Olgu Sunumu

A Case of Homocystinuria Presenting with Unilateral Cataract, Systemic Hypertension and Purpura Fulminans

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Abstract

In homocystinuria, clinical involvement may include the skeleton, brain, orbita, and vascular system. We report a 7-year-old male who initially presented with fever, edema on feet and legs, and bruising on the hands, and was followed-up with the diagnosis of homocystinuria. On account of the case we would like to emphasize homocystinuria should be considered in cases of cataract, systemic hypertension and purpura fulminans.

Key words: Homocystinuria, unusual presentation, child

Introduction

Deterioration in the metabolism of methionine which is an essential amino acid that contains sulfur leads to homocystinuria (1). The disease inherited is autosomal recessively (2). Skeleton, brain, ophthalmologic and vascular system involvement can be seen in clinical course (1,2). Among neurological symptoms, convulsion, spasticity, and psychiatric disorders may be observed (1,3). In this article, a 7-years-old-male with homocystinuria is presented because of unusual presentation. On account of the case we would like to emphasize homocystinuria should be considered in cases of cataract, systemic hypertension and purpura fulminans.

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Case Report

A-7-years-old male was referred to our clinic due to the complaints of fever, bruising on the hands, and legs and edema on feet. The child was healthy until the age of three, but after then sometimes headache, vomiting, dyspnea, fatigue, edema on the feet, and palpitations occurred. For month, some of the symptoms became severe and fever was also observed. Two days before admission to our clinic edema and bruising on the hands and legs and pain were noted. The personal history indicated that a cataract of the left eye developed 6 months ago. The family history displayed a 2nd degree relationship between the parents.

On physical examination, body weight and height were 21 kg (25-50 percentile), 114 cm (10-25 percentile), respectively. Body temperature was 36.4 ºC; pulse rate 120/min; respiratory rate 48/min; blood pressure measured from the right lower extremity 280/200 mmHg, from the left lower extremity 290/200 mmHg, from the right upper extremity 220/200 mmHg, and from the left upper extremity 200/180 mmHg. His general condition was good. A cataract was noted on the left eye. The patient was also suffering from tachypnea. Kyphosis and inspiratory rales were present on thorax examination. He had tachycardia, and 3/6 degree systolic ejection murmur. The liver was palpable 4 cm. Prebital and back of the feet an edema were present. Cyanosis was noted on the hand and feet nail

beds, scattered purpura on the back of the hand and feet. Non-marked necrotic wound, sized of 1x1.5 cm, were present on the second finger pulp of the both feet.

On laboratory investigation, hemoglobin was 14.6 g/dL; leukocyte count 12700/mm^3; thrombocytes 327.000/mm^3; sedimentation rate 31 mm/hr; prothrombin time 16.1 sec; active partial thromboplastin time 36.5 sec; fibrinogen 448 mg/dL; D-Dimer 0.45 ug/dL; protein-C 74% (N: %70-130), and protein S 77% (N: 60-140). Routine biochemical parameters were normal. Urinary blood amino acids and Tandem-MASS spectroscopy for metabolic screening were normal. Plasma lactic acid and pyruvate levels were 7.8 mg/dL (5.7-22 mg/dL) and 0.5 mg/dL (0.3-1 mg/dL), respectively. Serum aldosteron concentration was 155 pg/mL (20-240 pg/ml) and serum homocystine level was 13.5 umol/L (N: <12 umol/L). Staphylococcus epidermis was cultured from blood culture.

Anti-streptolysin-O 252 IU/mL, C-reactive protein 4.9 mg/L, antinuclear antibodiesc, Anti-deoxyribonucleas DNA, p-antinuclear cytoplasmic antibodies, c-antinuclear cytoplasmic antibodies were negative. Serum C_3 and C_4 levels 174.1 mg/dL (N: 88-177) and 28.2 mg/dL (N: 15-45), respectively. In telecardiograph, pulmonary artery segment was bulging and cardiomegaly was determined. Brain *magnetic resonance imaging* displayed cerebral focal atrophy and cerebral focal ischemic focuses (on the right centrum semiovale and on the right frontal lobe) were determined (Figure 1).

Cardiomegaly and left ventricle hypertrophy were determined in the thorax *magnetic resonance imaging* and dilatation was monitored on the ascending aorta and pulmonary artery. Thorax computerized tomography revealed a narrowing of the thoracic aorta. Renal angiography was normal. Echocardiography displayed pulmonary hypertension, right and left ventricle hypertrophy, advanced mitral failure, mild degree tricuspid failure and massive pulmonary failure. Cardiac catheterization was normal. Histopathological examination of liver showed increased connective tissue at the portal areas, chronic inflammed cells at portal areas, and vacuolization compatible with glycogenesis in the nucleuses of some hepatocytes.

The patient was hospitalized with the diagnoses of hypertension, congestive cardiac failure, purpura fulminans and congenital cardiac disease. Additional to the administration of dual antibiotics, fluid restriction was ordered. Because of high blood pressure, captopril and nifedipin were initiated.

