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On line submission of article: Case Study

TITLE OF ARTICLE: Case reports of previously undiagnosed cases of homocystinuria presenting as displaced lenses after trivial trauma

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ABSTRACT:

Eye is a window to a rare disease. Two children aged 9 year old male and 5 years old female presented with pain, redness and sudden diminution of vision in right eye and left eye respectively following trivial trauma while playing. On complete ocular examination it was found that in the involved eye of both cases the lens has dislocated anteriorly causing pupillary block glaucoma. Bio-chemical findings include increased levels of homocysteine in blood- 52 μ mol/L in Case-1 and 26.2 μ mol/L in Case-2 (normal levels: 5.9-16 μ mol/L). Both children were not a known case of homocystinuria. They were first diagnosed as a case of homocystinuria by an ophthalmologist.

KEY WORDS: homocystinuria, homocysteine, subluxation

INTRODUCTION:

Homocystinuria is a general term for a group of disorders that cause elevated levels of amino-acid homocystine in urine. These disorders primarily occur because of deficiency of any of several enzymes required for the proper degradation or reformation of an essential amino acid called methionine. Elevated levels of methionine can cause a variety of health problems. The classical homocystinuria due to cystathionine beta-synthase (CBS) deficiency is an autosomal recessive disorder of methionine metabolism that produces increased levels of urinary homocysteine and methionine. Ocular manifestations include progressive ectopia lentis, detachment of retina and significant myopia. Defect in amino-acid metabolism results in brittle zonules that rupture. This allows the lens to displace inferonasally. There is no accommodation and condition may progress. It manifests itself in other organ systems such as vascular, central nervous system, and connective tissue. Skin manifestations include malar flush easily seen after vigorous exercise or after exposure to cold, livido reticularis on the extremities, and thinning and diffuse hypopigmentation of the hair, CNS manifestations include mental retardation, grand mal seizures, depression, chronic behavioral disorders, obsessive compulsive disorders, and

personality disorders. Cardiovascular manifestations include thrombosis of both veins and arteries.^[1,2,3,4]

CASE REPORT:

Case-1: A nine year old male child (Figure-1) presented with sudden diminution of vision in his right eye following trivial trauma with the hand of other child while playing. Visual acuity in the right eye was hand movements which did not improve with pin hole, while in the left eye was 2/60 which improved with pin hole to 6/12. Intraocular pressure on day of presentation was 60mm Hg in right eye and 10mmHg in left eye which was measured with non contact tonometer (NCT). On slit lamp examination of right eye, there was ciliary and conjunctival congestion and full chamber hyphema with dislocated lens in the anterior chamber causing pupillary block glaucoma. In the left eye there was inferiorly subluxated lens (Figure.2). Ultrasound B-scan of both the eyes was normal. Fundus of left eye was normal which was examined with direct ophthalmoscope and 90 D lens on slit lamp biomicroscope. The child had typical associated features of homocystinuria i.e. malar flush (Figure-3), thinning and diffuse hypopigmentation of hair, pes pectus, pes cavus (Figure-4&5), and mental retardation due to which he was not sent to any school for his education. He had myopia of -21 D in his left eye. It was a lenticular myopia, as the axial length of eye and refractive power of cornea was within normal limits. It was not possible to assess the refractive error in right eye due to media opacity. On routine investigations his Hb was 11gm%, fasting blood sugar was 83mg/dl and on urinalysis the nitroprusside cyanide test was positive. Serum homocysteine was 52µmol/L (normal levels: 5.9-16µmol/L). The child was not a known case of homocystinuria. His right eye was operated in emergency under general anesthesia. Pre-operatively, 150ml of 20% Mannitol was given through intravenous route to reduce the IOP. Anterior chamber wash was done to aspirate the blood. Dislocated lens was removed along with the capsule. Vitrectomy was done to remove the vitreous from anterior chamber. Primary Anterior Chamber (AC) IOL implantation with peripheral iridectomy was done. On first post operative day IOP had reduced to 18mmHg. His best corrected visual acuity (BCVA) on follow-up after 3 months was 6/18. Decision of using ACIOL implantation was taken as the parents of the child were unable to take the child to the higher centre for Sulcus Fixation (SF) IOL implantation because of financial reasons. Parents were advised to give methionine-restricted, Cysteine-supplemented diet and pyridoxine in high doses (100 mg tid). Parents of the child were motivated to consult higher center for the other eye with the financial help from local panchayat (local administrative body at village level).

Case-2: A five year old female child (Figure-6) presented with sudden diminution of vision in her left eye following trivial trauma with the hand of other child while playing. Visual acuity in the right eye was 3/60 which improved with pin hole to 6/18, while in the left eye was Finger counting close to face which did not improve with pin hole. Intraocular pressure on day of presentation was 11mmHg in right eye and 45mmHg in left eye which was measured with NCT. On slit lamp biomicroscope examination there was inferiorly subluxated lens in the right eye (Figure-7). In the left eye there was ciliary and conjunctival congestion with dislocated lens in

the anterior chamber causing pupillary block glaucoma (Figure-8). The child did not have other associated features of homocystinuria except ectopia lentis and history of delayed milestones. She had myopia of -22D in her right eye. Refractive error could not be assessed in left eye due to media haze. On routine investigations her Hb was 13gm %, fasting blood sugar was 110mg/dl and on urinalysis, the nitroprusside cyanide test was positive. Serum homocysteine was 26.2 μ mol/L (normal levels: 5.9-16 μ mol/L). **Ultrasound B-scan of both the eyes was normal. Fundus of right eye was normal which was examined with direct ophthalmoscope and 90 D lens on slit lamp biomicroscope.** The child was not a known case of homocystinuria. This case represents an incomplete clinical form of the disease and may suffer from other associated features as she grows older if not managed in time by a pediatrician. Her left eye was operated under general anesthesia. Preoperatively 100 ml of 20% Mannitol was given intravenously to reduce the IOP. Lens was extracted from the anterior chamber. Vitrectomy and surgical peripheral iridectomy was done. IOP on first post operative day was 16mmHg. Parents were advised to give methionine-restricted, Cysteine-supplemented diet and pyridoxine in high doses (100 mg tid). Child was referred to higher institution for secondary IOL implantation in the left eye and further management for right eye.

