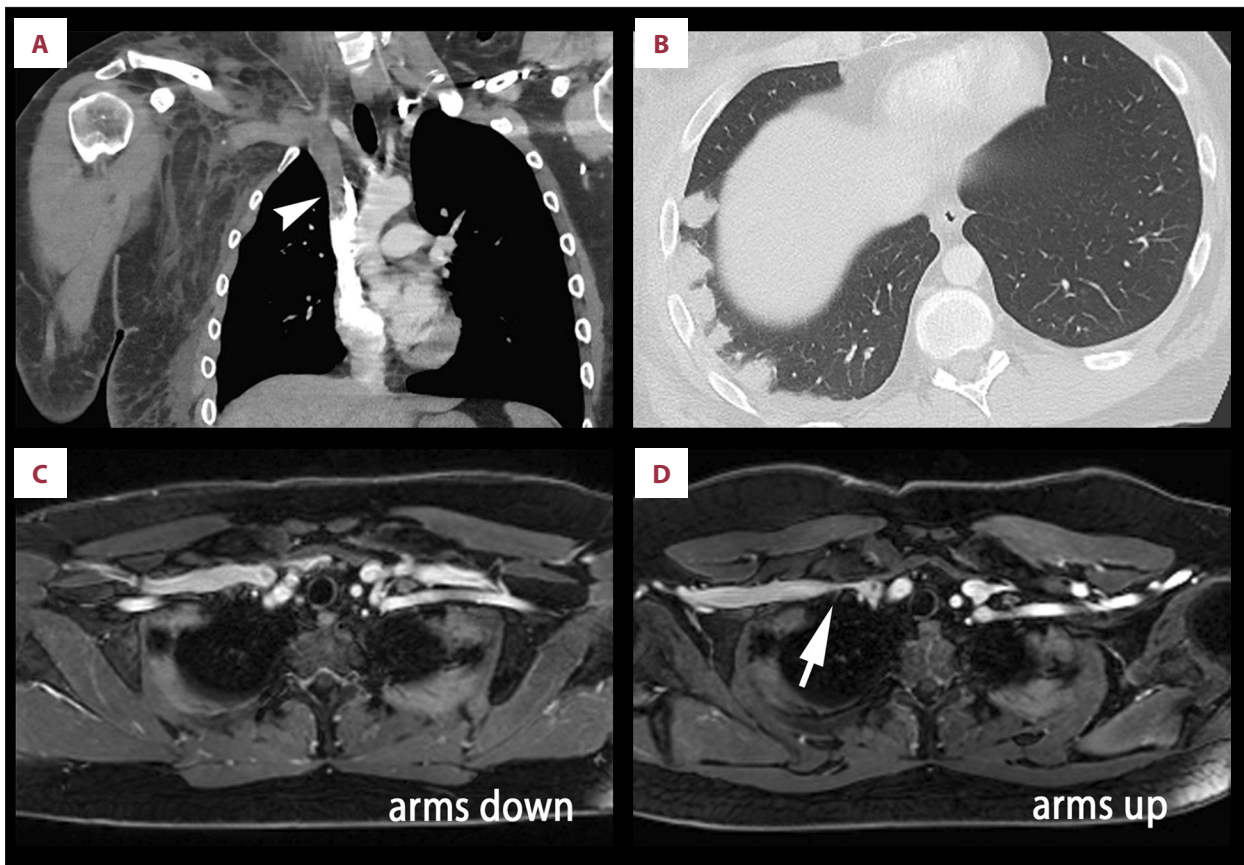
The hypercoagulability panel revealed normal levels of anti-thrombin, protein C, protein S as well as cardiolipin and beta2-glycoprotein I antibodies. He did not carry the Factor V Leiden or prothrombin G20210A mutations. Testing for lupus anticoagulant was negative. Other laboratory workup was notable for normal renal function. However, he was found to have a low serum albumin level of 1.7 g/dL (reference 3.3–5 g/dL). Given the low serum albumin, urine protein level was checked, and he was found to have nephrotic range proteinuria (urine total protein 1121 mg/dL, reference 0–13.5 mg/dL).

The patient underwent catheter-directed thrombolysis, thrombectomy, and angioplasty of the right subclavian and axillary veins. Given the location of the clot, venous thoracic outlet syndrome was suspected. Magnetic resonance venography showed stenosis of the right subclavian vein between the clavicle anteriorly and the anterior scalene posteriorly only with abduction and external rotation of the patient's arms (Figure 1C, 1D). Stenosis was not seen in the left subclavian vein with the same arm movement. This finding was consistent with unilateral thoracic outlet syndrome, which is also known as Paget-Schroetter syndrome in the presence of upper extremity clot [5].

He was transitioned from the intravenous heparin drip to rivaroxaban (15 mg twice daily for the first 3 weeks then 10 mg daily). Anticoagulation was planned for at least 6 months. At the time of discharge, the most likely renal diagnosis was primary minimal change disease given his age. He was started on glucocorticoid therapy (1 mg/kg daily) and lisinopril (40 mg daily). Renal biopsy was deferred given his need for anticoagulation. Three months later, he underwent right supraclavicular first rib resection, brachial plexus neuroplasty, subclavian venolysis, and scalenectomy. He recovered well from the surgery. As an outpatient, his renal disease was found to be resistant to glucocorticoids so was tapered to prednisone 5 mg daily and started on monthly injections of rituximab 1000 mg.