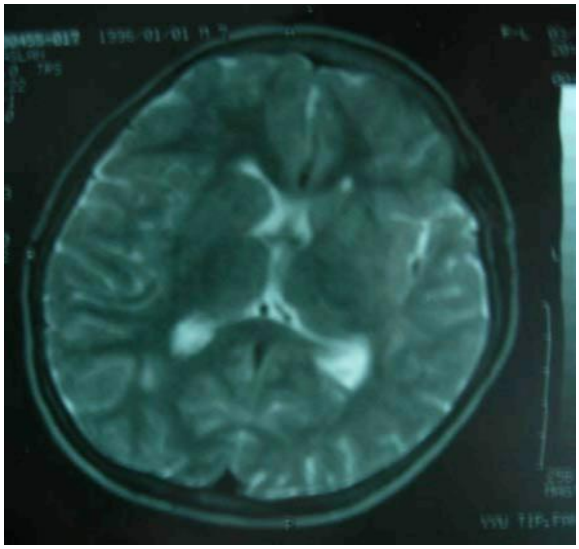

Fig. 1. Modified signal compatible with a few number of ischemia at the right centrum semiovale focal displayed in T2-weighted *magnetic resonance imaging*.

Despite triple antihypertensive drugs hypertension was continued. Thus sodium nitroprussid was administered, which successfully controlled blood pressure. On the other hand, heparine was initiated for purpura fulminans.

During follow-up, blood pressure was controlled and exanthemas decreased. Hepatomegaly was improved. However, a necrotic area occurred at the tip of the second foot finger. Based on the clinical and laboratory findings, the patient was diagnosed with homocystinuria. The patient was given a methionine-restricted diet, but a diet consisting from a rich content of cysteine, plus pyridoxine (vitamin B_6) and folic acid was initiated.

Discussion

The most frequent cause of homocystinuria is cystionin B-synthetase deficiency (2). The infant appears normal during labor, and clinical findings may be non-specific at the infancy, however, development and growth retardation may be present. The diagnosis is mainly determined after 3 years of age by seeing ocular lens sublocation (ectopia lentis) (2,3). By a certain period, miscellaneous variations may develop in patients, who involve the eye, circulating system, central nerveous system and bones. Several ophthalmologic problems such as ectopia lentis, cataract, severe myopia and iridodonesis, glaucoma, retinal separation and eye problems related to optic atrophy may be occurred (1,2,4,5). The complaints of our case were

compatible with the literature and started at age 3. The patient suffered from a cataract at the left eye, which spontaneously developed when the patient was approximately 6.5 years old; however, other ophthalmologic conditions that are seen in homocystinuria were absent.

Patients with homocystinuria can be more tented to thrombo-embolic events. Both large and small veins may be involved, and specially brain vessels are effected and the condition can be seen at any age (6). As a result of secondarily increased thrombocyte adhesion at high homocystine levels and modifications that formed in the vessel wall due to high levels of homocystine, optic atrophy, core pulmonale and severe hypertension which are severe sequels of thrombo-embolism can be observed (1,2,7). A Marphan syndrome-like appearance, arachnodactyly, scoliosis, pectus excavatum or carinatum, genu valgum, skeletal abnormalities such as high palate and especially spinal osteoporosis is frequent and are the main radiological finding for homocystinuria (1,8). In line of the literature, our case had core pulmonale, hypertension, purpura fulminans and kyphosis supports the diagnosis of homocystinuria. The diagnosis of homocystinuria can be determined by detecting methionine level in the plasma or urine and/or an increase in homocystine. Cysteine is totally absent in the plasma or may have decreased. For a definite diagnosis, enzyme assay in lymphocytes that are stimulated by phytohemaglutinin or in fibroblasts, which were cultivated must be present in the liver biopsy sample (1). In our case no any enzyme assay in the liver biopsy or lymphocytes were performed, however, plasma homocystine level was found high and then the patient was diagnosed with homocystinuria.

Patients who responded well to a high dose vitamin B_6 (200-1000 mg/day) treatment regime will dramatically improve (1,9). In some patients, folate deficiency may be the number one responsible factor, whereas in addition folic acid (1-5 mg/day) should be administered to patients who failed to respond to the vitamin B_6 therapy. Furthermore, a diet comprising from a metionin-restricted but rich from cysteine diet can be given. Betain (trimethylglycine, for children 200-250 mg/kg/day, for adults 6-9 g/day) may be benefit by providing the formation of metionin from homocystine (1,10).

Consequently, on account of the case we would like to emphasize homocystinuria should be considered in cases of cataract, systemic hypertension and purpura fulminans.

Tek taraflı katarakt, sistemik hipertansiyon ve purpura fulminans ile seyreden bir homosistinüri olgusu

Özet

Homosistinüri klininiğinde iskelet, beyin, göz ve vasküler sistem tutulumu görülebilir. Biz ateş, el ve ayaklarda ödem, ellerde morarma şikayetleri getirilen ve takiplerde homosistinüri tanısı alan 7 yaşında erkek olgu sunduk. Bu vaka dolayısı ile katarakt, sistemik hipertansiyon ve purpura fulminanslı hastalarda homosistinürinin düşünülmesi gerektiğini vurgulamak isteriz.

Anahtar kelimeler: Homosistinüri, olağandışı tutulum, çocuk

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