Case Report

Ocular manifestation in progeria: A case report

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Abstract

Introduction: Progeria also known as Hutchinson Gilford Progeria Syndrome (HGPS) (MIM176670) is a very uncommon fatal genetic untimely aging syndrome. It is characterized by retarded physical development, accelerated degeneration of the skin, cardiovascular and musculoskeletal abnormalities. Other features include prominent eyes, thin nose, small chin and thin lips. Eyebrow hair loss, madarosis and lagopththalmos are the common ocular manifestations.
Case: We report a case of five year old boy with complaints of discomfort in bright light and a whitish appearance in his right eye for two months. He was accompanied by the parents. They complained of loss of eyelashes and eyebrows. In the developmental history he was normal at birth till the age of one year then they noticed gradual hair fall, delayed growth, wrinkling of skin, increase in size of head and thinning of limbs.
Conclusion: This is the first case report from Nepal with the ocular presentation of progeria indicating the role of ocular senescence in patients with Hutchinson Progeria Gilford Syndrome.

Key words: Hutchinson-Gilford progeria syndrome, ocular manifestation, alopecia, premature aging syndrome, progeria

Introduction

Progeria also known as Hutchinson Gilford Progeria Syndrome (HGPS) (MIM176670) is a very uncommon fatal genetic untimely aging syndrome (Gordon et al, 2019; Merideth et al, 2008). It was initially represented with the guide of Jonathan Hutchinson in 1886 and further by Hasting Gilford in 1897 (Gilford, 1904; Hutchinson, 1886). Progeria is acquired from the Greek word where "pro" means "before" and "geras" means "agedness"(Stables and Morley, 1994). It is known to be caused by a single de novo nucleotide replacement at position 1824 (C→T) in the LMNA gene (gene map locus 1q21.2) (Eriksson et al, 2003). Mortality is mostly because of cardiovascular disease with life expectancy of mean age of 14.6 years (Gordon et al, 2014). Incidence is 1 in 4 million (Hennekam, 2006), and prevalence is 1 in 20 million; thus, 350-400 children are estimated living with Projeria worldwide today (Gordon and Gordon, 2014). Usually male are affected and the ratio of male-to-female is 1.5:1 (Sarkar and Shinton, 2001). They often have a normal intelligence, physical appearance in early infancy and affected children with this condition develop severe growth retardation, causing short stature, low weight at about one to two years of age (Sarkar and Shinton, 2001; Ullrich and Gordon, 2015).

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The diagnosis of the HGPS is done clinically with assessment of characteristic features. They are characterized by growth retardation, musculoskeletal, cardiovascular dysfunctions (Stables and Morley, 1994). Common ocular manifestations are eyebrow hair loss, madarosis, prominent eyes and lagophthalmos. In this we report the case of HGPS.

Case Report

Five year old boy from India presented to Mechi Eye Hospital with complaints of discomfort in bright light and a whitish appearance in his right eye for two months. He was accompanied by the parents. Parents gave the history of watering and on and off redness of both eyes since three years. They also complained of loss of eyelashes and eyebrows. In the developmental history he was normal at birth till the age of one year then they noticed gradual hair fall, delayed growth, wrinkling of skin, increase in size of head and thinning of limbs.

The prenatal period was unremarkable and there was a history of normal delivery. His parents were healthy, consanguinity was present and he has 5 unaffected older siblings.

General physical examination at age 5 years showed: height : 2 feet 11 inch (<5thpercentile), weight : 10 kg (<3rdpercentile), head circumference: 49 cm (<5th percentile). Systemic evaluation revealed craniofacial disproportion, prominent scalp veins and superficial veins, open anterior fontanelle, alopecia, prominent ears with nonappearance of ear lobes, thin and high-pitch voice, nail dystrophy, thin limbs, small irregular teeth, thin lips, beaked nose, lack of subcutaneous fat, wrinkled and thin 'sclerodermatous' skin, wide-based gait, prominent stiff joints. X-ray hand showed radiolucent terminal phalanges. ASD seccundum with left to right shunt was indicated by echocardiography.

His distance and near visual acuity was 20/20 and N6 respectively in both eyes. Head posture was normal with excessive wrinkling of forehead skin and superior sulcus deformity. There was loss of eyebrows and eyelashes. Eyeballs were prominent and hertels showed no significant proptosis. Inter canthal distance was 25mm and outer canthal distance 58 mm. Inter- pupillary distance was 45.5 mm with monocular pupillary distance right eye 22.5mm and left eye 23 mm. Horizontal fissure length was 24 mm, Palpebral fissure height 8 mm. Lid Lag was present and the amount of Lagophthalmos was 2 mm. Pupillary reaction was normal. Eye was orthophoric, extraocular movement was full in all gazes and syringing was patent in both the eyes. Schirmer II reading was Right Eye 5 mm, Left Eye 6 mm which shows dry eyes.

