The Indian Journal of Pediatrics (March 2018) 85(3):217–227
https://doi.org/10.1007/s12098-018-2623-2

REVIEW ARTICLE

Ocular Manifestations of Pediatric Systemic Diseases

Gopal S. Pillai[1] · Natasha Radhakrishnan[1]

Received: 22 March 2017 / Accepted: 8 January 2018 / Published online: 17 February 2018

Abstract
Ocular manifestations that occur directly or indirectly as result of a pathologic process that involves other parts of the body, in a pediatric population, will be discussed here. While a myriad number of systemic conditions have ocular manifestations, its importance cannot be undermined because it has implications for both diagnosis and treatment. Often, the eye findings can give a clue to the systemic diagnosis and at other times, not managing the eye manifestations can lead to irreversible blindness although the systemic condition was treated well. So, it is important for all clinicians dealing with pediatric population to be aware of ocular manifestations of the common systemic conditions. The authors discuss the ocular manifestations of the following systemic conditions: Genetic and chromosomal anomalies, phakomatoses, metabolic disorders, infectious diseases, craniofacial anomalies, muscular disorders, inflammatory disorders and miscellaneous.

Keywords Eye · Ocular · Ophthalmic · Pediatric diseases

Introduction

Eye is a window to the human body. It is an extremely good location to visualise vascular, neural and tissue pathology as we can directly see the blood vessels and nerves. There are many systemic diseases with widespread manifestations in the vascular and neural tree, which can manifest themselves within the eye. Eye examination will very often give a clue to the systemic pathology and can help us in clinching or negating a diagnosis, prognosticate a disease or even grade a disease activity. A simple torchlight and direct ophthalmoscopy can offer a practicing pediatrician a whole new set of findings which can have a bearing on the diagnosis. Eye manifestations in systemic diseases is an exhaustive topic which may need a full text book. But with a practicing pediatrician in mind, authors have tried to showcase the more common eye manifestations and have tried to classify it based on pure practical considerations.

✉ Gopal S. Pillai
gopalspillai@gmail.com

[1] Department of Ophthalmology, Amrita Institute of Medical Sciences and Research Centre, Amrita Vishwa Vidyapeetham, Kochi, Kerala, India

Genetic and Chromosomal Abnormalities

Many of the pediatric genetic disorders have distinctive eye findings that often provide a missing link to diagnosis.

The most widely described of these is the "cherry red spot"- this finding, seen as a dark red spot at the foveola surrounded by yellowish white elevated retina occurs due to the choroid shining through the thinner foveola while the surrounding ganglion cells have accumulations of various metabolic products, the exact nature of which depends on the primary disease [1]. In Tay Sachs disease, it is glycolipid accumulation in the ganglion cells due to deficiency of Hexosaminidase A that causes this appearance in the early years of life itself [2]. The other conditions in which a cherry red spot is seen include GM1 gangliosidoses, GM2 gangliosidoses, Neimann Pick disease, Sialidoses and Galactosialidoses [3] (Fig. 1).

Fabrys Disease

Angiokeratoma corporis diffusum- where there is alpha galactosidase A deficiency has ceramide trihexoside accumulation causing several ocular manifestations. In the cornea, it produces a characteristic whorled pattern called cornea verticillata or vortex keratopathy [2]. Conjunctival and retinal vessels can show tortuosity and dilatation (Fig. 2).

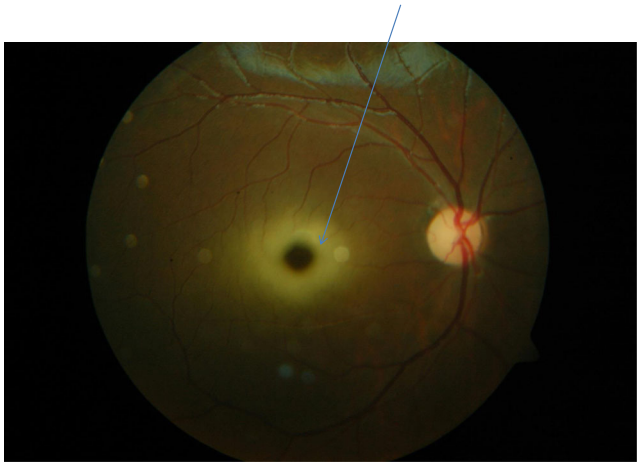

Fig. 1 Cherry red spot

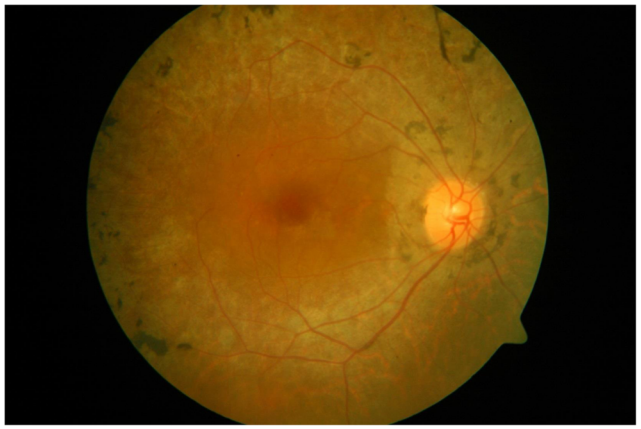

Fig. 3 Retinitis pigmentosa showing arteriolar narrowing, bone spicule pigmentation, waxy disc pallor

Retinitis Pigmentosa Associated Syndromes

Retinitis pigmentosa (RP) is a photoreceptor dystrophy predominantly affecting rods and is characterised by a classic triad of waxy disc pallor, arteriolar attenuation and bone spicule pigmentation. However, the clinical appearance may vary from a mild pigmentary change, then called pigmentary retinopathy to the classic RP appearance [4] (Fig. 3).

