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CASE REPORT

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Case series of intraorbital colobomatous cysts with anophthalmos/microphthalmos spectrum: a rare diagnostic conundrum simplified

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Abstract

Background Anophthalmos/microphthalmos spectrum is a rare congenital eye disorder and concurrence of a cystic intraorbital lesion is even rarer. Every so often it presents as a diagnostic enigma for the clinician as well as radiologist. The occurrence of anomaly is linked with early intraembryonic insult and is closely linked with neuroectodermal development of the eyeball. There is a wide range of differential diagnoses for the intraaorbital cysts associated with microphthalmos cases ranging from colobomas to teratomas. The radiological findings in the coloboma gamut are poorly understood with a paucity of the literature regarding the same. Early and correct diagnosis is imperative for the proper management of the patient.

Case presentation We present the radiological findings in three patients presenting at different ages with a basic approach pattern.

Conclusions Knowledge of the radiological findings in cases of intraorbital colobomatous cysts and associations along with their embryological basis would help in making the correct diagnosis ensuing timely and accurate patient management.

Keywords Intraorbital colobomatous cyst, Anophthalmos, Microphthalmos with congenital cyst, Cystic ocular lesions, Congenital cystic lesion in eye

Background

Colobomatous cyst with congenital anopthalmos/microphthalmos is a lesser known entity that often presents as a diagnostic dilemma for the clinician as well as the radiologist, time and again. These are associated with abnormalities of the palpebral fissure resulting in inadequate diagnosis on clinical examination [1]. Anopthalmos/microphthalmos spectrum represents a continuum of the disorder due to embryonic insult at different gestational age, with more severe abnormalities being the result of the early occurrence of insult [2]. There is a paucity of the literature regarding their imaging appearance leading to misdiagnoses as tumors and teratomatous lesions. Even though the diagnosis can be made at birth or even in utero, many a times the patients present in later stages of life owing to ignorance and later complications. Early and correct diagnosis of the associated neural and intracranial abnormalities help the clinician in prognosticating these patients and deciding the further course of management. Herein, we report imaging findings of three

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such rare cases with varied radiological findings and a simplified stepwise approach to diagnose the same.

Ethical consideration

Well-informed written consent of the patients/patient's guardians was obtained.

Case presentation

Case 1

A 2-year-old male child presented in pediatrics OPD with global developmental delay.

The birth history, antenatal and perinatal history was uneventful without any significant family history. On gross examination, frontal bossing was present with right anopthalmos, left micropthalmos (Fig. 1a) and normal spine. Sensorimotor examination revealed absence of neck holding, poor vocalization, adequate response to auditory stimulus and absence of vision in both eyes. Patient was referred to the Radiodiagnosis Department for MRI brain with both orbits. MRI revealed the presence of a fibrous structure in right anopthalmic intraconal compartment (Fig. 1b), likely representing remnant ocular tissue with normal extraocular muscles. There was grossly dysmorphic small dumbbell--shaped malaligned left eye globe with hypoplastic deformed intraocular lens, small inferomedially positioned fluid

