



Case report

Uncommon series of subclavian vein thrombosis in Emergency Department

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ABSTRACT

Introduction: Deep vein thrombosis (DVT) is one of the two possible clinical manifestations of venous thromboembolism (VTE), and the other one is the pulmonary embolism. The most common reasons behind the upper limb DVT can be central venous catheterization, compression of subclavian vein or anatomical abnormalities.

Aim: The aim of this study is to stress the importance of accurate diagnosis of the relatively rare subclavian vein thrombosis (SCVT). Due to low specificity of the clinical signs and symptoms, a careful risk assessment of VTE is extremely helpful in successfully reaching a diagnosis.

Case study: Authors are presenting a series of 4 cases of diagnosis and initial treatment in Emergency Department (ED) of the patients presenting with common symptoms of upper limb with uncommon SCVT. All patients presented to ED, of which 3 were seen in ED of our hospital and 1 patient, who is co-author of the publication, had the same diagnosis in other ED allocated in another city.

Results and discussion: Among the 4 patients only 1 has reached high risk in Caprini's score and moderate in Wells score. In Padua scale patient did not reach high risk. In other patients risks in each score were low.

Conclusions: In most cases, the Wells, Padua, Caprini scores can be used to evaluate the risk of VTE; this diagnostic tool cannot be efficiently utilized in patients with local anatomical anomalies, which can lead to problems with diagnostics and treatment of such patients.

1. INTRODUCTION

Subclavian vein thrombosis (SCVT) is a type of deep vein thrombosis (DVT), which is the second manifestation of venous thromboembolism (VTE) after pulmonary embolism. It is a relatively rare condition, observed in up to 10% of all DVT cases.¹⁻³ Primary upper extremity DVT, seen in 10%–20% cases, is known as the Paget–Schroetter syndrome. The remaining cases are secondary, most frequently following central vein catheterization and/or implantation of endovascular electrodes.³⁻⁷ Other causative factors include malignant tumors, hereditary thrombophilias and genetic factors, hemoglobinopathies, oral contraceptives, hormonal therapy, surgery, obesity and long-term immobilization.^{1-4,6,7} The condition remains a diagnostic challenge due to its non-specific clinical presentation (pain, edema, erythema, cyanosis) or asymptomatic course.^{2,6} The possible complications of upper extremity DVT include pulmonary embolism, post thrombotic syndrome and death.^{1-3,7} Their incidence, however, is lower than in lower extremity DVT.^{3,4,8} Most of these complications can well be avoided by a timely diagnosis and initiation of treatment. The non-specific and mild symptoms call for a careful assessment of risk factors. An accurate diagnosis can be reached based on clinical symptoms, risk assessment and laboratory/imaging results.⁶

2. AIM

The aim of this study is to stress the importance of accurate diagnosis of the relatively rare SCVT. Due to low specificity of the clinical signs and symptoms, a careful risk assessment of VTE is extremely helpful in successfully reaching a diagnosis. In most patients the risk of VTE can be accurately assessed with the help of Caprini, Wells, Padua prediction score. Based on a retrospective analysis of 4 cases we will show that the predictive value of these scoring systems is limited.

3. CASE STUDY

3.1. Patient 1

A 63-year-old woman reported to the Emergency Department (ED) complaining of left upper extremity edema persisting for 4 days. She also reported increased abdominal circumference and lower extremity edema in the preceding month, that seemed to get reduced by initiating torasemide. Past medical history revealed treatment with bisoprolol, ramipril, atorvastatin due to hypertension and hypercholesterolemia.

On admission, the patient's overall condition was good. The abnormal findings upon physical examination were swollen superficial veins of left side of the chest and palpable supraclavicular lymph nodes on the same side; left forearm and arm were swollen and erythema, with palpable pulse on radial artery.

