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Unilateral subclavian vein and brachiocephalic vein occlusion presenting as unilateral facial and arm swelling: a case report and review of the literature

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Abstract

Asymmetric left face edema due to left subclavian vein thrombosis and its management is presented in this case report. 30 years-old woman with left arm and face edema had thrombosis from the middle part of left subcavian untill superor vena cava and brachiocephalic vein. Low molecular weight heparin and oral anticoagulant therapy were shown to provide clinical improvement, although it did not provide improvement in the anatomy. The literature is reviewed.

Key words: vein thrombosis, edema,subclavian vein thrombosis

Introduction

Upper-extremity deep vein thrombosis (UEDVT) is an increasingly important clinical entity with potential for considerable morbidity. Pulmonary embolism (PE) is present in up to one third of patients with UEDVT. Other complications, such as persistent upper-extremity pain and swelling, the superior vena cava (SVC) syndrome, and loss of vascular access, can be disabling and devastating. UEDVT has become more common over the past several decades.

This is directly related to the increasing use of central venous catheters. UEDVT has been reported in up to one fourth of patients with these catheters. For these reasons, it is imperative that physicians understand UEDVT risk factors, diagnostic options, treatment alternatives, and prophylaxis regimens. UEDVT most commonly refers to thrombosis of the axillary and/or subclavian veins. UEDVT is classified as primary or secondary on the basis of pathogenesis.

First described in the late 1800s, spontaneous primary thrombosis of the upper extremity, or Paget-Schroetter syndrome, accounts for approximately 20% of UEDVT. Primary UEDVT includes both idiopathic and "effort-related" thrombosis. Effort-related thrombosis usually develops among young people after strenuous or repetitive exercise. Secondary UEDVT characterizes thrombosis in which an endogenous or exogenous risk factor is present.

Endogenous risk factors include coagulation abnormalities, such as antithrombin, protein C and protein S deficiencies; factor V Leiden gene mutation; hyperhomocysteinemia; and antiphospholipid antibody syndrome. Exogenous risk factors include CVC pacemakers, intracardiac defibrillators, malignancy, previous or concurrent LEDVT, oral contraceptives, trauma, and IV drug use (especially cocaine).Catheter-related thrombosis is caused by vessel wall damage during catheter insertion or during infusion. Blood flow is most rapid in the SVC, which may sufficiently dilute the infusate and reduce the risk of thrombophlebitis. Therefore, catheter tips should be positioned in the lower third of this vessel or at the junction of the superior vena cava and right atrium [1]. We presented here a case with subclavian and brachiocephalic thrombosis and its management and showed the improvement in face and arm edema and reviwed the literature.

Case presentatıon

A 30- year-old woman presented with one and a half year history of left arm, left face edema and pain . Her complaints started since the operation of her for mature cystic teratoma in anterior mediastinum half years ago in another center. Venous doppler ultrasonography and venography revealed thrombosis that started from the middle part of left subcavian until superor vena cava and occlusion in brachiocephalic vein. Superior vena cava was visible with neck collaterals in the venography .On physical examination, lungs and heart were normal. Adson test was positive on the left arm. There was no pain on palpation of left arm. There was no palpable cervical, axillary or inguinal lymph node. Body temperature was 36.6 ºC, pulse was 75/min, and the respirations were 16/min.

The blood pressure was 120/70 mmHg. Chest radiography showed a normal sized heart, normal lungs. Hemoglobin value was 13 g/dl, white cell blood was 10000/mm3. Erythrocyte sedimentation rate (ESR) was 20/ hour, D- dimer was 2.47µg/ml. Tumor markers were normal. Transthoracic echocardiography showed normal findings. Serum levels of antitrombin III, protein S and protein C were normal. Antinuclear antibodies, anti-DNA antibodies, anti neutrophil cytoplasmic antibodies, antiglomerular basal membrane antibodies, serum IgG and IgM anticardiolipin antibodies and rheumatoid factor were negative. Repeat venous doppler ultrasonography revealed chronic thrombosis in the same location.

Tinzaparin Na 175 IU/kg was given to the patient for 15 days. At the end of 15th day edema and pain decreased in the left arm and left face. Tinzaparin Na was given for one month and then oral anticoagulant therapy was costarted. After anticoagulant therapy, doppler ultrasound showed no recanalization of the internal jugular vein, but the response of the patient to the treatment was better than we expected, although it did not provide improvement in the anatomy.