DISCUSSION:

First case of homocystinuria was reported from Northern Ireland in 1960⁵. The patient was a 7 year old child. Child was mentally retarded with thin and fair hair, pale skin and flushed cheeks. He had arachnodactyly, dolichostenomelia, pes cavus, a high arched palate, and bilaterally dislocated lenses. At age 10 years, the urine of the patient was found to contain a large quantity of homocysteine; urinalysis results for the nitroprusside cyanide test were positive. Mutation in the CBS gene (21q22.3) causes Homocystinuria, which is inherited as autosomal recessive. Cruysberg et al^[6] stated that there was a mean delay of 11 years between the first major signs of the disease and final diagnosis of homocystinuria. Lens dislocation is observed in 85% of the patients with homocystinuria. Myopia in excess of 5D is extremely rare in children under 5 years of age. If ocular fundus of a highly myopic patient shows no clear ophthalmoscopic signs of axial myopia and the corneal curvature is not abnormal, then lenticular myopia due to ectopia lentis should be suspected and searched for. **So an ophthalmologist may be the first** person to diagnose the case of homocystinuria.^[5,6]

Clinical manifestations of homocystinuria vary markedly from severely affected to nearly normal. The clinical characteristics develop after birth and are progressive. On comparing both these cases, the elder child (9 year old), had more clinical features than a five year old child. Ectopia lentis is a zonular disease where alteration of zonular fibres weakens the zonular support of lens which becomes vulnerable to dislocation with trivial trauma. After surgical management both children were put on medical management. Parents were advised to give methionine-restricted, Cysteine-supplemented diet (Max.500mg/day) and pyridoxine in high doses (300-600mg/day). Folic acid and Vit.B₁₂ are used in partial responders. Betaine (3-methyl glycine) is used in pyridoxine resistant patients. Treatment is aimed at maintaining the plasma **homocysteine**

concentration below 11 $\mu\text{mol/L}$ and the plasma homocysteine concentration as close to normal as possible. Serum homocysteine levels are done regularly to monitor response to treatment.^[7,8,9,10,11]

CONCLUSION: Eye is a window to a rare disease. Both children were not known cases of homocystinuria. They were first diagnosed as a case of homocystinuria by an ophthalmologist. In children presenting with dislocated lens after trivial trauma, detailed ocular examination of the uninvolved eye should also be done. Since children are operated under general anesthesia, measures should be taken to prevent development of thromboembolism and use of nitrous oxide should be avoided as it causes increase in the levels of blood homocystine by inhibiting methionine synthase.

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FIGURE-1: Case-1. Nine year old male child with trivial trauma in right eye.

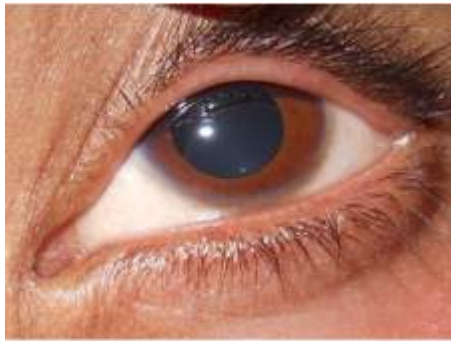


FIGURE-2: Case-1. Inferiorly subluxated lens in left eye.



FIGURE-3: Case-1. Malar Flush.



FIGURE-4: Case-1. Pes pectus



FIGURE-5: Case-1. Pes cavus



FIGURE-6: Case-2. Five year old female child with trivial trauma in left eye



Figure-7: Case-2. Inferiorly subluxated lens in right eye.

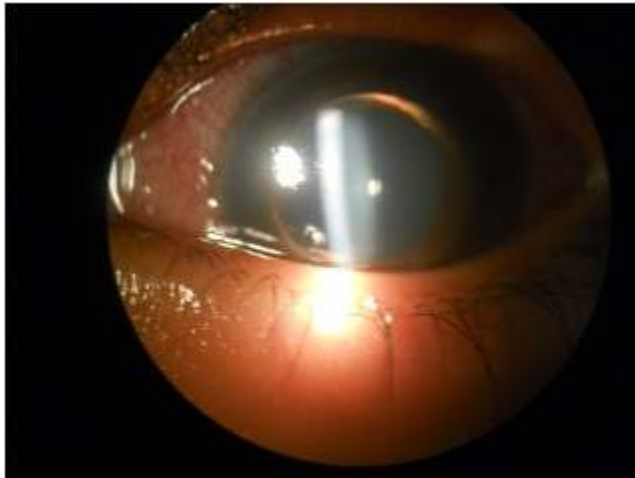


Figure-8: Case-2. Dislocated lens in anterior chamber in left eye causing pupillary block glaucoma.