

Anterior lenticular opacities in Costello Syndrome

Anchal Thakur^a, Vishal Thakur^b, Tripti Choudhary^a, Rahul Mahajan^b, Ashish Kulshrestha^a, Amit Gupta^{a,*}

^a Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh, 160012, India

^b Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

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ABSTRACT

Purpose: A case of anterior lenticular opacities in a patient of Costello Syndrome is reported.

Observations: Bilateral anterior capsular plaque along with anterior lens opacities (Anterior Segment Optical Coherence Tomography) has been demonstrated in a patient of Costello Syndrome presenting with atopic dermatitis.

Conclusions: All patients with Costello Syndrome require a detailed anterior segment examination and a close follow up, as even minute lenticular opacities cause visual impairment leading to amblyopia and may require an early surgical intervention.

1. Introduction

Costello syndrome is a rare congenital malformation characterized by growth retardation, characteristic facies, skin laxity, and developmental delay.¹ Most of the children are diagnosed clinically when they have the aforementioned group of signs or symptoms. The reported prevalence all over the world is 1 in 300,000. The diagnosis is confirmed by identification of an HRAS mutation; which is present in more than 80% patients of this syndrome. Ocular findings in these patients include nystagmus due to delayed visual maturation, strabismus and myopia. We report for the first time lenticular changes in a patient of Costello syndrome who presented with severe atopic dermatitis.

2. Case report

A 14-year-old female presented with complaints of severe itching all over body and eczematous lesions predominantly over flexures since early childhood. Past history revealed that the patient had delayed milestones. On general physical examination, patient was short statured and had a distinctive coarse facial features (Fig. 1A) with unusually curly hair, sparse hair on the front (anterior) of the head, low-set ears with large, hemangioma over right eyebrow, thick lobes; unusually thick lips; a large, depressed nasal bridge and abnormally wide nostrils (nares). Cutaneous examination revealed few skin coloured papules around the upper lip above the vermilion border. Skin over the dorsum

of hands and feet were thickened (Fig. 1B) with diffuse palmoplantar keratoderma, deep palmoplantar creases (Fig. 1C) and pachydermatoglyphia (thick dermatoglyphics) (Fig. 1D). Cutaneous papillomas were present over the nape of neck along with acanthosis nigricans (Fig. 1E). Eczematous plaques were present in the cubital and popliteal fossa and lichenification over the upper and lower extremities. Patient was given prednisolone 20 mg/day and topical steroids and tacrolimus 0.1% ointment for her eczematous lesions, which improved partially after 2 weeks of treatment. Steroids were tapered gradually and she was started on azathioprine 50mg/day along with topical steroids, tacrolimus and oral antihistamines for long-term remission of disease. Her cardiac, neurological and endocrine evaluation was normal.

On ocular examination, her unaided visual acuity was 20/80 in right eye and 20/70 in left eye. The patient had a horizontal jerk nystagmus with right eye exotropia. Corrected distance visual acuity was 20/40 in the right eye with -1.5 D sphere and 20/30 in the left eye with -1.5 DS sphere. On dilated slit lamp examination, the cornea was clear and the anterior chamber was quiet in both the eyes. The intraocular pressures were normal. There was presence of a linear central 2mm capsular opacity along with a speck of nuclear opacity in the right eye (Fig. 2A). The left eye examination also revealed small wool like central capsular opacity with a speck of anterior lenticular opacity (Fig. 2B). The fundus examination was unremarkable.

Swept-source optical coherence tomography (SS-OCT) showed a plaque like deposit on the capsular surface of both the eyes. Also we

* Corresponding author.

E-mail addresses: thakur_anchal@yahoo.co.in (A. Thakur), amitguptaeye@gmail.com (A. Gupta).

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Fig. 1. A. Clinical picture of the patient showing coarse facial features along with low set ears, hair on the forehead, hemangioma over the right eyebrow, depressed nasal bridge and unusually thick lips. B. Clinical picture of abnormally thickened skin over the dorsum of both the hands. C. Clinical image of the planter aspect of the hands showing deep palmoplantar creases. D. Picture (magnified view) of the palmer aspect of the fingers showing pachydermatoglyphia. E. Picture of the nape of the neck showing cutaneous papillomas along with acanthosis nigricans.



Fig. 2. A. Slit lamp diffuse examination of the right eye showing linear capsular plaque along with a small lenticular opacity. B. Slit lamp diffuse examination of the left eye showing round capsular plaque along with a wool like central lenticular opacity.

could see anterior nuclear opacities, which were present in the adult nucleus (Fig. 3A and B). Corneal topography parameters as seen on Pentacam HR (Oculus Surgical, Inc., Germany) were normal. Since the patient had no visual complaints, the patient was advised to follow up for ophthalmic evaluation every 3 months.

On molecular testing, a mutation in HRAS with p.Gly 12 serine alteration, variant c.34G>A at exon 2 location was detected confirming the diagnosis of Costello syndrome.