## Discussion

This is an unusual case of a young adult who developed life-threatening venous thromboembolism due to a combination of rare anatomic and physiologic risk factors. This patient had 2 conditions, including 1) acquired hypercoagulability from nephrotic syndrome and 2) dynamic anatomic occlusion of the



**Figure 1.** (A) Venous thromboses in the superior vena cava and right brachiocephalic/subclavian veins with associated arm/chest edema. Coronal reformatted computed tomographic angiography of the chest shows filling defect in the superior vena cava (arrowhead), right brachiocephalic and subclavian veins with associated right arm/chest edema, suggestive of upstream thrombosis. (B) Pulmonary infarcts in a patient with Paget-Schroetter syndrome and nephrotic syndrome. Axial computed tomography of the chest shows multiple pulmonary infarcts in the peripheral right lower lobe. (C, D) Dynamic compression of right subclavian vein with patient's arms raised. Following endovascular treatment of venous thrombosis, magnetic resonance venography of the chest (T1-weighted fat saturated post-contrast images) with the arms down (C) and arms up (D) shows dynamic severe compression of the right subclavian vein between the clavicle anteriorly and the anterior scalene muscle posteriorly at its insertion near the first rib (arrow).

right subclavian vein, which is called Paget-Schroetter syndrome in the presence of upper extremity clot. This case highlights an important lesson for practicing physicians. In patients with venous thromboembolism, additional testing may be needed beyond the initial admission labs and screening hypercoagulability panel. Despite a normal hypercoagulability panel, this patient's low serum albumin level prompted providers to check for proteinuria. Furthermore, the location of the right subclavian vein thrombosis prompted providers to check for dynamic occlusion of the subclavian vein via magnetic resonance venography.

Approximately 7% of patients with nephrotic syndrome have a venous thromboembolism event, although the risk of venous thromboembolism varies depending on the underlying pathology [6,7]. The risk is highest at the time of diagnosis of nephrotic syndrome and increases as the serum albumin

decreases. If the serum albumin is  $<2.5$  g/dL [8], patients with nephrotic syndrome have ~4% absolute risk of a venous thromboembolic event. This patient's serum albumin was in fact below this threshold. However, patients with nephrotic syndrome are particularly prone to deep vein thromboses in the legs and renal veins [9,10], not upper extremities.

Studies of the mechanism underlying the hypercoagulable state in patients with nephrotic syndrome point toward changes in the levels of antithrombin, protein C, protein S secondary to loss in the urine. Interestingly, these levels can be normal, as they were in this patient, despite being functionally hypercoagulable [11].

Quantifying the urine protein is not part of the standard laboratory workup for an unprovoked venous thromboembolism [11,12]. In this particular case, it was the low serum

albumin that prompted providers to check for proteinuria. Additionally, not all patients with nephrotic syndrome have abnormal serum creatinine at the time of diagnosis, such as was true in this case. The other signs or symptoms that should prompt an evaluation of the urine include new or unexplained hypertension, hypercholesterolemia, and edema. Performing a thorough review of systems and physical examination would hopefully prevent clinicians from missing these signs.

Renal biopsy is typically recommended in adults with new onset nephrotic syndrome. Unfortunately, biopsy was not possible for this patient, given his risk of recurrent clot if taken off anticoagulation. In terms of his response to therapy, we are hopeful that he will have a favorable response to rituximab despite not being steroid responsive. Adults have ~80% chance of remission at 7 months with immunosuppressive therapy [13].

The name Paget-Schroetter syndrome refers to the specific clinical situation in which a patient with venous thoracic outlet syndrome develops an upper extremity clot. The pathogenesis of venous thoracic outlet syndrome is thought to relate to repetitive overhead movements causing trauma and inflammation to the thoracic bundle [5]. Because not everyone who routinely does overhead lifting develops this syndrome, people with certain anatomy of the shoulder are thought to be predisposed to this syndrome. While this patient did do some overhead weightlifting for exercise, he did not do daily overhead lifting for his job, for instance. He was right-handed, however, so likely favored his right arm to perform single arm tasks.

Timely surgical decompression is recommended for patients with Paget-Schroetter syndrome [14]. However, the type of surgical intervention often depends on the exact anatomic abnormality. The procedure can involve first rib resection, cervical rib resection, division of anomalous bands or musculotendinous insertion, and scalenectomy. This patient underwent successful surgical decompression within 3 months of diagnosis.

This case highlights the important lesson that 3-dimensional, dynamic vascular imaging can be helpful to diagnose a vascular occlusion that occurs only with certain arm positioning. This patient's right subclavian vein stenosis was not appreciated on computed tomography. The axial image from magnetic

resonance venography was required for the diagnosis, specifically when the patient lifted and externally rotated his arms. Although Paget-Schroetter syndrome is rare (1–2/100 000 people per year) [5], this key concept about provoking maneuvers could be applied in other contexts as a universal lesson in clinical diagnosis.

After careful review of the literature, we have not found an association between proteinuria and Paget-Schroetter syndrome. Thus, we believe that this patient had 2 unrelated, uncommon conditions. In terms of timing, the onset of minimal change disease likely prompted the clot to form at the location that was anatomically vulnerable to venous stasis due to repetitive movement of the right arm during exercise and daily living. In this particular case, advanced laboratory and imaging tests were necessary to fully appreciate his risk factors for venous thromboembolism, treat him appropriately and arrange for proper follow-up.

## Conclusions

This case highlights 2 important lessons for practicing physicians. First, clinicians should formulate a broad differential diagnosis for venous thromboembolism and consider combinations of rare genetic, anatomic, and physiologic risk factors. Second, additional diagnostic testing beyond the initial admission labs and screening panel for hypercoagulability should be considered in patients with venous thromboembolism when there is enough clinical suspicion. This may include laboratory tests to check for proteinuria as well as imaging tests with dynamic provoking maneuvers.

## Department and Institution where work was done

Massachusetts General Hospital in Boston, MA, USA as a collaboration between the Division of Pulmonary/Critical Care and the Department of Radiology.

## Conflicts of interest

None.

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