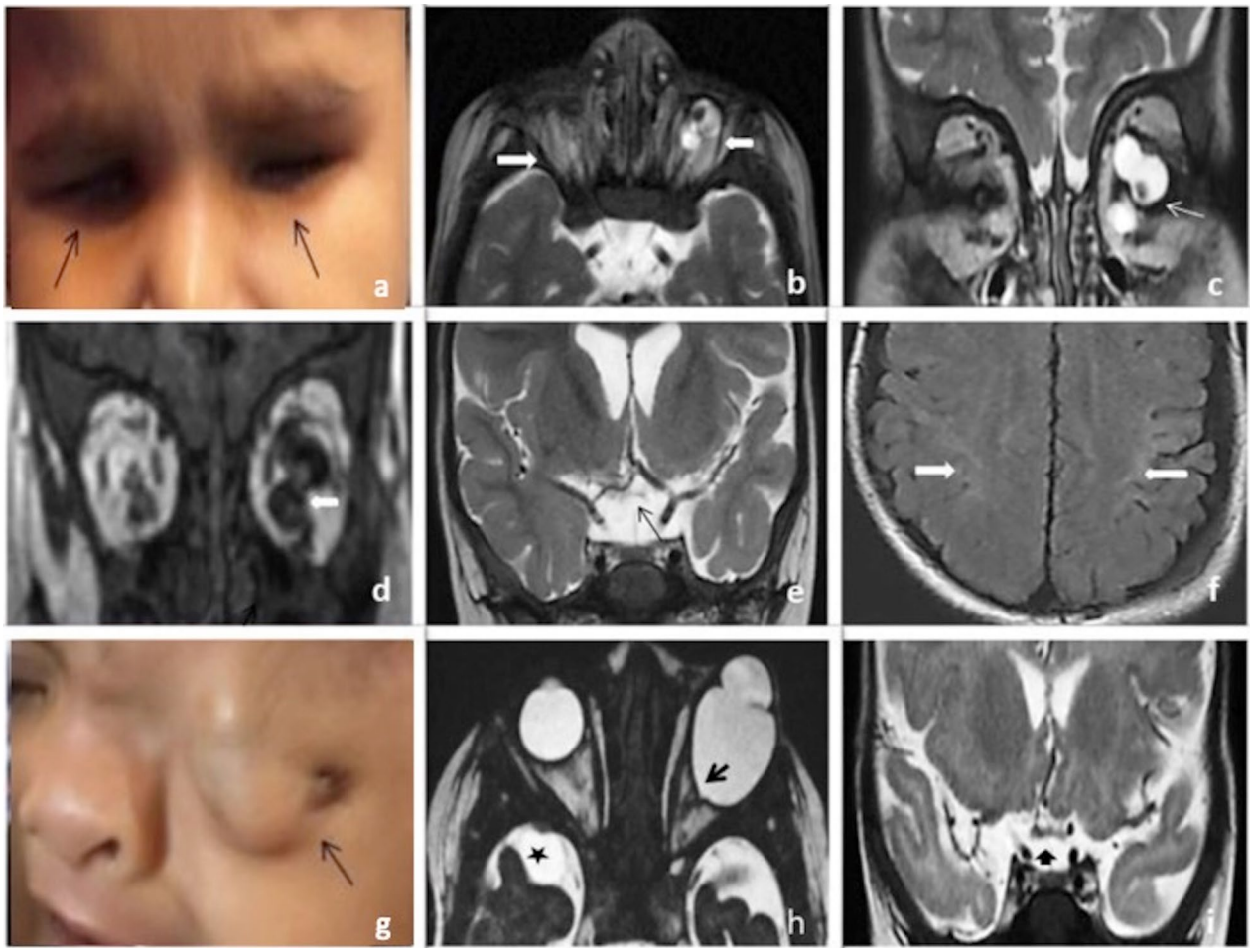

Fig. 1 Case 1: On clinical examination, (**a**) right anopthalmos and left micropthalmos were seen. MRI axial T2WI (**b**) and coronal T2WI (**c**) and coronal T1WI (**d**) showed fibrous structure in intraconal compartment (long solid arrow in b) of right orbit, with grossly dysmorphic small dumbbell-shaped malaligned left eye globe,hypoplastic deformed intraocular lens and small inferomedially positioned fluid intensity colobomatous cyst (small arrow). Coronal T2WI (**e**) showed severe attenuation of right optic nerve with moderate attenuation of left optic nerve and optic chiasma (thin black arrow). Axial FLAIR image (**f**) showed FLAIR hyperintensity in bilateral perirolandic subcortical white matter (solid arrows). Case 2: On clinical examination, (**g**) left-sided cryptophthalmia (thin black arrow) with normal right eye was seen. MRI axial T2WI (**h**) showed enlarged left eye globe with aphakia, a defect in the iridal contour, a focal defect with beaking in the chorioretinal rim of the posterolateral aspect of globe just adjacent to the optic disk (solid black arrow) and a small right anterior temporal lobe arachnoid cyst (black star). Coronal T2WI (**i**) showed normal optic chiasm with minimal thinning of left optic nerve (short small solid arrow)

intensity colobomatous cyst and normal extraocular muscles (Fig. 1b–d). There is severe attenuation of right optic nerve with moderate attenuation of left optic nerve and optic chiasma (Fig. 1e). Mild cerebral cortical atrophy was seen with area of T2/FLAIR hyperintensity in bilateral perirolandic subcortical white matter, bilateral external capsules, periventricular and subcortical white matter in the parietooccipital lobes and along cingulate gyri (Fig. 1f). Final diagnosis was right-sided degenerative anophthalmia, left-sided complex microphthalmia with colobomatous cyst, bilateral optic nerve atrophy and term pattern of perinatal hypoxic injury.

