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Case report

A Case of Venous Thrombosis of the Upper Extremity in Patient with Minimal Change Disease

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Abstract

Introduction. Thromboembolism is unexpected in nephrotic syndrome in remission unless there are other factors causing thrombosis. Herein, we present a case of deep venous thrombosis in the upper extremity in a patient with nephrotic syndrome in remission during an excessive exercise program.
Case. A 33-year-old male was diagnosed with minimal change disease. He had complete remission with steroid treatment. He was admitted to our Clinic with swelling of the left arm; and was found to have acute thrombus lying from left brachial vein to left subclavian vein. He had no additional diseases causing hypercoagulability, but he had been swimming for about 30-60 minutes every day. The symptoms resolved with low molecular weight heparin treatment followed by warfarin therapy within one month.
Conclusions. Thromboembolic events may rarely occur in patients with nephrotic syndrome in remission although there are no other inducing factors. Paget-Schroetter syndrome should be kept in mind in cases with UEDVT together with excessive physical activity of the specific muscles of the upper arm.

Key words: nephrotic syndrome; Paget-Schroetter syndrome; remission; thrombosis

Introduction

The hypercoagulabilty state with changes in the proteins of coagulation cascade and increased thrombocyte aggregation may lead to deep venous thrombosis (DVT), especially of the renal veins in patients with nephrotic syndrome (NS). Immobility, infections and hemoconcentration are other facilitating factors. DVT has been reported in 10% of adult patients with NS [1]. The most commonly used parameter for determining thrombosis risk is serum albumin level, which values under 2g/dl increase the risk substantially [1-4]. Thromboembolism is unexpected in NS in remission unless there are other concomitant factors such as immobility, malignant disorders, inherited causes of procoagulant states etc.
Upper extremity deep vein thrombosis (UEDVT), the term used for thrombosis of the brachial and subclavian veins, is fairly rare composing 4-6% of cases with DVT [5-7]. Most of the cases (80%) are secondary to central vein catheterization and malignancy [5-7]. Primary UEDVT may be either idiopathic or due to thoracic outlet syndrome or effort related thrombosis (Paget-Schroetter syndrome). Hereditary or acquired thrombophilia may underlie in idiopathic UEDVT (8-11). But, it is speculated that the frequency of thrombophilic disorders is lower in UEDVT compared with thrombosis of the lower extremity deep veins [12,13].
Herein, we present a case of acute UEDVT in a patient with NS in remission during an excessive exercise program.

Case history

A 33-year-old male was diagnosed with minimal change disease (MCD) by renal biopsy three years ago when he had been admitted to our Clinic with clinical findings of NS. He responded well to corticosteroid treatment; followed by two attacks of relapses that also responded well to the same treatment. He was accepted as steroid resistant and was treated with low dose corticosteroid treatment under which no relapse occurred again. The patient, who was in remission for the last 12 months, was admitted again to our Clinic with pain and swelling of the left arm for the last three days.
His past medical history revealed no history of concomitant disease, immobilization, surgical procedure, catheterization or trauma; and no history of smoking and alcohol use. He was right-handed and had been swimming for about 30-60 minutes every day. He was using ramipril, asetylsalycilic acid, lansaprazol and methylprednisolone (4mg methylprednisolone every other day) at the time of admission. Pathological findings on physical

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examination were edema of the left arm and hand without change in the color and temperature of the overlying skin. Basic laboratory results were within normal limits as follows: Leukocyte: 11600/mm³, hemoglobin: 14.5g/dl, thrombocyte: 359000/mm³, creatinine: 1.0mg/dl, albumin: 4.8 g/dl, proteinuria: 180 mg/day. Doppler ultrasonographic examination of the left arm revealed an acute thrombus extending from left brachial vein to left subclavian vein. He was given low molecular weight heparin followed by warfarin; and screened for diseases associated with thrombophilia. PT G20210A allele, FV Leiden mutation, antiphospholipid antibodies, anti-nuclear antigen and anti ds-DNA were negative. Levels of homocysteine, protein C and S were within normal levels. He was thought to have idiopathic UEDVT and discharged with warfarin therapy. His symptoms resolved completely within one month. Warfarin was stopped after six months at which time no thrombus was detected with Doppler ultrasonography. He has been followed up in our outpatient clinic without relapses for 12 months since the time of the thrombotic attack.

Discussion

Thromboembolism is a frequent extrarenal complication of NS. Decreased levels of anti-thrombin III and plasminogen, thrombocyte activation, hyperfibrinogenemia, inhibition of plasminogen activation, systemic effects of procoagulant activity due to immune complex injury within the glomeruli are among the defined hemostatic abnormalities [14-17].

Risk of thromboembolism is directly correlated with the severity of the disease and hypoalbuminemia with the highest risk encountered in patients with serum albumin levels below 2 g/L [14-18]. Thrombotic risk is not the same in NS of various origin; with membranous nephropathy having the highest risk followed by membranoproliferative glomerulonephritis and MCD [19,20]. MCD is the most common cause of NS in childhood; whereas it represents 10-15% of cases in adults [21,22]. Thromboembolic events usually occur in case of hypoalbuminemia in MCD as in other etiologies of NS. In a review by Waldman, *et al.* [5], severe hypoalbuminemia (0.6-1.5g/L) was detected in all four cases with thromboembolic events (three cases of DVT and one with arterial thrombosis) among 95 patients with NS. Kerlin, *et al*. [23] detected older age and proteinuria as predictive of thromboembolic events in 326 children with MCD. With these data and the current knowledge, it can be said that thromboembolic events are unexpected in patients with NS in remission. It has been shown that thrombin activation products (fibrinopeptide A and thrombin-antithrombin III complex) and prothrombin activation products (prothrombin fragment 1 and 2) are increased in patients with proteinuria less than 1gr/day [17]. This may support the existence of a subclinical state of coagulation in those patients; although there is a need for further studies to correlate these findings with clinical events.

Our case has a peculiar presentation due to atypical localization of the thrombus, atypical timing ie. one year after complete remission with serum albumin level of 4.8 g/L, and lack of congenital or acquired risk factor for thrombosis. The only risk factor delineated for this patient was history of forceful activity of upper extremities associated with regular swimming exercise.

UEDVT is fairly rare composing 5% of all cases with DVT. In more than 80% of cases, there are secondary factors like central venous catheterization, malignancies, pregnancy and use of oral contraceptives [5-7,11]. The presented case had none of these in his medical history.

Primary UEDVT may be either idiopathic, or related to thoracic outlet syndrome or Paget-Schroetter syndrome. Paget-Schroetter syndrome (effort related thrombosis) was described in the end of the 19th century in young (mostly aged 24-37 years) and otherwise healthy subjects presenting with UEDVT after repeating and forceful activity of the upper extremities like painting, swimming and heavy lifting [24-26]. Costoclavicular joint abnormalities may accompany this syndrome [11]. The presented case has similarities with the mentioned syndrome with his age and history of regular swimming exercise. It was thought that the procoagulant state of NS and prior corticosteroid treatment together with regular swimming facilitating Paget-Schroetter syndrome has led to UEDVT in the presented case.

Conclusions

Thromboembolic events may occur rarely in patients with NS in remission, unless there is a predisposing factor. Thoracic outlet syndrome and Paget-Schroetter syndrome should be kept in mind in cases with UEDVT together with excessive physical activity of the specific muscles of the upper arm.

Conflict of interest statement. None declared.

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