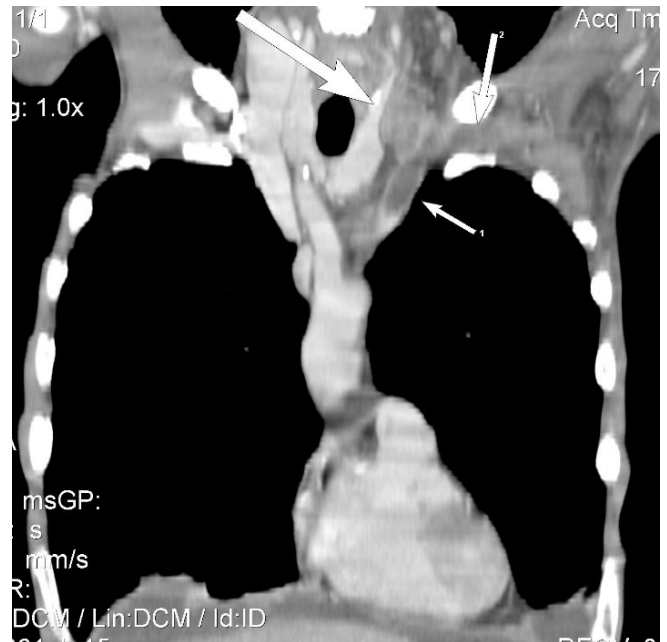


Figure 1. Patient 1: (1,2) Thrombus visible in the subclavian vein; (3) Thrombus visible in the carotid vein.

Based on clinical suspicion of SCVT or Pancoast's tumor on the left side, chest computer tomography (CT) was performed. A CT-angiography of the chest (Figure 1), with a contrast enhanced in arterial and venous phase, revealed thrombus in brachiocephalic vein, on the level of sternoclavicular joint on the left side, extending to jugular and subclavian vein, with presence of partial flow in both veins. CT also showed bullae in apex of lungs bilaterally and multiple enlarged mediastinal and jugular lymph nodes. A large quantity of free fluid in the peritoneal cavity was observed in abdomen, homogenous tumors in liver, spleen, and the tail of pancreas. Abdominal ultrasonography (USG) showed, masses in mesentery, greater omentum, multiple enlarged lymph nodes and solid tumor in hypogastrium (140 × 100 mm).

Abnormal laboratory findings included low activated partial thromboplastin time (APTT) of 23.6 s (reference range: 24–37 s) and a significant elevated serum D-dimer of 10.8 $\mu\text{g}/\text{mL}$ (reference <0.5 $\mu\text{g}/\text{mL}$) was observed.

The patient was admitted to the Gynecological Ward for further diagnosis and treatment of small pelvis tumor. Treatment with small molecule heparin at a dose of 1 × 100 mg sub cutaneous (s.c.) was initiated.

Based on histopathological examination diagnosis of metastatic ovarian cancer was made. No further documentation on follow-up.

3.2. Patient 2

A 65-year-old male reported to the ED complaining of pain in the left upper extremity and coexisting edema, that appeared on the day of notification. Past medical history of patient included myocardial infarction (5 and 17 years before the episode), disseminated prostate cancer (diagnosed 14 months before the episode), ventricular tachycardia with

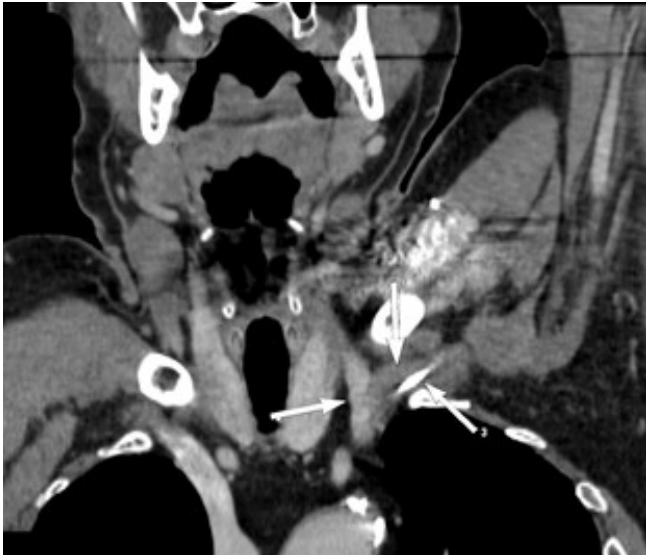


Figure 2. Patient 2: (1) Thrombus visible in the subclavian vein; (2) Patent brachiocephalic vein; (3) Catheter in the subclavian vein.

cardioverter defibrillator implantation (ICD) (1 year before the episode), coronary angioplasty with releasing stent implantation (4 years before the episode). Patient has been on coagulation treatment since ICD implantation, starting with clopidogrel at dose 75 mg per day and later dabigatran 300 mg per day.

