

Bilateral Acute Lower Limb Arterial Occlusion after Long Term Tranexamic Acid Usage

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Received on 23.09.2017,

Accepted on 13.10.2017

Abstract

Tranexamic acid is widely used as an anti-fibrinolytic agent in different conditions including menstrual bleeding, trauma, dental procedures etc. though considered safe, its use on a long term basis in an abnormal dose is not without adverse effects. Both arterial and venous thrombosis in different vascular beds has been described with its use. Here in, we report a rare case of bilateral acute lower limb arterial thrombosis in a young female who had used tranexamic acid inadvertently for a long period of time. Our patient presented with sudden onset of weakness of both lower limbs and progressively worsening blackish discoloration ascending from foot to mid leg. Her evaluation revealed bilateral common femoral and superficial femoral arterial occlusion on CT angiogram, moderate renal insufficiency, and evidence of rhabdomyolysis. Her pro-coagulant screening and connective tissue disease profile were negative. She has been managed with anti-coagulation as per hospital protocol and also been given anti-platelets. She progressed to bilateral lower limb gangrene for which fore quarter amputation was done. It is advisable to exercise caution in using long term tranexamic acid usage especially in people who have thrombophilic tendencies.

Keywords: Tranexamic Acid; Arterial Thrombosis.

Introduction

Tranexamic acid is an anti-fibrinolytic agent that reversibly binds with lysine receptor sites on plasminogen and prevents its conversion to plasmin, thereby preventing plasmin from binding and degrading fibrin [1]. This preserves the framework of fibrin matrix. Therefore, tranexamic acid is a competitive inhibitor of plasminogen activation and at much higher concentrations, a non-competitive inhibitor of plasmin. Tranexamic acid is ten times more potent than any other anti-fibrinolytic agent. It is mainly excreted through glomerular filtration and has a half-life of four hours. Usually tranexamic acid is used to prevent and treat blood loss in variety of situations like dental procedures in hemophiliacs, heavy menstrual bleeding and in major trauma [2]. The long-term usage of tranexamic acid very rarely can lead to deep vein thrombosis, pulmonary embolism and visual disturbances.

Case Report

A 22 year old female was admitted to emergency department with history of pain and weakness of both lower limbs for the last 10 days. Claudication distance reported was around 50 feet. There is progressively ascending blackish discoloration of both lower limbs starting from toes. She also complains of vague ill health, reduced urine output and shortness of breath. She has been using oral tranexamic acid at a dosage of 500mg twice a day in the last 4 weeks for menorrhagia. No other significant past medical history except she has been using oral contraceptive pills for the last two years. On physical examination, her vitals are stable. There are no distal pulses felt in both lower limbs. Dry gangrenous patches noted on both feet extending up to ankles. Her Hb% was 12.4gm/dl, Total leucocyte count 11,400, Lactate dehydrogenase 900 IU/ml, Creatinine phosphokinase was 1,89,800 IU/lit, platelet count 1.3lacs/mm³ and

serum total bilirubin 1.8 mg/dl. Her urine examination revealed 1+ protein and plenty of RBCs. Urine myoglobin was positive. Renal function showed eGFR of 40ml/min/1.73m². After adequate hydration

CT angiogram of lower limb vessels was performed. It revealed total occlusion of right common femoral, superficial femoral, popliteal artery and left superficial femoral artery. Pro-coagulant factor screening (protein



C, protein S and anti-thrombin III) was negative. Her antinuclear antibody and anti-phosphate antibody were negative. Her ultrasound abdomen was within normal limits. She was given anti-coagulation (UFH 5000units/hr for 48 hours), anti-platelet agents and three sessions of hemodialysis through right internal jugular catheter over the next one week. Initially fasciotomy was attempted to try and salvage the limbs. As she developed frank gangrene bilateral lower limb fore quarter amputation was done. Her renal function improved over the next one week. LDH and CPK became normal.

Discussion

Tranexamic acid widely used in bleeding tendencies though generally safe is not without any major side effects. It has the potential to cause major arterial thrombosis and is contraindicated in patients with thrombophilic tendencies and also in patients with active thrombotic or embolic disorders. In our patient inadvertent long term high dose tranexamic acid has resulted in bilateral acute arterial occlusion. Renal failure in our patient could be attributed to

Rhabdomyolysis. In the literature this agent causing venous thrombosis has been reported. There are 56 reports of deep vein thrombosis, pulmonary embolism or both and these include reports of cerebral and retinal vein thrombosis in the World Health Organization's international drug monitoring database. But, there are only few reports of arterial thrombosis so far [3]. Two reports of arterial thrombosis have been reported in literature, both of whom were on oral TA for menorrhagia and developed cerebral arterial thrombosis [4]. Additionally, there are 22 reports of cerebral embolism and 9 of arterial thrombosis [5]. In our patient bilateral lower limb arterial thrombosis was developed after the usage of high dose tranexamic acid for one month. She has no additional risk factors for development of thrombosis except for she has been using oral contraception for the last 2 years.

Conclusion

Early recognition of this rare entity could salvage vital organs. The extent of arterial or venous thrombosis depends on the dosage and duration of

tranexamic acid therapy in susceptible patients. The tendency to develop arterial or venous thrombosis in high risk population should be kept in my mind before prescribing long term tranexamic acid.

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