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ANKYLOSING SPONDYLITIS - AN ALARMING RISK OF VENOUS THROMBOEMBOLIC DISEASE

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Abstract

Venous thrombo-embolic disease (VTE) is a potentially life threatening clinical event. Ankylosing spondylitis (AS) is a chronic inflammatory disease with a significantly increased risk of developing VTE. Management of acute proximal deep venous thrombosis (DVT) depends on the clinical status of the affected limb, extent of the thrombus and comorbidities of the patient. Semba and Dake introduced Catheter directed thrombolysis (CDT) to treat 21 patients of DVT in 1994. CDT is a life or limb saving procedure, despite limitation of efficacy and associated complications. We hereby present a case of a 48 years old gentleman, diagnosed to have acute right lower limb proximal DVT extending up to IVC, and was also known to have AS and DVT of the left lower limb in the past. He was successfully managed with CDT and anti coagulation therapy.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease with a significantly increased risk of developing VTE. Coagulation and innate immunity have a common origin. Thrombin, which has an important role in coagulation, also increases the secretion of angiogenic growth factors and inflammatory cytokines. Studies have demonstrated a statistically significant increase VTE risk among patients with Ankylosing spondylitis. Our patient was diagnosed to have acute right lower limb proximal DVT extending up to IVC, and was also known to have AS and DVT of the left lower limb in the past. He was successfully managed with CDT and anti coagulation therapy.

Case report

A 48 years old, non-diabetic and normotensive gentleman presented to the emergency room with complaints of acute onset of right lower limb swelling, involving the ankle and calf which was extending up to mid thigh for a period of 5-6 hours. The swelling was sudden in onset, gradually increasing in nature and was associated with pain. He had no complains of parasthesia or weakness of the lower limbs, shortness of breath or chest pain. He did not have any history of recent trauma, surgery, hospital stay, prolonged immobilization or any thrombo embolic disease (MI, CVA or acute limb ischemia) in the past.

He was diagnosed to have AS 14 years ago (Lab markers – HLAB27 +ve, raised ESR, CRP and X-ray - sacroilitis), and had complains of severe back pain which improved on exertion and exacerbated on taking rest. Following 3 years time, he noticed to have hip joint instability, which was due to sacroilitis and fusion of sacroiliac joint, and had to undergo left Total Hip Replacement (Fig: 1).

After 6 years of the surgery, he developed left proximal DVT extending up to the lower 1/3rd of external iliac vein and was immediately initiated on oral anti coagulation therapy and continued for 2 years. In spite of being on oral anticoagulation therapy, he developed chronic non-healing ulcer associated with hyperpigmentation around the ankle in the left lower limb that is possibly due to post-thrombotic syndrome (PTS). He had been off oral anticoagulation for 3 years prior to the present episode.

General examination of the patient revealed a conscious, oriented and afebrile patient with tachycardia (116 b/min), B.P 130/70mmHg, RR 18/min and SpO2 – 99%. Systemic examination was unremarkable. Local examination of the right lower limb revealed diffuse tender swelling of the ankle, calf and thigh. There was calf tenderness on

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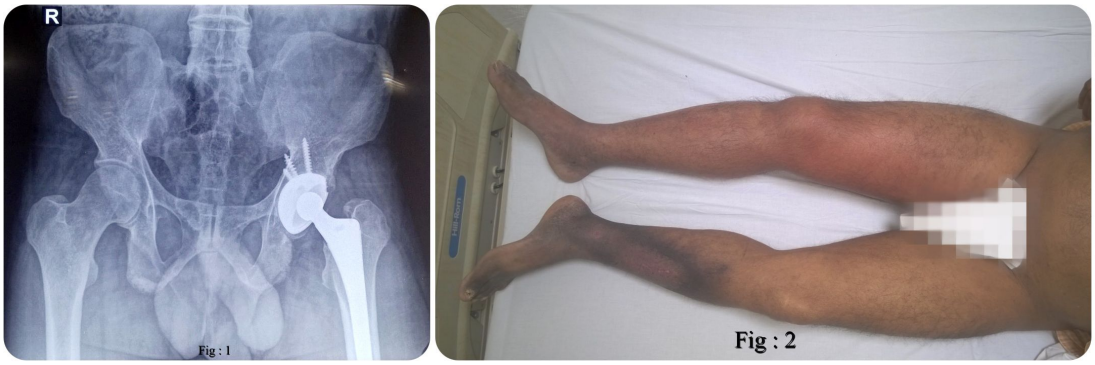
dorsiflexion of the foot (Homan's sign) associated with reddish purple hue involving the thigh and calf. Peripheral pulses were feeble due to edema but had good Doppler signals.