Case 2

A 3-month-old female child presented in pediatrics OPD with left-sided cryptophthalmia since birth. The birth history, antenatal and perinatal history was uneventful without any significant family history. On gross examination, there was left-sided cryptophthalmia with normal right eye (Fig. 1g) add normal spine. Sensorimotor examination was unremarkable. Patient was referred to the Radiodiagnosis Department for MRI brain with both orbits. MRI revealed enlarged left eye globe with aphakia and absence of any focal intraocular mass. A focal bulge was seen along the anterolateral aspect of anterior segment with a defect in the iridal contour, which was isointense to the vitreous humor (Fig. 1h). Focal defect with beaking was also seen in the chorioretinal rim of the posterolateral aspect of globe just adjacent to the optic disk (Fig. 1h). Extraocular muscles were normal. Right orbit showed normal eye globe with normal anterior and posterior segments, no mass and unremarkable extraocular muscles. Mild atrophy of left optic nerve was seen with normal right optic nerve and chiasm (Fig. 1i). A small fluid signal intensity arachnoid cyst was also seen in right anterior temporal lobe (Fig. 1h) Final diagnosis was left-sided cryptophthalmia with congenital anterior and posterior colobomas and anterior segment dysgenesis (presence of aphakia and enlarged eye globe).

Case 3

A 20-year-old adult male presented to ophthalmology OPD with bulging of right eye since childhood and progressively increasing size since last 1 year. On clinical examination, cystic right eye with positive transillumination was noted (Fig. 2a, b). B scan demonstrated anechoic cystic cavity with a small disorganized globe (Fig. 2c, d). Patient was referred to the Radiodiagnosis Department for MRI brain with both orbits. MRI revealed a lobulated intraconal cystic lesion appearing hypointense on T1WI, hyperintense on T2WI, getting partially suppressed on FLAIR without evidence of diffusion restriction or blooming on SWAN. It was communicating with a small round to oval well-defined structure seen in superolateral part of the orbit, closely abutting the cyst, appearing hypointense on T1WI, hyperintense on T2WI/FLAIR, with a focus of calcification and optic nerve seen reaching till its posterior aspect, suggestive of severe microphthalmia with calcified lens (Fig. 2e–h). Final diagnosis was right-sided severe microphthalmia with phthisis bulbi and colobomatous cyst. Patient was treated by aspiration of cyst contents and bleomycin injection (Fig. 2i).

Discussion

In the third week of gestation, the rudimentary eyes develop as two diverticula extending from lateral aspects of diencephalon (forebrain) on either side of the neural groove. These diverticula deepen to form optic vesicle that comes in close contact with the overlying ectoderm forming the lens placode, which further invaginates to form lens vesicle, while the optic vesicle transforms into a goblet-shaped optic cup attached by a hollow optic stalk. The inner wall of the optic cup gives rise to the neural retina, whereas the outer wall gives rise to the pigment layer of retina. Axons from the neural retina grow through the optic stalk to the brain, converting the optic stalk into the optic nerve. Terminal branch of the ophthalmic artery, the hyaloid artery, enters the optic vesicle via a groove in the caudal portion of the optic cup called the optic fissure and traverses the vitreous body to reach the lens. It degenerates during fetal life, and the remainder becomes the central artery of the retina. Mesenchyme coverings the optic cup forms two layers—the thin inner vascular choroid and the fibrous outer sclera. The mesenchyme at edge of the optic cup differentiates to form the iris and ciliary body. Mesoderm adjacent to the optic cup also differentiates in 5–6th weeks to form the extrinsic ocular muscles. The connective tissue components of the extrinsic ocular muscles are derived from neural crest cells. The eyelids arise as folds of surface ectoderm and are fused from the eighth week to about the fifth month [3, 4].

Anophthalmos/microphthalmos spectrum, resulting from an early embryonic insult in the neurodevelopment of eyeball, is significant causes of congenital blindness and can be isolated or syndromic. Several genetic mutations involving *PAX6, SOX2* and *RAX* genes are associated with these conditions [5].