Discussion

Upper extremity deep venous thrombosis (UEDVT) is a rare condition. According to the literature, approximately 4-10% of all cases of venous thrombosis may involve the subclavian, axillary or brachial veins. In the last few decades, the incidence of UEDVT has increased because of more frequent use of central venous catheters (CVCs) and cardiac pacemaker implantation. In addition, another common risk factor for UEDVT is cancer.

UEDVT is classified as primary, approximately one-third of cases, which refers either to effort thrombosis or idiopathic UEDVT, or secondary, due to the presence of overt predisposing causes. The onset of UEDVT is usually characterized by arm swelling and pain, but may also be completely asymptomatic especially in patients with a long-term presence of a CVC. Axillary or subclavian vein thrombosis may occasionally be completely asymptomatic [2] .

Swelling (80% of patients) and pain (40% of patients) are the most common UEDVT symptoms at presentation. Physical examination may reveal low-grade fever attributable to thrombosis. Higher fevers may suggest septic thrombophlebitis or may be related to the underlying malignancy in patients with cancer. SVC syndrome reduces venous return to the heart and, like PE, may cause sinus tachycardia. Patients with UEDVT may have mild cyanosis of the involved extremity, a palpable tender cord, arm and hand edema, supraclavicular fullness, jugular venous distension, and possibly dilated cutaneous collateral veins over the chest or upper arm. The signs and symptoms of UEDVT , however, are non-specific and may occur in patients with lymphedema, neoplastic compression of the blood vessels, muscle injury, or superficial vein thrombosis. If thrombosis causes obstruction of the superior vena cava, the patient may complain of arm and facial edema, head fullness, blurred vision, vertigo, or dyspnea. Fewer than half of these symptomatic patients will have imaging evidence of an UEDVT. Therefore, it is important to confirm or exclude the diagnosis with objective testing [1] .

Ultrasonography represents a simple and accurate diagnostic tool to demonstrate the problem. Accurate diagnosis of deep venous thrombosis is very difficult and imaging plays a crucial role in the diagnosis or exclusion of DVT. The initial test of choice for diagnosis of acute thigh as well as upper extremity DVT is ultrasound, because of its high accuracy, relatively low cost, portability, and lack of ionizing radiation. Although contrast venography is the gold standard for the demonstration of venous occlusion, there are many inherent risks of this modality. Other noninvasive investigations, such as CT and MR, can establish the diagnosis of upper extremity deep vein thrombosis easily and have replaced the venography, which carried significant risks, such as dislodgement of the clot and dissemination of septic emboli or trauma to the vein. CT venography can be performed as a part of the examination. MR has a problem-solving role, and conventional venography is now limited to specific scenarious including evaluation of central DVT in the upper extremities . Accurate diagnosis of chronic DVT remains problematic on all imaging modalities. Findings

of chronic DVT include increased clot echogenicity, irregularly thickened venous walls, small caliber veins, and collateral veins. MR may reveal ancillary findings that may be contributing to the DVT. MR may be superior to US [3] . In our patient venography was done before we saw the patient but the patient did not obey the doctor and came to us because of her face and arm swelling.

UEDVT has major clinical consequences including pulmonary embolism, recurrences, post-thrombotic syndrome, and death. The post-thrombotic syndrome(PTS) varies from mild edema with little discomfort to incapacitating limb swelling with pain and ulceration. A meta-analysis of clinical studies on UEDVT noted that PTS occurs in 7% to 46% (mean 15%) of patients. Graduated compression stockings markedly reduce the rate of the post-thrombotic syndrome in patients with lower extremity DVT. Those with refractory swelling may need to use these sleeves indefinitely[1].Up to one third of patients with UEDVT have PE. PE is less common on presentation among patients with UEDVT when compared to patients with LEDVT, but when PE occurs, the three-month outcome is similar. PE appears to be more frequent in patients who have a CVC, with an incidence as high as 36% of DVT patients[4] . Other complications include SVC syndrome, septic thrombophlebitis, thoracic duct obstruction, and brachial plexopathy [1] .