Slit Lamp Examination showed corneal opacity (2×2mm) in the peripheral cornea in the right eye. Rest other findings and fundus examinations were within normal limits. We have managed this case with topical lubricating drops, antibiotic ointments and lid taping was advised at bed time as the patient had lagophthalmos. With all these clinical presentations and findings the child was diagnosed as HGPS.

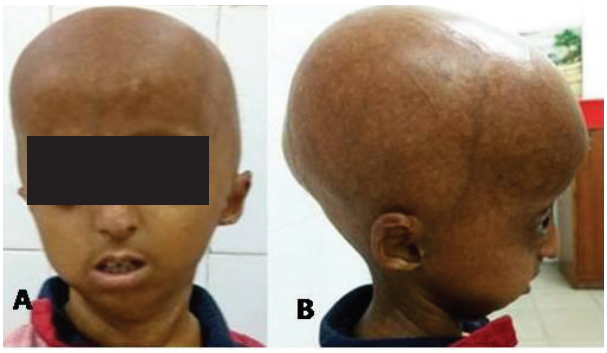

Figure 1: External photograph of patient showing disproportionate small face in contrast to the head, micrognathism, thin lips, beaked nose (A) and alopecia, protruding ears with nonappearance of earlobes, prominent scalp veins (B)

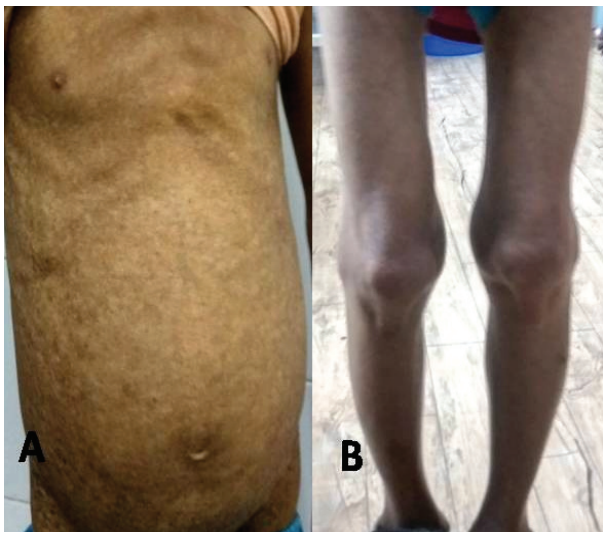

Figure 2: Thin and wrinkled pigmented 'sclerodermatous' skin, lack of subcutaneous fat (A). Thin limbs, prominent and stiff joints, wide-based gait (B)

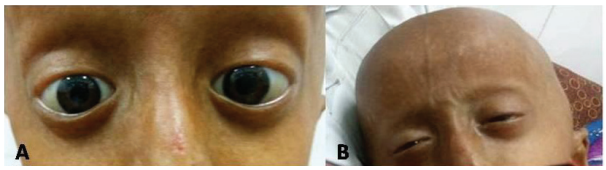

Figure 3: Superior sulcus deformity, loss of eyebrows and eyelashes, prominent eyes (A). Lagophthalmos (B)

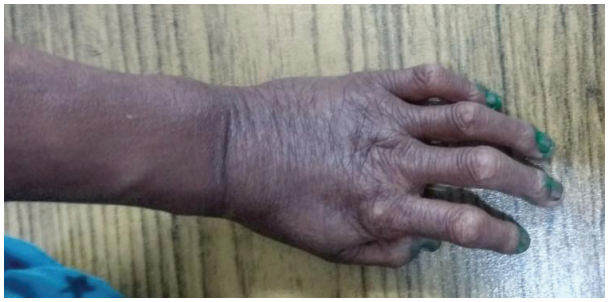

Figure 4: Prominent metacarpophalangeal joints, interphalangeal joints with lack of subcutaneous fat, sclerodermatous skin and nail dystrophy

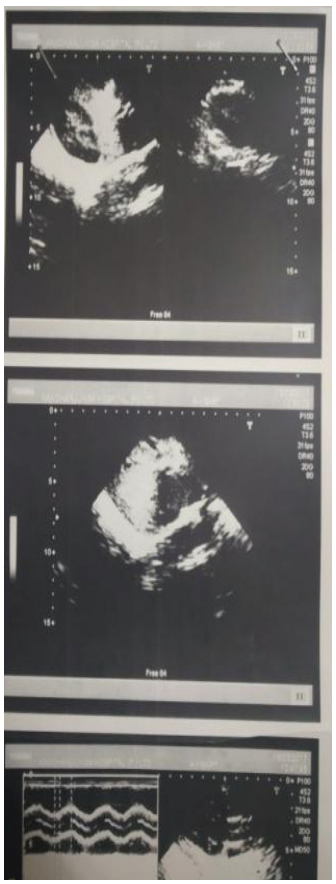

Figure 5: Echocardiography showing ASD seccundum with left to right shunt.