Anophthalmos refers to congenital absence of the eye. Primary anophthalmos is bilateral in approximately 75% of cases and occurs because of failure of optic vesicle development at approximately 22–27 days of gestation. Secondary anophthalmos is lethal and occurs when the entire anterior neural tube fails to develop. Degenerative or consecutive anophthalmos occurs when the optic vesicles form but subsequently degenerate; consequently, neuroectodermal elements may be present in

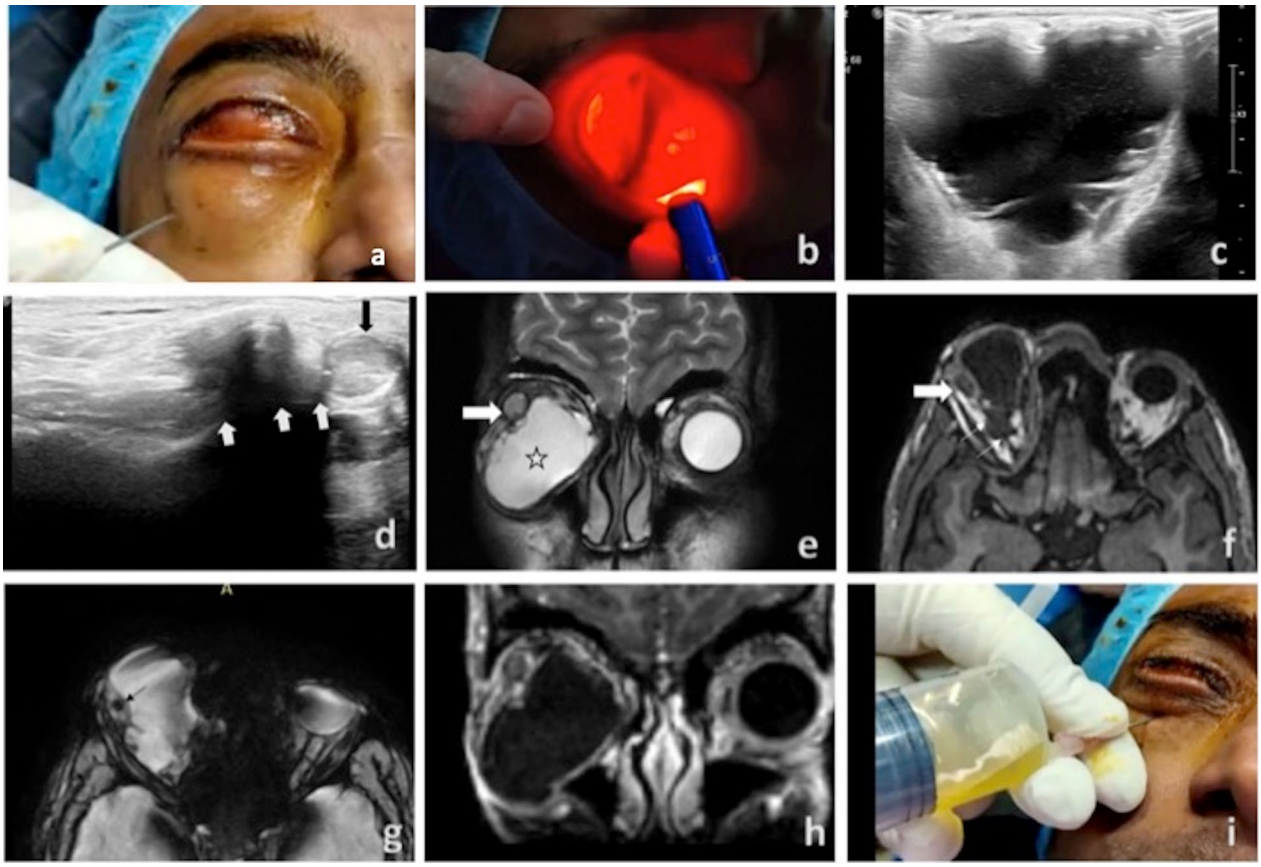

Fig. 2 Case 3: On clinical examination (**a**, **b**), cystic right eye with positive transillumination was noted. B scan (**c**, **d**) demonstrated cystic cavity with lobulated margins, low level internal echoes and few thin partial septations. A small globe (black arrow) was seen in the periphery with optic nerve (bold white arrows) at its posterior aspect. MRI coronal STIR (**e**) images shows intraconal lobulated cystic lesion (star) in right orbit. Small globe (white bold arrows) can be seen in superolateral aspect of the right orbit. A thin optic nerve (thin white arrows) can be traced till the posterior aspect of right globe on Axial 3D FSPGR (**f**). A focus of blooming (black arrow) is seen within the microphthalmic globe on SWAN images (**g**) which likely represents calcified lens. Contrast-enhanced coronal FSPGR image (**h**) shows thin peripheral wall enhancement of the cyst and globe. Cyst aspiration (**i**) revealed clear serous contents