On admission the patient's overall condition was good. The abnormal findings upon physical examination were edema and swelling of superficial veins of upper left extremity with active hyperaemia with no abnormal findings in pulse, sensation, warmth, and capillary refill.

Abnormal laboratory findings included elevated serum D-dimer of 1500 $\mu\text{g/L}$ (reference 500 $\mu\text{g/L}$).

The clinical picture corresponded to venous thrombosis of the upper limb and therefore CT-angiography of the chest was performed, which revealed occlusion of the left subclavian, axillary, basilic and cephalic vein (Figure 2). Only fragments of the brachial vein showed contrast enhancement. The patient was diagnosed with the thrombosis of venous angle, left subclavian, axillary, cephalic and basilic veins. The patient was qualified for conservative treatment, low molecular weight heparin (LMWH) at therapeutic dose with I and II-degree compression therapy was initiated in ED.

Patient was discharged from ED the next day in good condition, with the following recommendations: LMWH at a dose of 1 mg/kg s.c. for 14 days, later to be changed to oral anticoagulant by General Practitioner (GP). Patient was advised to follow up in the vascular and cardiology outpatient clinics. Follow up angio-CT was performed which revealed collateral vasculature in left axillary and infraclavicular fossa and thrombi in course of left subclavian vein. The follow-up USG of the effected extremity performed 1 month after episode revealed patency of all previously obstructed veins was confirmed.

3.3. Patient 3

An 82-year-old male reported to the ED complaining of persisting edema and erythema of the left upper extremity, with no pain, lasting for 4 days. In past medical history, implantation of ICD with unknown year of the procedure was noted. Patient was treated with: piracetam, nebivolol, torasemide,

On admission the patient's overall condition was good. Abnormalities upon physical examination included: distended veins within the left upper extremity and chest wall; erythema and edema of the left arm, with palpable pulse on radial artery. Abnormal laboratory findings revealed elevated serum D-dimer of 1.9 $\mu\text{g/mL}$ (reference <0.5 $\mu\text{g/mL}$). Plain chest x-ray showed the tip of the endovascular electrode within the right ventricle.

An ultrasound of the venous system of the left upper extremity revealed parietal thrombi, up to 6 mm in thickness, within the axillary vein, as well as a thrombotic occlusion of the distal subclavian vein, with well-developed collateral vasculature. The patient was seen by a consultant surgeon, who recommended conservative treatment with subcutaneous injections of LMWH – 150 mg once a day for 30 days. The patient was referred to the surgical and hypertension outpatient clinic for follow-up. Several episodes of ventricular fibrillation were noticed that led to ICD treatment, no history of heart failure and venous thrombosis were notified.

3.4. Patient 4

A 17-year-old girl (medical student) without any past medical history, no smoking, no oral contraception, was reported to the ED of a different hospital complaining of pain, edema, cyanosis and hypothermia to left upper extremity, lasting for few hours. Three days before onset of symptoms, the patient had been carrying a backpack, while being on a cycling trip lasting for a few hours.

The patient's overall condition was good, without significant abnormalities in the physical examination, except for the presence of swollen superficial veins of the left side of the chest with bruising, cooling and swelling of the left extremity. Based on presented history, complaints and clinical setup, upper extremity thrombosis was suspected.

The only abnormality present in laboratory tests was slight elevated serum D-dimer of 655 $\mu\text{g/L}$ (reference <500 $\mu\text{g/L}$). An USG revealed signs of thrombosis confined to left subclavian vein only.

The patient was admitted to the Vascular Surgery Ward where the treatment was induced: LMWH therapeutic dose was initiated for the first 2 days, followed by oral rivaroxaban 30 mg per day for 3 weeks, then 20 mg per day. The patient was discharged with the following recommendations: to elevate the arm, use compression therapy, control in the Vascular Surgery Outpatient Clinic, and avoiding vigorous physical activity involving the affected extremity. After 3 months of follow-up, with normal D-dimer levels, patient didn't reveal any clinical symptoms, the consulting physician decided to discontinue the medication. However, 11 days after discontinuation of rivaroxaban, symptoms (pain, edema, cyanosis) to the left upper extremity appeared again. Rivaroxaban was reintroduced at 20 mg per day.