(Fig: 1 – Pelvis X-ray – post op left hip replacement with minimal sclerosis and erosion of right femoral head, Fig: 2 –Swelling of the right lower limb involving ankle, calf and mid thigh associated with reddish purple hue and hyperpigmentation of around the ankle in left lower limb)

Initial blood investigations revealed normal haemogram, kidney function test and bleeding parameters. Right lower limb Venous Doppler showed no flow in external iliac vein and non-compressible femoral vein, which were suggestive of DVT. The upper extent of thrombosis could not be assessed clearly due to edema and hence he was taken for a CT Venogram that revealed acute thrombosis of right external iliac vein (EIV), common femoral vein (CFV), popliteal vein (PV) and sapheno-femoral junction (SFJ) causing luminal distension and non-enhancing filling defect with partial recanalization of right superficial femoral vein (SFV). There was chronic thrombosis noted in the infra-hepatic IVC, bilateral common iliac vein (CIA) and left EIA with significant reduced caliber and formation of numerous collaterals in the peritoneum, retro peritoneum and thoraco-abdominal subcutaneous fat which was draining through the azygous system. These were probably sequelae to the previous episode of DVT. The left EIV, left CFV, SFV, SFJ and PV were normal.

ECG was normal and Echo revealed no left ventricular regional wall motion abnormality, LVEF 60% with normal Cardiac chamber dimensions and no intra-cardiac clot.

Systemic anticoagulation therapy was administered in the emergency room and was then taken for CDT in the cathlab. He was positioned prone and right popliteal vein access was obtained under USG guidance and 6F sheath was inserted. The Venogram showed non-enhancing filling defects in right PV, SFV upward to CFV with complete flow cut off from right EIV upwards. (Fig: 3)

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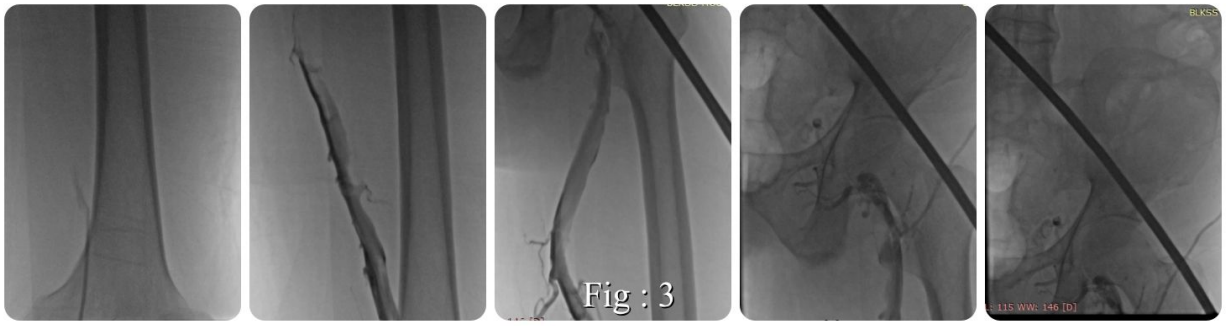
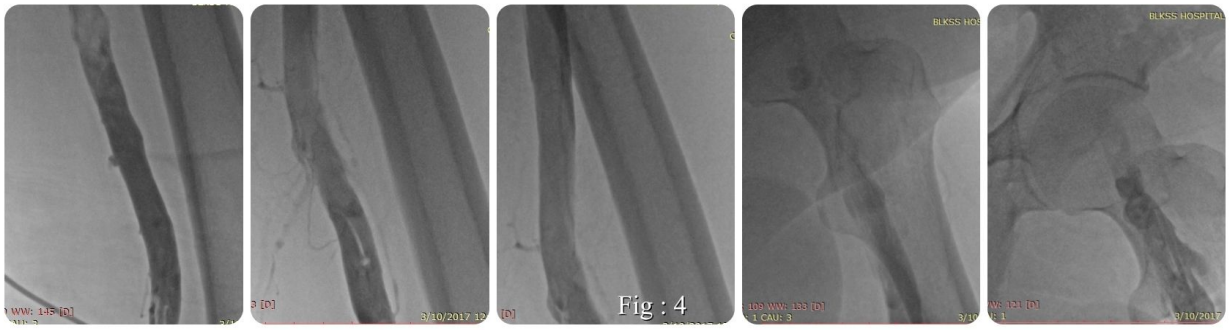


(*Fig: 3 - Non-enhancing filling defect in right external iliac vein, common femoral vein, popliteal vein and sapheno-femoral junction)*

He was initiated on catheter directed thrombolysis through the popliteal vein (Fig: 3) with Alteplase 1mg/hour. Check Venogram at 36th hours of thrombolysis revealed patent right PV, SFV, and CFV had no filling defect. However, intraluminal-filling defect was observed in the right EIV. At this point a 5F pigtail catheter was inserted into the thrombus via the sheath and CDT was continued.