degenerative anophthalmos but are absent in primary and secondary anophthalmos which can be very well delineated on MRI [2]. MRI will further help in assessing the size of the optic nerves and ruling out other associated intracranial abnormalities. As hypoxic injuries constitute a significant prenatal insult, other associated neural differentiation as well as migrational disorders may be seen [6, 7].

An insult to the embryo after outgrowth of optic capsule results in microphthalmos which is defined as a small ocular globe with an ocular total axial length (TAL) 2 standard deviations less than those of the population age-adjusted mean. It is further classified as severe (TAL < 10 mm at birth or < 12 mm after 1 year of age), simple or complex depending on the anatomic appearance of the globe and the degree of TAL reduction [2]. Simple microphthalmos refers to an intact globe with mildly decreased TAL. Complex microphthalmos refers to a globe with anterior and/or posterior segment dysgenesis (developmental abnormalities of the globe anterior/posterior to the lens, respectively) [1]. Severe microphthalmos may be difficult to differentiate from degenerative anophthalmia as they both contain neuroectodermal tissues. The diagnosis is usually based on clinical and imaging criteria [7] (Fig. 3).

Failure of the optic vesicle to invaginate to form the globe results in congenital cystic eye. On imaging, a cystic, sometimes septated, orbital mass is seen in place of the normal globe. The bony orbit is enlarged with widened superior orbital fissure and thinned out optic nerve remnant [2]. The differential diagnosis includes microphthalmia with colobomatous cyst, microphthalmia with cystic teratoma, ectopic brain tissue and meningoencephalocele [6, 8].

Coloboma results from incomplete closure of the embryonic optic fissure, resulting in ectasia and