Figure 3. Patient 4: MR angiogram 3D reconstruction, visible thrombosis of the left subclavian vein.

Six months after, A follow-up ultrasound revealed a 50% obstruction of the medial part of the left subclavian vein, along with the thickening of its walls.

Due to all above, the differential diagnosis was further taken out in hematology institute. The search for the causative factor was then broadened to include protein C and S, antithrombin, factor VIII, anti-cardiolipin and anti-beta-2-glycoprotein I antibodies, Factor V Leiden mutation and G20210A prothrombin gene were also examined. All the results were within normal range, which excluded congenital thrombophilia and antiphospholipid syndrome.

CT revealed patency of both subclavian and axial veins with weak enhancement within the vessels on the left side. A phlebography revealed a tight permanent short stricture within the left subclavian vein at the clavicle level, with prominent collateral circulation. An attempt at percutaneous angioplasty (via the right femoral vein) was unsuccessful. All the above findings revealed probability of a thoracic outlet syndrome.

Magnetic resonance (MR) angiography (Figure 3) revealed presence of a left subclavian vein stenosis located laterally from the junction with the (patent) external jugular vein between the clavicle and the insertion of the anterior scalene muscle on the first rib. The compression was exacerbated by an upward curving of the first rib at the insertion of the costoclavicular ligament. The MR also revealed the presence of parietal material (most likely an organized thrombi of 2 mm thickness) within the subclavian trunk proximal to the stenosis site and within its small tributaries. The patient was placed on oral rivaroxaban 20 mg daily.

4. RESULTS

In Patient 1 the presence of a disseminated malignant process was undoubtedly a risk factor of DVT, and in patient 2, not only the disseminated malignant process, but also the invasive cardiological procedure and implementation of

ICD were the high-risk factors for DVT. In Patient 3, invasive cardiological procedure and central venous cannulation for ICD placement could be considered as high risk for DVT. Apart from all 3 patients, the patient 4 had no risk factors of DVT at all. The only correlation factor that could lead to DVT would be the pressure implied by a simple backpack while cycling.

Considering the lack of a well-established risk assessment model for DVT in the upper extremity, the authors have attempted to evaluate retrospectively the above cases using the Caprini's risk model, the Padua risk score, and the Wells DVT risk assessment score (with respect to the upper extremity) (Table 1).

Caprini score is intended to assess the risk of vein thrombosis in surgical patients and is based on more than 20 variables, such as age, type of surgery, past medical history including obesity, cancer, history of thrombosis and other risk factors. On the other hand, Padua prediction score for risk of VTE is used to determine need of anticoagulation in hospitalized patients and is based on 11 risk factors in past medical history. Wells DVT risk assessment score is created to assess the probability of DVT in lower extremity based on current symptoms and risk factors such as active cancer and bedridden.

Patient 1 received 5 points in Caprini's score (high risk), 3 points in the Padua score (high risk starts at 4 points), and 2 points in the Wells score (medium risk). Patient 2 received medium risk in Caprini's score, just because of a disseminated malignant process in the past. The patient could have received a score in other scales only if the malignant process would have been diagnosed or treated in last 6 months from the presenting complaints of DVT. Patients 3 and 4 did not receive points in any of the scoring systems.

It is worth to mention, that none of above scales is a dedicated scale for risk assessment of DVT in upper extremity. The Wells' score is applicable to lower extremities only, the Padua and Caprini's scores do not consider the well-established DVT risk factors as vascular catheters or implantable cardiological devices. Caprini's score considers central venous catheters only at the moment of assessment, but not in the past medical history. Adopting a new risk assessment model or modifying those currently in use might facilitate diagnosing upper extremity DVT. It must, however, be emphasized that this condition may occur even if no risk factors at all are present (as in patient 4).

Table 1. Caprini's, Padua and Wells DVT risk assessment scores.

