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General Medicine

HYPERHOMOCYSTEINEMIA CAUSING EXTENSIVE LEFT UPPER LIMB DEEP VEIN THROMBOSIS- A RARE CASE REPORT

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ABSTRACT Hyperhomocysteinemia is a common prothromboticcondition predisposing to venous thrombosis. We are reporting a case of hyperhomocysteinemia with extensive left upper limb deep vein thrombosis. A 44-year-old male presentedwithprogressive swelling and painin his left upper limb. He had marked knuckle hyperpigmentation. His left upper limb doppler ultrasonography was suggestive ofdilated leftinternal jugular vein, subclavian vein , axillary vein,brachial vein and cephalic vein with intraluminal contents suggestive of deep vein thrombosis. Blood investigations were suggestive of increased levels of homocysteine.The patient was evaluated extensively but no other cause could be found out. The patient was treated with low molecular weight heparin and oral warfarin along with folic acid.

KEYWORDS : homocysteine, deep vein thrombosis, prothrombotic.

INTRODUCTION

Hyperhomocysteinemia is a well-recognized risk factor for thrombotic and atherosclerotic vascular disease. It is one of the common causes of cerebral venous sinusthrombosis. Lower limb deep vein thrombosis is common but upper limb is rare. The patient was elaborately evaluated for other causes of thrombosis but all were negative. There are very few casereports of extensivedeep vein thrombosis due to hyperhomocysteinemia.The patient improved with anticoagulation and folic acid. This case report is of one such rare cases of deep venousthrombosis which had increased homocysteine levels in patient.

History

A 44-year-old male, vegetarian, presented with 2-month history of gradually progressive swelling and pain in his left upper limb and neck. There was no h/o trauma to the limb, prolonged immobilization, any neck or mediastinal surgery, and no h/o drug intake. Patient was not a diabetic, hypertensive nor any history of taking antitubercular medicines. Patient was a smoker and his smoking index was 12 cigarette pack years. Patient was a non alcohol consumer and there was no high risk sexual history.On examination, his pulse was 84/min regular, normal character without vessel wall palpable. Blood pressure checked in right upper limb supine position was 132/78mmHg. His respiratory rate was 16/ minute. Saturation checked in right index finger by pulse oximeter was 98% on room air. On examination patient was conscious cooperative and oriented to time place and person. There was no pallor, cyanosis, lymphadenopathy, raised jugular venous pressure, jaundice, clubbing. General examination revealed knuckle hyper-pigmentation. His left arm was edematous and tenderness was present. There were no visible veins. Skin was shiny over arm and forearm. Examination of cardiovascular, abdominal, respiratory and nervous system revealed no abnormality.

Investigations were done which showed Hemoglobin - 16.1 gm/dl, Mean Corpuscular Volume of 97.4 fl, Total Leukocyte Count 12500/mm3, platelet count was 190,000/mm3, prothrombin time of 14.6 and International normalized Ratio (INR) of 1.08. Liver Function Tests showed serum glutamic pyruvic transaminase levels of 38 IU/L, serum oxaloacetic transaminase levels of 34 IU/L, alkaline phosphatase levels of 104 IU/L, Bilirubin total 0.8 mg/dL, albumin 4.2 g/dL. Renal function tests showed blood urea nitrogen -13mg/dL and serum creatinine-0.8 mg/dL. Electrolytes were done and the values were sodium- 140, potassium-4..7, chloride-111. His lipid profile showed Total cholesterol of 210 mg/dL, Low density cholesterol was 116mg/dL and triglycerides were 162mg/dL. His viral markers for human immunodeficiency, hepatitis B and C were negative.His glycated hemoglobin levels were 5.2%. D-dimer was raised and the value was 2.5 mcg/mL His left upper limb USG doppler was suggestive of incompressibility, dilatedveins and absence of blood flow on color and spectral mode in left internal jugular, subclavian, axillary,brachial and cephalic veins was suggestive of deep vein thrombosis. USG abdomen and pelvis was normal. electrocardiogram, chest X-ray and 2D echocardiography were normal. Anti-phospholipid antibodies were negative, anticardiolipin antibodies were negative , lupus anticoagulant was absent, dilute Russel viper venom time(Plasma) was normal and prothrombin time and mixing studies were normal. Factor five Leiden mutation was negative. Protein C and S were negative. Fasting plasma homocysteine levels > 50 µmol/L.A final diagnosis of upper limb DVT due to hyperhomocysteinemia was made. The patient was treated with low molecular weight heparin, overlapped with warfarin and was discharged when he achieved an INR of > 2.0. Patient was also given folic acid 5 mg once a day. He was advised elevation of upper limb. On follow up after one month patient improved, pain and swelling of left upper limb was decreased.

DISCUSSION

Venous thrombosis of upper limbs is a rare clinical condition. The primary complications that can result from upper limb venous thrombosis are pulmonary embolism and postthrombotic syndrome1,4. Standard treatment is clinical, with oral anticoagulants and heparin. Thrombolysis may occasionally be a treatment option.Hyperhomocysteinemia, which is a disorder of homocysteine metabolism, has recently been recognized as a risk factor for thromboembolic disease5. Homocysteine is a by-product of sulfur-containing amino acids and in excess it appears to be related to endothelial damage caused by oxidative and inflammatory mechanisms, and by reducing bioavailability of nitric oxide, which is a powerful endogenous vasodilator4-8. Elevations in the plasma homocysteine concentration can occur dueto genetic defects in the enzymes involved in homocysteine metabolism (e.g.thermolabile variant of methyltetrahydrofolate reductase), nutritional deficiencies of vitamins – folate, B12, B6, or due to other factors – including some chronic medical conditions and drugs9. Some drugs used in the treatment of hypercholesterolaemia, such as fibrates and nicotinic acid, can raise homocysteine levels by approximately 30 per cent; however, the clinical significance of this is uncertain.Cigarette smoking also may elevate homocysteine levels.Chronic kidney failure can increase homocysteine levelsdue to decreased renal removal and impaired metabolism. The normal range is from 5 to 15 µmol/L; figures above this level characterize hyperhomocysteinemia8. There is increasing evidence that hyperhomocysteinaemia is a risk factor for venousthromboembolic disease 10-12. Meta-analyses of case-control studies have found an odds ratio of 2.5 to 2.95 for venous thromboembolic disease in patients with homocysteine levels more

than two standard deviations above the mean value of control groups11-12.

Treatment for thrombosis should be initiated as soon as diagnosis is made, but there is no consensus regarding duration of treatment13. Some authors prefer perennial anticoagulation because of the thrombophilia. In contrast, other choose to treat the first event for 3 to 12 months during the acute phase and only prescribe continual anticoagulation in cases of repeat thrombosis. High risk patients (two or more thrombosis episodes, atypical site, a DVT and more than one genetic mutations, cancer patients, and others) should be considered for indefinite anticoagulation in order to avoid recurrence5 , 13.

For hyperhomocysteinemia, folic acid and vitamin B6 and B12 supplementation and dietary changes can reduce plasma levels effectively, but the impact this has on cardiovascular disease morbidity and mortality is a controversial subject and different studies contradict each other14-16.

The case described here is of importance because of its rarity, but this possibility should not be forgotten when investigating patients complaining of pain in an upper limb, even when there is no obvious cause of venous thrombosis as discussed here to prevent the reoccurrence. Serum homocysteine levels should be part of work up for prothrombotic conditions.

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