Case Report

Congenital Lens Dislocation and Fatal Cerebral Vein Thrombosis in a Patient with Homocysteinemia: A Lesson for Urgent Screening of Pediatric Population

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Abstract

Congenital homocysteinemia is a genetic disease with various clinical manifestations such as thrombosis, lens dislocation and mental retardation and osteoporosis, so early diagnosis is important for decreasing the mortality and morbidity especially in pediatric populations. Here we describe a child with a presentation of coma with a past history of lens operation with unfortunate fatal clinical course, and a final diagnosis of congenital homocysteinemia.

Keywords: Cerebral vein thrombosis, congenital homocysteinemia, lens dislocation

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Introduction

Congenital thrombophilia is a treatable, but life- threatening, disease. The main problem is that it needs to be diagnosed before the onset of thrombosis at least to prevent the morbidity and mortality of thrombotic sequellae.

Antithrombin III, protein C and S, activated protein C resistance-factor V leiden, methyl tetrahydrofolate reductase mutation, prothrombin20210 A mutation, and plasma homocysteine level[1] all might be checked to find the causes of the thrombosis. Also, the acquired causes, such as anticardiolipin antibody syndrome, paroxysmal nocturnal hemoglobinuria, high factor VIII level, systemic disease such as cancer and vasculitis, and drugs like estrogenic compounds needs to be considered. Here we present a case of fatal cerebral thrombosis, because of the severe homocysteinemia.[1]

Case Report

The patient was an 11-year-old girl with the complaints of headache and decreased level of consciousness few hours before referral to our hospital. The patient's magnetic resonance imaging of the brain showed a widespread cerebral vein thrombosis (Figure1). At first she was suspected of having subarachnoid hemorrhage (Figure 2) and therefore, there was a delay to start anticoagulants. Unfortunately, the clinical courses lead to a fatal outcome despite using proper anticoagulants.

The most important point in diagnosis of this case was in history. She, from the age of four, had congenital dislocation of lenses of both eyes without any medical or mental problem. There was no suspicion of homocysteinemia (Marfan syndrome and congenital homocysteinemia are the two main causes of congenital lens dislocation). The parents were far relatives and the other sibling was healthy, but had a slight degree of homocysteinemia (22 micromol /l) without any ophthalmic or medical problem.

One month prior to the problem of central nervous system (CNS), she had surgical correction of both eyes due to lens dislocation with a two-week interval. During the last hospital admission, all laboratory profiles of thrombophilia were done, and the only abnormality detected was homocysteinemia. The patient's plasma homocysteine level was 75micromol/l (normal level: 5 – 15 micromol/l). The attached images are in favor of high degree of cerebral Vein thrombosis.

Discussion

Homocysteinemia is a contributing factor for thrombosis, and can be combined with other thrombophilic factors in thrombophilia. In this case all the above-mentioned thrombophilic factors except plasma homocysteine were normal.

Homocysteinemia can be seen secondarily in folate and cobalamine deficiencies (the serum level was normal in our case), smoking, advancing age, renal failure, hypothyroidism, leukemia, and inflammatory bowel disease. It causes endothelial damage by low-density lipoprotein oxidation and disturbances in protein C pathway.[2–4] Musculoskeletal defects such as tall and thin body (marfanoid picture), pescavatum and pescarinatum, high- arched palate, genu valgum, and pescavus are some related musculoskeletal abnormalities seen in congenital homocysteinuria. Mental retardation, seizure, and psychiatric abnormality together with subluxation of lens, glaucoma, optic atrophy, and myopia, also are reported with congenital homocysteinuria. Cystathionine B synthase deficiency as a heterozygote inheritance is a major enzyme deficiency in this category especially in this case with congenital lens dislocation and hyperhomocysteinemia.[5,6]

Magnetic resonance imaging findings in cystathionine B synthase deficiency include vessel occlusions or mural irregularity

