Superficial vein thrombosis in a child with methylene tetrahydrofolate reductase (MTHFR) heterozygous mutation: a case report

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ABSTRACT

Methylene Tetrahydrofolate reductase (MTHFR) mutation leads to increased plasma homocysteine levels which is associated with increased risk of thrombosis. MTHFR mutation might be one of the unusual cause of thrombosis besides the usual risk factors like trauma, venous procedures, surgery, malignancy and immobility. We report a case of 13 years old male presenting with superficial venous thrombosis in bilateral forearm who later on evaluation was found to have heterozygous Methylene Tetrahydrofolate Reductase (MTHFR) mutation.

Keywords: Child; homocysteine; MTHFR; thrombosis

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INTRODUCTION

Thrombosis in the superficial veins is termed as superficial thrombophlebitis or superficial vein thrombosis. It occurs most commonly in saphenous veins and their tributaries in the lower limbs followed by the cephalic and basilic vein in the upper extremities. Bilateral cases are reported in 5–10%.[1] It is found to be more common in older people, and in women compared to children.[2] Most common cause of superficial venous thrombosis of the upper limbs consists of iatrogenic conditions like intravenous catheters, infusion of different drugs such as chemotherapy, heroin.[3] Prolonged immobility, a hypercoagulable state may also predispose to thrombophlebitis. Hypercoagulable states associated with venous thrombosis are due to deficiencies of antithrombin, protein C, and protein S; the presence of the factor (F) V Leiden mutation; hyperhomocysteinemia; and methylene tetrahydrofolate reductase (MTHFR) gene mutation.[4]

Here, we present a case of 13 years male with superficial venous thrombosis with heterozygous MTHFR mutation along with positive family history. Studies with MTHFR mutation associated with thrombosis in children have not been adequately reported. This case report may aware clinician to consider MTHFR mutation as one of the causes of thrombosis in children.

Case Report

A 13 years old male presented with history of fever for 5 days associated with swelling over bilateral forearm (right more than left). Swelling was acute on onset extending from middle third of the forearm up to the wrist bilaterally and was associated with pain and redness over right forearm. There was no history of trauma, chest pain, cough, prolonged immobility, swelling over any other site or any significant past medical or surgical history. On examination, child was average built with stable vital signs with pulse rate of 90 bpm with no radio-radial or radio-femoral delay and blood pressure of 110/60 mm of Hg measured at right forearm in sitting position which falls between 50th and 90th centile for that age and sex. Local examination of the swelling revealed ill-defined border along with redness, local rise in temperature of the overlying skin and tenderness over the dorsum of right distal forearm. Other systemic examinations were unremarkable.

His father is a known case of MTHFR heterozygous mutation which was diagnosed during the evaluation of stroke at the age of 35 years for which he was taking Tablet Aspirin 150 mg and Tablet Atorvastatin 40 mg.

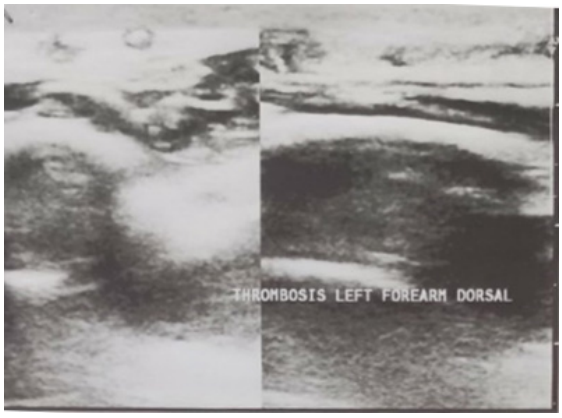

Figure 1. Ultrasound showing thrombus in left upper limb

His investigations reports showed leucocyte count of 8800/mm^3 with neutrophil of 72%, platelet count of 279000/mm^3 and CRP of 5mg/l. Prothrombin time was 14 sec with INR of 1.16. Ultrasound Doppler study showed echogenic thrombus with non compressible vein noted in distal dorsal branch of cephalic vein along with extensions in right forearm and echogenic thrombus with non compressible cephalic vein noted in the mid left forearm extending upto dorsal aspect of the superficial hand vein, showing evidence of superficial vein thrombosis in bilateral upper limb. ANA was done to rule out vasculitis, which was negative. As there was positive family history, child was evaluated for MTHFR mutation as the possible cause which showed the presence of heterozygous mutation. Child was managed with Aspirin 75mg PO OD for 2 weeks and discharged after clinical improvement. He is under regular follow up every 2 weeks and is symptom free with no evidence thrombus at the same or different sites in the last 2 months of follow up.

DISCUSSION

There is a wide range of predisposing conditions of superficial venous thrombosis that have been delineated, including prolonged immobilization, trauma, obesity, hypercoagulable states, use of oral contraceptives or hormonal therapy, prior history of SVT or DVT, intravenous catheter use, malignancies and autoimmune disorders.[5]

MTHFR is a rate limiting enzyme that catalyses the irreversible conversion of 5, 10 methylenetetrahydrofolate to 5-methyltetrahydrofolate, which serves as a methyl donor in the reaction converting homocysteine to methionine. Mutation in this gene may impair this

conversion resulting in elevated level of homocysteine. Hyperhomocysteinaemia may lead to cardiovascular disease or DVT and pulmonary embolism though exact mechanism is not known. However, MTHFR gene mutation may not necessarily always cause elevated homocysteine level especially when food is fortified with folic acid.[6] There are two MTHFR genes; one inherited from each parent. Mutation is said to be heterozygous if present in only one gene and homozygous or compound heterozygous if present in both genes. MTHFR A1298C and MTHFR C677T are the types of MTHFR gene mutation where latter is more common.[6] Heterozygous MTHFR C677T mutation was detected in our patient. American College of Medical Genetics recommends against the routine testing of MTHFR mutation for evaluation of risk of blood clots or recurrent pregnancy loss.[7] Genetic testing was done in our case as there was positive family history and there was no other obvious cause for thrombosis. Detection of mutation doesn't change the management of the patient and use of vitamin B6 or B12 or folic acid though found to lower homocysteine level; doesn't lower the risk of recurrent clots and hence are not prescribed.[8] We managed the patient with NSAIDs alone and no supplementation with vitamin B6 or B12 or folic acid was done. Similarly, we didn't look for the homocysteine level in our patient as elevated level of homocysteine will not influence the management plan of the patient.

MTHFR mutation has also been linked with increased incidence of neural tube defect.[9] Venous thrombosis has been uncommonly reported in children as compared to adults. Moreover, genetic cause associated with venous thrombosis has also been rarely reported in children in our part of the world. Hence, this case report can be of scientific significance as well as contribute to further research in this area.

CONCLUSION

When there is no obvious cause of superficial venous thrombosis, rare causes of thrombosis like MTHFR gene mutation should be sought. Though MTHFR gene mutation is not regularly tested and doesn't require specific treatment, it helps in counselling of the patient and predict future risks.

Consent

Informed consent received from the patient's parents.

Conflict of Interest

None

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