These patients have very high short-term mortality rates compared with patients who have lower extremity deep vein thrombosis. Most die from underlying medical problems such as infection, cancer, or multisystem organ failure rather than from complications of the UEDVT. The mortality among UEDVT patients has been described as 10% to 50% in the 12 months after diagnosis, which is much higher than the ratio in LEDVT patients. This in part is due to sicker cohorts getting UEDVT [4] .

The role of thromboprophylaxis for those patients with a long-term CVC is still controversial. Anticoagulation is the cornerstone of therapy of UEDVT. Unfractionated or low molecular weight heparin, followed by an oral anticoagulant are the most common treatments, with strategy of management similar to that of deep vein thrombosis of the leg.. It helps maintain patency of venous collaterals and reduces thrombus propagation even if the clot does not completely resolve. Recent ACCP guidelines recommend treating UEDVT patients with unfractionated heparin (UFH) or LMWH and warfarin, with an INR goal of 2 to 3 for at least three months depending upon the overall clinical scenario. Typically, unfractionated heparin is used as a "bridge" to warfarin. Low molecular weight heparin as a bridge may be safe and effective for outpatient treatment, or for reducing the duration of hospitalization. Warfarin or other anti-vitamin K agents are typically continued for a minimum of 3 months, with a goal INR of 2.0 to 3.0. At least 6 months of anticoagulation therapy is recommended if a coagulation abnormality is detected. Patients with UEDVT who have contraindications to anticoagulation, such as major gastrointestinal bleeding, or patients who develop PE despite adequate anticoagulation may be candidates for SVC filter placement. SVC filters are not widely used because data regarding their safety and efficacy are sparse. There are concerns that the risks of SVC filters, including filter migration, dislodgment, fracture, and precipitation of SVC syndrome, outweigh the benefits, especially because fatal PE from UEDVT is considered rare [(1).] Our patient was started on subcutaneous tinzaparin Na 175 IU/kg once time a day. Left face edema and arm edema resolved on 15th day of the therapy. Low molecular weight heparin treatment was continued for one month just because of difficulties in the setting of INR values untill the improvement in edema is stable. Then oral warfarin was started simultaneously untill INR of 2.0-3.0 was achived and low molecular weight heparin was stopped. Oral warfarin therapy was continued life long because the thrombosis of the subclavian and brachiocephalic vein did not resolve.

The prevalence of hypercoagulable states in patients with UEDVT is uncertain because observational studies report varying results. Furthermore, screening for coagulation disorders is controversial and has never been shown to be cost-effective. The yield of these tests is highest for patients presenting with idiopathic UEDVT, a family history of deep vein thrombosis (DVT), a history of recurrent, unexplained pregnancy loss, or a personal history of a prior DVT. Physicians who recommend life-long anticoagulation for protein C, protein S, and antithrombin III deficiencies should test for these rare causes of inherited thrombophilia. Factor V Leiden, the prothrombin gene mutation, hyperhomocysteinemia, and antiphospholipid antibodies are studied in clinical practice. Elevated antiphospholipid antibodies in the presence of UEDVT establish the diagnosis of the antiphospholipid antibody syndrome. These patients are managed with indefinite, intensive anticoagulation with a target international normalized ratio (INR) of 3.0 to 4.0. Hyperhomocysteinemia is easily corrected with folic acid supplementation. The optimal duration of anticoagulation for a thrombotic event associated with other hypercoagulable disorders, such as factor V Leiden or coexisting thrombophilias, is unknown [1].

Thrombolysis/thrombectomy and surgical decompression are often successful in the treatment of

UEDVT, but less frequently used. Randomized controlled trials are warranted to clarify the optimal management of UEDVT, and to identify patients at the highest risk of recurrence who might benefit from long-term anticoagulation [2].