	Caprini's score, points	Padua score, points	Wells DVT risk assessment score, points	Interpretation
Patient 1	5	3	2	High risk in Caprini's score
Patient 2	3	0	0	Medium risk in Caprini's score
Patient 3	0	0	0	Low risk
Patient 4	0	0	0	Low risk

5. DISCUSSION

Evaluation and correct diagnosis of DVT in upper extremities can be a huge challenge for ED, because of its non-specific symptoms and relatively rare occurrence. There is no good scale for risk assessment for upper extremity deep venous thrombosis (UEDVT). Padua, Wells or Caprini scores are not specific enough for this group of patients. In the diagnostic process, the helpful areas should be the patients' medical history, clinical evaluation and the symptoms suggesting the DVT. Edema, pain, venous collaterals, erythema or other symptoms like cyanosis and hypothermia should highlight the bulb of DVT, especially in patients with risk factors, such as malignancy, ICD implementation.^{7,8} DVT can also be spotted in young patients doing sports or other activities associated with upper extremity movement.^{5,9,10} D-dimer is a marker of thrombosis, and it can be a useful tool for the initial diagnosis. Nonetheless, due to its low specificity, it cannot be the suitable method for certain group of patients, e.g., patients with ICD, malignancy, during pregnancy or with thrombosis in other localizations that might have elevated D-dimer level.^{2,11–17} However, as its negative predictive value is high, it can be used to rule out thrombosis.⁶ Imaging methods should be crucial for the final diagnosis.^{2,5,6} Plebography is considered as the gold standard, but other imaging methods are widely used as a replacement.^{11,14} Although there are limitations connected to possible difficulties with visualizing some fragments of veins beneath the bones,^{2,11} USG is preferable diagnostic tool because of its accessibility, no radiation no need of using contrast.⁷ MR can be used as another diagnostic tool, but its sensitivity and specificity is lower in comparison with USG.¹¹ A relatively new method is intravenous ultrasonography, which is more sensitive than venography, but not widely used.¹⁸ In the diagnostic process imaging method should be chosen based on accessibility and patient overall condition.

The treatment of SCVT doesn't differ from the treatment of DVT. The basis of conservative treatment is anticoagulation with LMWH which can be combined with vitamin K antagonists.³ The treatment with new group of anticoagulants, monitoring of treatment effectiveness with the help of INR (international normalized ratio) or APTT, can be safe and effective in this group of patients. Anticoagulant therapy should be continued for at least 3 months.¹⁴ Treatment protects the patient from developing pulmonary embolism which is potentially a fatal complication.^{2,3,19} According to Thompson,⁹ one of goals of the treatment is to reduce the risk of the recurrence. Additional procedures can be necessary in some cases, for example, surgical treatment in thoracic outlet syndrome or catheter removal (if needed).^{5,9,14} DVT of upper extremity is more common in pediatric population than in adults, but in our group of patients DVT was predominantly connected to other clinical states (e.g., venous catheters, malignancy, genetic mutations).^{3,4,20,21} Primary UEDVT is more common in population of older children and in young adults, especially physically active.^{5,9,22} This specific group of patients, if presenting

above mentioned symptoms, should be suspected for DVT in upper extremity because suspected risk factor in above case is microtrauma during repetitive movements leading to persistent local inflammation and fibrosis in surrounding tissues that causes the activation of coagulation pathways.^{5,9,14,22} For this reason, in younger patients with a negative history of other risk factors, questions pertaining to sports and physical activity should be included in standard patient history. It may also be caused by anatomical abnormalities (cervical ribs) or postural defects, as suspected in patient 4.^{6,14} In the case of anatomical variants the course of action should often include a surgical intervention to correct the underlying defect.²³

6. CONCLUSIONS

- (1) SCVT, considered to be a diagnostic challenge in EDs, requires high awareness and development of the diagnostic standard. Our work reveals that above mentioned scores are not the efficient diagnostic tool to evaluate the risk of UEDVT. There is a need to adapt a new risk assessment tool or modify those currently in use, that might facilitate diagnosing upper extremity DVT, and in consequence avoid underdiagnosis and lack of prophylaxis
- (2) Risk factors for UEDVT in young patients are anatomical abnormalities and intense effort, while in older patients more common to cause this condition are underlying disease or medical intervention. However, if no other possible mechanism is present, it may be necessary to extend diagnostic measures in search of cancer.
- (3) Apart from easily accessible USG, one more diagnostic imaging technic, most available in each medical center, should be considered to obtain good quality imaging, regardless the location of the thrombosis.

Conflict of interest

None declared.

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