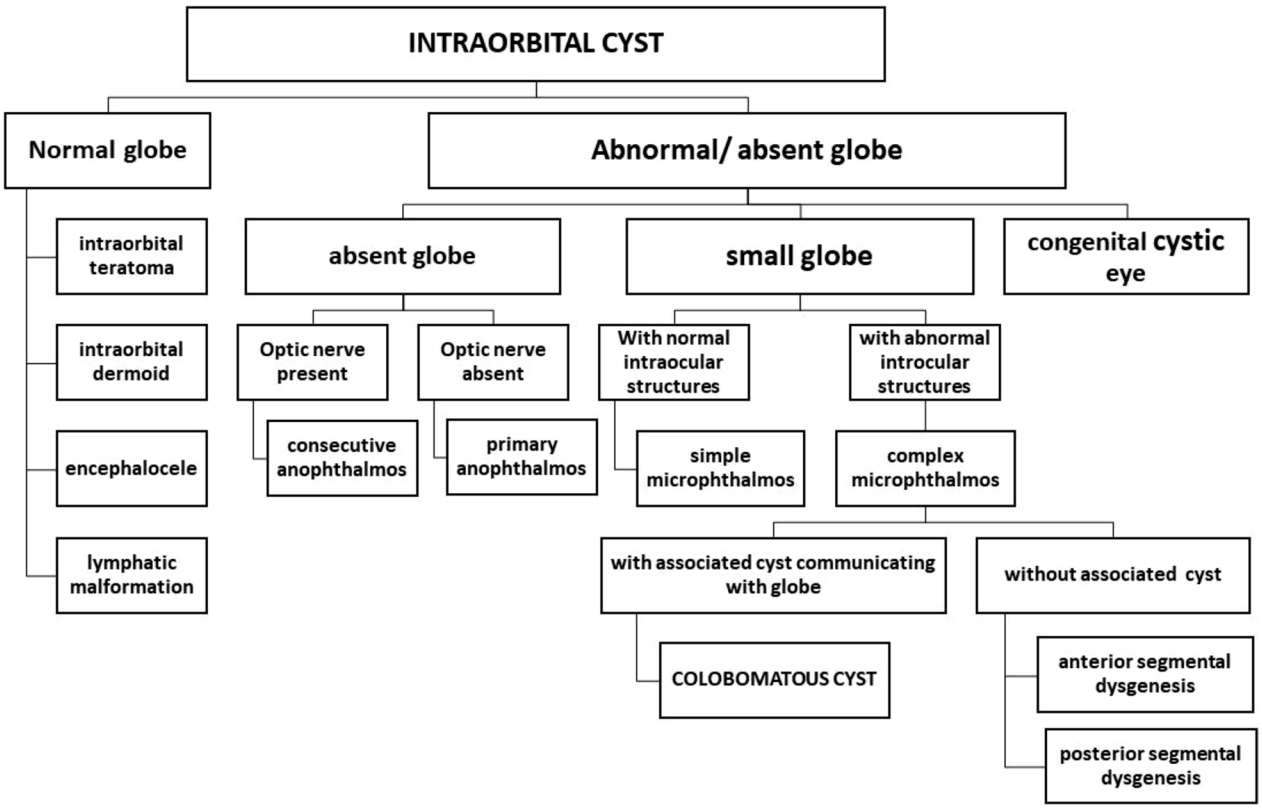

Fig. 3 Stepwise approach to intraorbital cystic lesion

herniation of intraocular neuroectoderm and/or vitreous into the retro-ocular space. A complete coloboma extends throughout the entire eye (from optic nerve to iris), whereas more localized colobomata may occur, as in coloboma of the iris as was seen in our cases. Colobomas may be unilateral or bilateral and can be isolated or syndromic, as seen in CHARGE syndrome (coloboma, heart defects, choanal atresia, retarded growth and development, genital malformations and ear anomalies). Coloboma may exist with microphthalmos or a normal sized eye. On MR imaging, coloboma appears as a focal defect of the posterior wall of the globe. A small defect leads to small excavation along the posterior globe while a larger defect produces a retrobulbar cystic cavity. MRI also helps in localizing the extremely microphthalmic globe in difficult cases where clinical examination is incomplete [2, 6, 8]. In cases of crypopthalmos, ultrasound of the abdomen is also warranted as these may be associated with urogenital abnormalities as is Fraser's syndrome [9]. Thus, a stepwise imaging approach to the intraorbital cystic lesion should be followed to differentiate these cystic lesions from more sinister neoplasms (Flowchart1).

Microphthalmia and anopthlamia are usually managed conservatively using endo-orbital volume replacement with implants of periodically increasing size. This allows growth of the orbit, palpebral fissure and conjunctival cul-de-sac. Severe cases may require orbital osteotomies. Cosmetic surgeries may include conjunctival sac reconstruction and blepharoplasty. Colobomatous cyst is usually aspirated followed by bleomycin injection, as recurrence rate in higher is aspiration alone [5, 7].

Conclusions

Colobomatous cyst with congenital anopthalmos/microphthalmos, an unusual rare presentation consequent to embryonic insult in the neurodevelopment of eyeball, is a significant causes of congenital blindness. A sound knowledge of the embryonic development of the eyeball and stepwise approach in imaging may help us in reaching the correct diagnosis, which may possibly further help in decision making and patient management.

Abbreviations

MRI Magnetic resonance imaging
FLAIR Fluid-attenuated inversion recovery
TAL Total axial length

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Author contributions
Dr. JG and Dr. AR conceived and designed the study, collected data and prepared the manuscript; Dr. JG, Dr. AR, Dr. NB, Dr. RY and Dr. AB reviewed the results and approved the final version of the manuscript.

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Declarations

Ethics approval and consent to participate
Well-informed written consent of the patients/patient's guardians was obtained.

Consent for publication
Consent to publish was obtained from the patient or legal guardian where ever applicable.

Competing interests
The authors declare that they have no competing interests.

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