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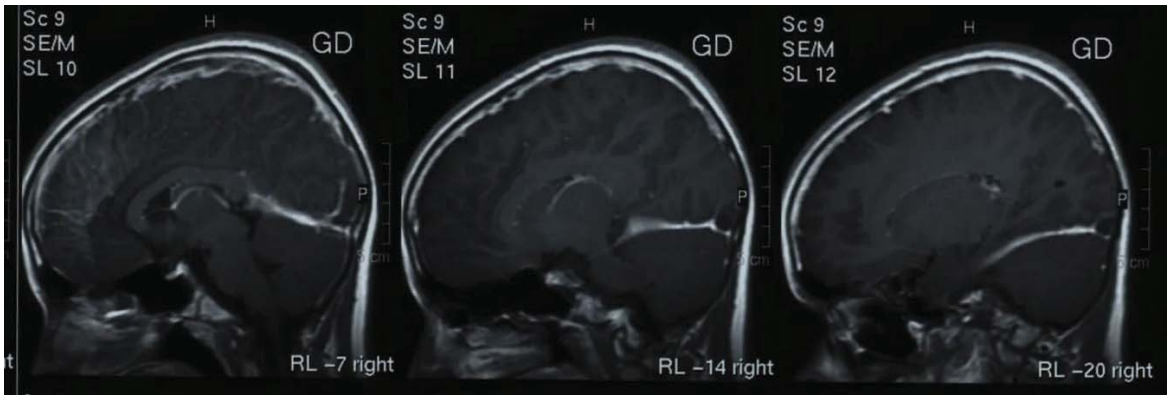

Figure1. Extensive cerebral thrombosis in lateral and sagital sinus thrombosis?

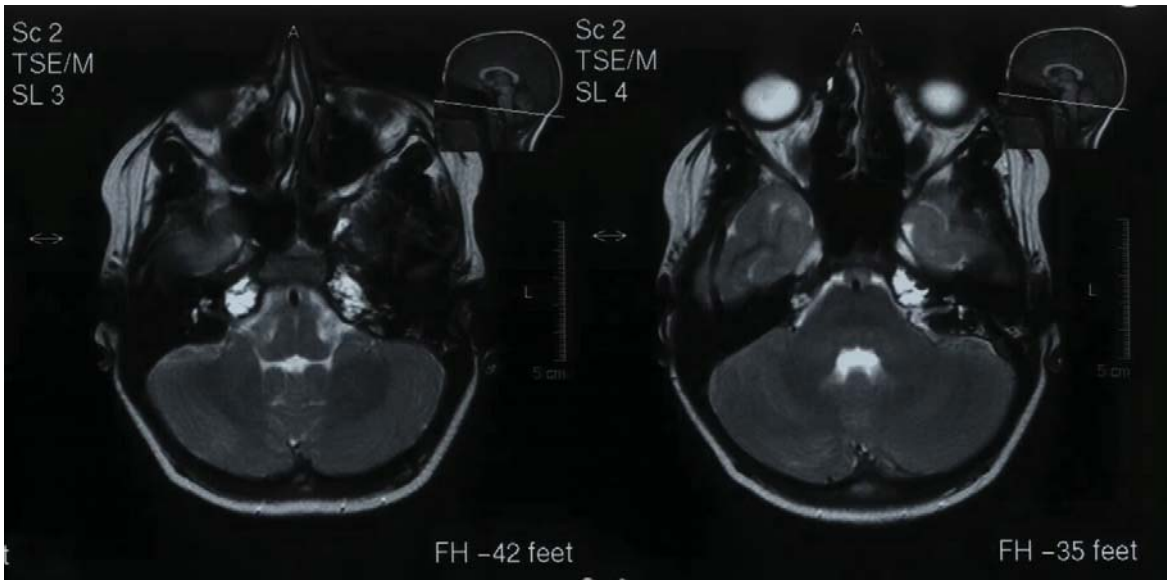

Figure 2. Axial view of the magnetic resonance image of the brain stem showing the extensiveness of thrombosis in the bright areas

reflecting accelerated atherosclerosis.[7] The unfortunate course of this case denotes that it is necessary to screen for homocysteinemia and homocystinuria at birth, and even more importantly when signs of disorders such as mental retardation, lens dislocation, osteoporosis, skeletal defects exist.[8,9]

What could we do for this case after the insult, except early detection? At first, early full-dose anticoagulants, prophylactic anticoagulation during a thrombogenic stress such as operation, (in this case, lens operations was a contributing factor for the thrombosis) and finally diet restriction such as low methionine and protein[10] are beneficial; also screening for homocystinuria in the siblings and pedigree is recommended.

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