Thrombolysis restores venous patency early, minimizes damage to the vessel endothelium, and reduces the risk of long-term complications, especially the troubling post-thrombotic syndrome. Catheter-directed thrombolysis achieves higher rates of complete clot resolution with lower doses of medication and reduces the risk for serious bleeding compared with systemic thrombolysis. The catheter should be positioned as close to the clot as possible; otherwise, collateral circulation will carry the medication away from the thrombus. Thrombolysis works best if used within several weeks of the onset of symptoms. Many case series of thrombolysis in carefully selected patients have reported excellent outcomes with only minor bleeding complications. The thrombolysis studies are small, however, so the risks of intracranial or gastrointestinal hemorrhage may not be fully appreciated.Those with primary UEDVT are usually young and healthy, more active, live longer, and are not troubled by other chronic medical conditions. Therefore, they should receive more aggressive treatment, such as thrombolysis and correction of outlet obstruction, to reduce the risk of chronic venous insufficiency. The best thrombolysis candidates are young, otherwise healthy patients with primary UEDVT, patients with symptomatic SVC syndrome, and those who require preservation of a mandatory central venous catheter. Patients with secondary UEDVT are less bothered by symptoms and are often not candidates for surgery or thrombolysis, so conservative treatment with anticoagulation alone is generally recommended. These patients have very high short-term mortality rates compared with patients who have lower extremity deep vein thrombosis. Most die from underlying medical problems such as infection, cancer, or multisystem organ failure rather than from complications of the UEDVT. Contraindications to thrombolysis include active bleeding, neurosurgery within the past 2 months, a history of hemorrhagic stroke, hypersensitivity to the thrombolytic agent, and surgery within the preceding 10 days. Heparin is usually given concurrently with the thrombolytic agent to prevent thrombus formation around the catheter [1].

Venipunctures, intramuscular injections, and invasive procedures should be minimized. Factors predicting success were as follows: (a) the use of urokinase compared with streptokinase; (b) the presence of a central venous catheter; and (c) a duration of symptoms < five days [5].

Small, single-center trials have shown that active intervention, such as thrombolysis, surgery, or multi-staged approaches are associated with increased vein patency and decreased rates of post-thrombotic syndrome. However, ACCP has withheld general recommendations for these interventions based on a lack of sufficient data to comment on their overall safety and efficacy, as well as comparable rates of post-thrombotic syndrome (15% to 50%) in studies that directly compared surgical and medical intervention. In fact, the ACCP recommends against interventional treatments unless the patient has failed anticoagulation therapy, has severe symptoms, and expertise is available [4].

Axillosubclavian vein thrombosis, also known as Paget-Schroetter syndrome, is a rare presentation of thoracic outlet syndrome (TOS) representing approximately 5% of all cases Venous thoracic outlet syndrome is a classic example of an entity which if treated correctly has minimal long-term sequelae but if ignored is associated with significant long-term morbidity. The subclavian vein is highly vulnerable to injury as it passes by the junction of the first rib and clavicle in the anterior-most part of the thoracic outlet. In addition to extrinsic compression, repetitive forces in this area frequently lead to fixed intrinsic damage and extrinsic scar tissue formation. The treatment of Paget-Schroetter syndrome is controversial and varies according to individual, institutional, and regional preferences. In general, the trend is toward more aggressive endovascular treatment. Prompt anticoagulation is generally accepted as the minimal treatment offered. Once primary thrombosis is recognized, catheter-directed thrombolytic therapy is usually successful if initiated within ten to 14 days of clot formation, but often unmasks an underlying lesion [6].

The importance of relieving the anatomic compression of the subclavian vein by first rib resection remains controversial, with some experts advocating surgical intervention in all affected patients, whereas others perform this procedure selectively in cases of persistent venous stenosis or ongoing symptoms. Angioplasty with or without stenting is generally discouraged in the absence of anatomic decompression but may play an adjunctive role in patients undergoing first rib resection [7].

The vast majority of investigators believe that decompression of the venous thoracic outlet, usually by means of first rib excision, partial anterior scalenectomy, resection of the costoclavicular ligament, and thorough external venolysis, is necessary, although opinion is less uniform as to the need for and method of treatment of the venous lesion itself. Using this

algorithm, long-term success rates of 95 to 100% have been reported by many investigators [6].

We treated our patient with low molecular weight heparin and then coumadin with an acceptable outcome. However future research should assess the safety and efficacy of low molecular weight heparin as monotherapy or as a bridge to warfarin and also define the optimal duration of anticoagulation for UEDVT. Although aggressive multimodal treatment, such as thrombolysis and surgical decompression, is generally recommended for patients with primary UEDVT, this practice should be evaluated critically with prospective clinical trials.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images.

Conflit of interest

There is no conflict of interest in the article.

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