Case report

Homocystinuria masquerading as vitamin B12 deficiency

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Abstract

Background: Homocystinuria is a rare metabolic disorder charcterised by excess homocysteine in the urine. Vitamin B12 deficiency has diverse cutaneous, nervous and ophthalmic manifestations. **Objective**: To report a case of homocystinuria masquerading as vitamin B 12 deficiency. **Case**: We hereby are presenting an interesting case of a 4 year old boy who was being treated for Vitamin B 12 deficiency on the basis of history of delayed milestone, abdominal pain and hyperpigmentation of skin which was diagnosed as homocystinuria. **Conclusion**: It is important to carry out ophthalmological examination in every case of megaloblastic anemia if associated with blurring of vision and mental retardation.

Key-words: Homocystinuria, vitamin B12 deficiency, lens subluxation, mental retardation.

Introduction

Vitamin B 12 deficiency is an important cause of megaloblastic anemia, skin hyperpigmentation, vitiligo, angular stomatitis, hair changes, peripheral neuropathy, subacute combined degeneration of the spinal cord and psychosis (Fenton & Rosenberg, 1995; Devalia, 2006). We report case of a four year old child with vitamin B-12 deficiency who was diagnosed as a case of homocystinuria when he was referred to us in eye OPD for blurring of vision.

Case report

A 4-year-old boy was admitted in pediatric department of our hospital with chief complaints of abdominal pain and vomiting for 4 days. There was a history suggestive of delayed milestones of development since birth, along with history of generalized increased pigmentation of skin and mucus membrane of oral cavity for past three years. On general physical examination, the child had streaky thin yellow hairs and his gait was suggestive of genu valgum. Examination of respiratory, abdominal and cardiovascular systems was normal. On the basis of history of delayed milestone, abdominal pain and hyperpigmentation of skin, a provisional diagnosis of Vitamin B 12 deficiency was made.

On further investigation, hemoglobin was 9 gm%, vitamin B12 levels were 100 p mol/L and a peripheral smear revealed megaloblastic anemia. Serum electrolytes, liver and kidney function were within normal limits (sodium-133, potassium-4.5, blood urea-24, serum creatinine-0.6mg/dl, serum bilirubin-0.6mg/dl). His ultrasound abdomen showed mild liver and spleen enlargement. The head MRI showed nonspecific hyperintense foci in the right frontal/ periventricular and in left frontal, subcortical white matter region. The chest X- ray was normal on radiological study. The child was sent for ophthalmic examination for complaints of blurring of vision.

The child's visual acuity was 2/60 in both eyes. Pupils were normal in size and both direct and

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consensual pupillary reactions were within normal. Anterior segment slit -lamp examination revealed iridodonesis. On pupillary dilatation, bilateral inferiorly subluxated lens with zonular dialysis (Figure 1) and phacodonesis were noted. The rest of the central and peripheral fundus examination and optic disc were within normal limits. Refraction showed myopia of -5.5DS OU.

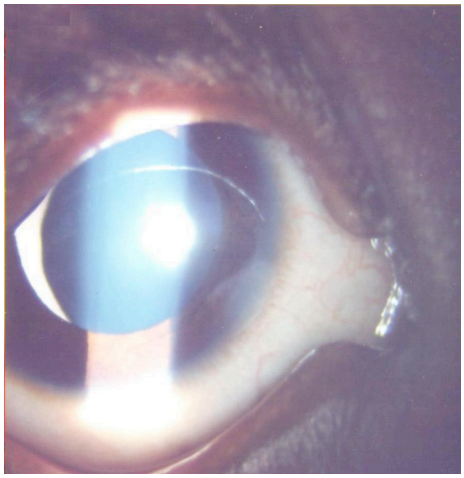

Fig 1: Inferiorly subluxated lens

On the basis of streaky thin yellow hairs, mental retardation since birth, genu valgum in gait with inferiorly sub-luxated lens; a differential diagnosis of homocystinuria was kept in mind, and serum for estimation of homocystine level was sent. It was found to be 225 µmol/l (normal level = 5-15 µmol/l). The key laboratory test for homocystinuria is sodium nitroprusside test which also came out to be positive in this patient. Thus, a final diagnosis of homocystinuria was reached.