3. Discussion

Costello syndrome, first reported in 1971, is a RASopathy caused by germ-line mutations in HRAS gene, located on chromosome 11p15.5. Approximately 80% mutations result in p.G12S missense change and is associated with classical phenotype of Costello syndrome as seen in our patient. Second most common mutation is p.G12A which is highly associated with increased chances of malignancies.² Various other mutations have been reported which may be associated with severe fatal

phenotypes while some mutations result only in milder phenotype. Apart from characteristic cutaneous features, Costello syndrome may have cardiac, neurological, musculoskeletal, endocrine, and ocular abnormalities. Cutaneous features include coarse facies with relative macrocephaly, fine, sparse, curly hair, downward-slanting palpebral fissures, low-set ears, broad nasal base and thick lips. Loose redundant skin, cutaneous papillomas, palmoplantar hyperkeratosis with deep creases, skin tags, and acanthosis nigricans are seen commonly.³ Most of these cutaneous findings were also seen in our patient. Cardiac abnormalities include atrial tachycardia or other arrhythmias, hypertrophic cardiomyopathy and thickened mitral valve. Costello syndrome has to be differentiated from Noonan and cardio-facio-cutaneous (CFC) syndrome and cutis laxa. Management of cutaneous manifestations include destructive modalities such as cryotherapy or electrocautery for papillomas. Acitretin has been reported to be effective in palmoplantar keratoderma. Topical or oral retinoids may be tried in acanthosis nigricans also. Associated eczema should be treated with adequate emollients, topical or oral steroids and antihistamines.

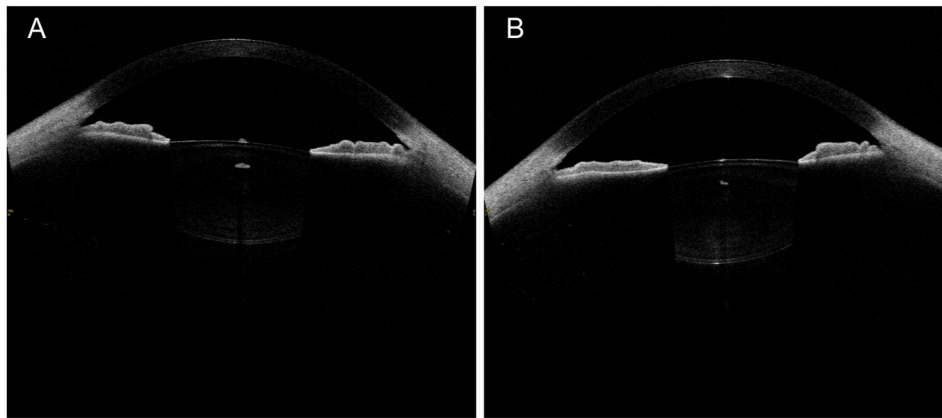


Fig. 3. A. Swept-Source OCT of the right eye showing anterior capsular plaque along with opacity in the anterior part of the lens. B. Swept-Source OCT of the left eye showing anterior capsular plaque along with opacity in the anterior part of the lens.

Children with Costello syndrome can have varied ocular findings. Studies have reported nystagmus, myopia, esotropia as well as an association of keratoconus with this syndrome.⁴ Decrease in visual acuity can be due to multiple aetiologies or a combination of all. Moreover these patients have developmental delay, which can lead to optic nerve hypoplasia leading to a significant decrease in vision. Lenticular opacities in these patients have not been reported till date.

Congenital and developmental cataracts encompass a broad spectrum of lens opacities in children. Out of these, anterior lens opacities (ALO) are found in 3–14% of pediatric patients.⁵ About half of anterior lens opacities are less than 1mm in size and do not contribute in decrease in vision. Our patient had two types of opacities, one on the anterior capsular as a plaque and other as a speck of nuclear opacity. The age of onset can be inferred from the association between the layer of opacity and the fetal nucleus.⁵ In our patient, the nuclear opacities correspond to adult nucleus, thus it may be categorized as a developmental cataract. Studies have shown that the human lens grows throughout life by a process of cell turn over, wherein the anterior layers of lens epithelial cells grow to form a central mass of fibers. Also anterior capsular plaques are present congenitally and it may be assumed that the later may form nuclear opacities during development of the lens.⁶ The etiology behind may be a common mutation in the gene since few studies have reported cataract in patients with RASopathy (Noonan's syndrome).⁷

Patients with Atopic dermatitis alone have an associated cataract with an incidence from 0 to 20%; as reported by many studies.⁸ However, the type of cataract in these patients is usually anterior or posterior sub-capsular unlike in our patient who had anterior capsular plaques as well as nuclear lenticular opacities.^{8,9}

There are no specific guidelines on the management of these opacities; small lens opacities do not progress and are visually non significant, whereas others can be central, involving the visual axis and can cause severe visual impairment leading to amblyopia if not treated at the right age.⁵ We followed up our patient closely as there was presence of a small central cataract, which may grow later in life and may need surgical intervention.

Thus the presence of such opacities in this subset of patients signifies the importance of detailed anterior segment examination and a need for close follow up.

4. Conclusions

Anterior lenticular opacities in a patient of Costello Syndrome are reported. All such patients require a detailed anterior segment examination and a close follow up, as even minute lenticular opacities may cause visual impairment leading to early surgical intervention.

Patient consent

Patient consent was obtained prior to the documentation of this report.

Declaration of competing InterestCOI

None.

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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