(Fig: 4 - Patent CFV, popliteal vein and had no filling defect with intraluminal-filling defect in the right external iliac vein)

At the 45th hour of thrombolysis, patient developed oozing from the puncture site; hence CDT was stopped and was started on unfractionated heparin (weight adjusted dose).

He was subsequently started on new oral anticoagulation (NOAC) therapy (T. Rivaroxaban 15mg twice daily for 21days and then 20mg once daily to continue for life long). The clinical condition (pain/swelling) improved gradually and he was discharged in a stable condition.

Discussion

Immune mediated disease, such as Rheumatoid Arthritis; Systemic Sclerosis; Psoriasis; Systemic Lupus Erythematosus and AS have an increased risk to develop VTE. AS is a type of seronegative spondylo-arthritis characterized by Enthesitis and axial joint involvement, which mostly affects young males (1). Back pain and progressive stiffness are the common clinical features but may also have extra articular manifestation such as uveitis and urethritis. Recent studies have demonstrated significant elevated VTE risk among patients with AS (2,3).

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Coagulation and innate immunity have a common origin. Inflammatory cytokines such as interleukin 6 (IL-6), interleukin 8(IL-8), Tumor necrosis factor - Alpha (TNF – **α**) inhibits the anticoagulation pathway and impair the fibrinolytic pathway rendering these patients to a *thrombophilic state*. Again patients suffering from AS are at a state of higher oxidative stress which itself is a cause of *endothelial cell injury*. On the contrary, patients suffering from AS are usually less active in comparison to normal individual because of arthritis and joint immobility and hence making them a risk of *venous flow stasis*. Hence *thrombophilic state, endothelial dysfunction and venous flow stasis* (Virchow's triad) could possibly serve the pathophysiology of the increased clotting tendency (3).

Phlegmasia cerulean dolens is a form of DVT occurring three times more in the left leg compared to right leg (5). Its is characterized by pain, diffuse swelling and red/bluish discoloration which may lead to venous gangrene, tissue ischemia or limb loss if delayed in treatment (5). The different modalities of treatment are systemic anticoagulation, surgical thrombectomy and CDT (4).

Common initial management of DVT includes systemic anticoagulation, compression stockings and limb elevation. Surgical thrombectomy leads to blood flow in very less time but have more risk of developing re thrombosis and post thrombotic syndrome (6). Studies have demonstrated that CDT has more advantages over conventional anticoagulant therapy as it helps in prompt resolution of symptoms, prevention of pulmonary embolism, restoration of normal venous circulation, preservation of venous valvular function and prevention of post thrombotic syndrome (7).

CDT was introduced by Semba and Dake in 1994 to treat 21 patients and reported a complete lysis in 72%, partial lysis in 20% with a technical success rate of 85% and had no major complications in those cases (8). Mewissen et al reported 221 ilio-femoral and 79 femoro-popliteal DVT case who were treated by CDT and Urokinase infusion and demonstrated complete lysis in 31%, partial lysis (50-90%) in 52% and less than 50% lysis in 17% while at the end 33% needed stent placement (9). CDT may have adverse effects such as neurological events, bleeding, hematoma, fever, nausea vomiting or even death. Mewissen et al also reported excessive blood loss in 11% and retroperitoneal bleeding in 1% of the patients and 2 0f 6 patients who developed pulmonary embolism had died (9). However, thrombolytic therapy does not prevent clot propagation, re-thrombosis or subsequent embolization and therefore Heparin therapy and oral anticoagulant therapy must always follow a course of CDT (10).

Our case was successfully treated by Catheter directed thrombolysis and no complication or adverse effect was noted after intervention.

Conclusion

Catheter directed thrombolysis is associated with significant reduction in the risk of post thrombotic syndrome, venous obstruction and also have more effective lysis and lysis monitoring (11). Studies defers about the duration of anticoagulation therapy required in patients with DVT secondary to AS. However considering the quality of life and risk to life involved in such cases we advocate life long anticoagulation, if there are no other gross contraindications to the same

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Conflicts of interest

There are no conflicts of interest.

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