Discussion

Vitamin B12 deficiency can present with diverse cutaneous, nervous and ophthalmic manifestations. The cobalamin (B 12) in methyl derivative form is necessary to methylate homocysteine to methionine (Fenton & Rosenberg, 1995). In the absence of B12, there is accumulation of both methylmalonic acid and homocysteine levels, therefore leading to homocystinuria. Homocystinuria is an autosomal recessive disorder of methionine metabolism and is an important cause of dislocated lens in mentally retarded children. A child with this disorder presents with genu valgum, vertebral collapse, osteoporosis and life threatening thrombo-embolic events (Fenton & Rosenberg, 1995; Ubbin et al, 1993). The screening of newborn infants for classic homocystinuria has been performed and the incidence is estimated to be 1 in 344,000 (Ubbin et al, 1993). Early diagnosis of homocystinuria is important to prevent visual and CNS complications.

In homocystinuria, there is deficiency of the enzyme cystathionine beta synthetase. This enzyme converts homocystine to cystathionine in the trans-sulphuration of methionine cycle. The initial presentation of the disease may be ophthalmic. Ectopia lentis is the hallmark, indeed many cases of homocystinuria have been diagnosed because of it, and other frequent ophthalmic findings are iridodonesis and myopia. Zonular and other cataracts are found in one fifth of patients. Lens subluxation occurs in childhood in 90% of the children by the age of 10 years, most often in the inferonasal direction. Zonular and other cataracts are seen in one fifth of the patients. Central Nervous System findings include mental retardation and seizures. The cardinal vascular sign in classical homocystinuria is thromboembolism. The occurrence of thromboembolic events is noted in only one third of patients (Ubbin et al, 1993; Carson et al, 1963). Genu valgum and pescavus are usually the first skeletal signs. In our case, classical features of homocystinuria such as cubitus valgus, high arched palate, mental retardation, iridodonesis, phacodonesis, inferiorly subluxated lens and myopia were found, but an initial diagnosis of B12 deficiency was made due to presence of hyperpigmented skin, abdominal pain and loose motions.

With the prompt and early diagnosis of homocystinuria, the development of ocular, skeletal, intravascular, thromboembolic complications can be arrested and the child can be assured normal intelligence (Carson et al, 1963, Schimke et al, 1965; Mudd et al, 1985). To achieve these the treatment should consist of Pyridoxine, folate,

methionine restricted, cysteine supplemented diet, and Betaine (Carson et al, 1963 Chandler, 1964; Burke et al, 1989). Combined pars plana vitrectomy with lensectomy is the treatment of choice (Schimke, 1965). If the lens surgery is successful, and amblyopia is managed well before and after surgery, the visual prognosis is good after surgery (Chandler et al, 1964). Important diagnostic tests include serum and urine levels of homocysteine. The cyanide nitroprusside test in urine is an important screening test (Ubbink, 1993).

In our case, the child was prescribed glasses and was given a diet chart with folic acid and vitamin B-12 supplements. After 2 months of follow up, the lens was found to be dislocated in anterior chamber in left eye and his vision had dropped. An emergency lens aspiration was done and posterior chamber intraocular lens with capsular tension ring was implanted.

In all cases of vitamin B12 deficiency with mental retardation and visual complaints, homocystinuria must be first on the line of differential diagnosis and a sodium nitroprusside test is warranted. These children must be kept on cysteine, vitamin B6 and B12 rich diet and at each visit an anterior and posterior segment examination along with examination for visual acuity and glaucoma should be done for timely intervention.

Conclusion

It is important to carry out ophthalmological examination in every case of megaloblastic anemia if associated with blurring of vision and mental retardation.

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