Discussion

HGPS is a rare fatal genetic premature aging syndrome. Life expectancy is 8 – 21 years with an average of 14.6 years with significant systemic morbidity (Gordon et al, 2014). 97% of reported cases reported Caucasians (Stables and Morley, 1994). Studies have revealed that a sporadic autosomal dominant mutation of the fertilizing sperm or the ovum is often a likely mode of inheritance (Brown, 1987; Brown et al, 1985a; Brown et al, 1985b). Diagnosis is established with the identification of characteristic features and exclusion of other progeroid syndromes (Kliegman et al, 2007). Physical appearance of a child with HGPS is generally known to be normal in early infancy (Sarkar and Shinton, 2001; Stables and Morley, 1994). After one to two years of age children with HGPS commonly have a delayed anterior fontanel closure, short stature and are underweighted due to severe growth

retardation. Half of patients have alopecia and other cutaneous abnormalities. Skin appears thin, atrophic and pigmented. Frontal and parietal bossing is often in affected patients. Lips are thin and circumoral cyanosis is likely present which indicates plucked-bird-like appearance sign. Common systemic features contain typical facial presentation characterized by a disproportionate small face in contrast to the head, micrognathism, dental abnormalities and crowding, delayed dentitions, beaked nose, prominent eyes and scalp veins, loss of subcutaneous fat giving the wrinkled skin, nasolabial circumoral cyanosis, generalized alopecia, eyebrow hair loss and loss of eyelashes (Merideth et al, 2008). In our case study we had similar ocular features like other reported cases (Eriksson et al, 2003; Hennekam, 2006; Sarkar and Shinton, 2001; Stables and Morley, 1994; Chandravanshi et al, 2011). Ocular features of HGPS may have eyelid deformities like senile ectropion, lagophthalmos, ptosis with Marcus-jaw winking phenomenon, bands of skin from upper eyelid to cornea (Hennekam, 2006). In additional, they might have different type of keratopathy, dry-eye syndrome, iridocorneal touch, corneal clouding and opacities, lens opacification, nystagmus, refractive error, strabismus, retinal angiosclerosis, narrowing and tortuosity of retinal arterioles (Hennekam, 2006). Chandravanshi et al. also reported poor pupillary dilatation, decrease of horizontal palpebral fissure length, superior sulcus abnormality, lid retraction and lid lag in depression (Chandravanshi et al, 2011). Narrowing of horizontal palpebral fissure and reduced inner and outer canthal distance and decreased interpupillary distance is likely due to undeveloped facial skeleton (Hennekam, 2006). Pseudoproptosis is possibly due to lid retraction (Hennekam, 2006). Superior sulcus deformity is caused by lipodystrophy of the orbital fat. Patients can experience significant ocular morbidity and vision loss due to exposure keratopathy and nocturnal lagophthalmos. They are significant factors to the ocular surface disease, with corneal limbal stem cell deficiency and induction of inflammatory mediators possibly contributing factors (Mantagos et al, 2017).

Our case have systemic findings like craniofacial disproportion, prominent scalp veins, open anterior fontanelle, protruding ears with absent ear lobes, thin and high-pitch voice, small irregular teeth, thin lips, beaked nose, thin limbs, prominent and stiff joints, nail dystrophy, wide-based gait, generalized alopecia, lack of subcutaneous fat, sclerodermatous skin, prominent superficial veins. Patients with HGPS are highly prone for developing complications due to dry eyes. So they should undergo a detailed ocular examination at presentation. Ocular lubrication should be done aggressively and lid tape must be used at bedtime. Our objective of this case report is to describe the ophthalmologic clinical features of HGPS and share our clinical approach to the management of ocular surface disease.

Although urine test, lipid profile, radiological images should be done to rule other differential diagnosis of HGPS, it could not be done due to patient's economic constraints and we lose the follow up of patients. Clinical highlights assist for diagnosing HGPS as there is no single demonstrative test. However, increased urinary secretion of hyaluronic acid (10 – 20 times greater compared with controls) had been shown and may account for the phenotype of HGPS (Brown, 1992; Tokunaga et al, 1978; Zebrower et al, 1986). Also mRNA level and levels of elastin production at the protein is increased in progeroid skin fibroblasts (Sephel et al, 1988). This combination are seen with HGPS which helps to differentiate from different other similar progeroid syndromes, for example, Wiedemann-Rautenstrauch syndrome, Werner's syndrome, Oculomandibulofacial syndrome, Cockayne'ssyndrome, Rothmund-

Thomson syndrome, mandibuloacral dysplasia, metageria and acrogeria (Sarkar and Shinton, 2001; Stables and Morley, 1994; Dyer and Sinclair, 1998).

Conclusion

Ophthalmic manifestation like madarosis, pseudoproptosis, deep superior sulcus, lagophthalmos, decreased ophthalmic measurements like inter canthal distance, inter pupillary distance and palpebral fissure height, lid lag, lagophthalmos and ocular surface disorder was seen in this case. Ocular dryness and exposure keratopathy can be vision threatening so ocular lubrication and regular eye checkup is advised. As this disease is very rare, it's ocular and systemic manifestation has been less reported. Although it had similar features like other reported cases, this type of case is first to be reported in Nepal.

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