Ushers Syndrome

It is the most frequent syndromic form and in this, typical RP is associated with neurosensory deafness. About 14% of all RP cases are Ushers syndrome [5]. Deafness, usually congenital and nonprogressive, may be profound (type 1) or moderate/medium (type 2) or may occur during the first decade and worsens progressively (type 3) [6].

Bardet Biedl Syndrome (BBS)

It is less frequent than Usher syndrome (prevalence 1/150,000) [7]. It is characterised by RP (often of cone-rod dystrophy type) with obesity, mental retardation or mild psychomotor delay, post axial polydactyly, hypogenitalism and renal abnormalities that lead to renal failure. A characteristic fundus appearance called Bulls' eye maculopathy is associated with this condition. Bulls eye maculopathy is also seen in conditions like Juvenile neuronal ceroid lipofuscinoses (Batten Mayou), Hallervorden-Spatz syndrome and chloroquin toxicity [8] (Fig. 4).

Abeta Lipoproteinemia

It is due to an inability to produce chylomicrons and very low density lipoprotein (VLDL) in intestine and liver leading to fat malabsorption and is characterised by acanthocytes in blood

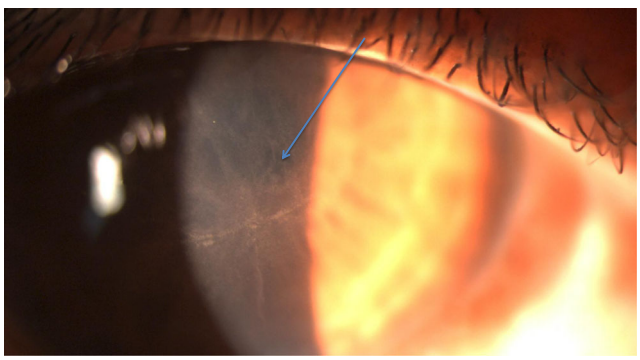

Fig. 2 Cornea verticillata showing filamentous lines on the cornea

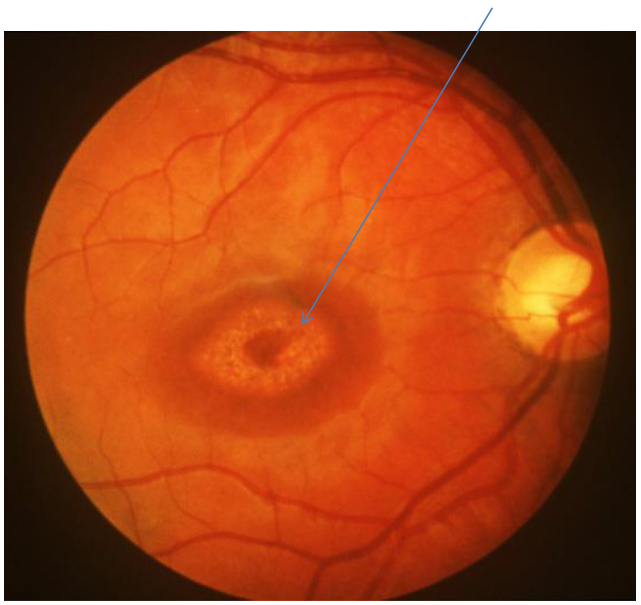

Fig. 4 Bulls eye maculopathy showing the concentric rings at the macula

smear. Failure to thrive, spinocerebellar degeneration and night blindness results, if not treated. Timely intervention with low fat diet and fat soluble vitamin supplementation can prevent progression and blindness [8] (Fig. 5).

Refsums Disease

Refsums disease with night blindness, cerebellar ataxia, peripheral neuropathy, ichthyosis and cardiomyopathy results due to a deficiency of the peroxisomal enzyme, phytanyl CoA hydroxylase causing accumulation of phytanic acid. Fundus has typical RP like picture [8].

Rare diseases with pigementary retinopathy include *Cohens syndrome* with facial dysmorphism, microcephaly, myopia, hypotony and obesity (Fig. 6).

Sjogren Larsson Syndrome

It has typical retinal glistening yellow white dots that are pathognomonic (Fig. 7).

Gyrate Atrophy

Gyrate atrophy due to ornithine aminotransferase deficiency has sharply demarcated areas of chorioretinal degeneration in the first decade with variable visual dysfunction (Fig. 8).

Allagille Syndrome

Allagille syndrome with hepatic cholestasis usually presents with neonatal jaundice. In the eye, there will be posterior embryotoxon, iris stromal hypoplasia, microcornea and sometimes, pigmentary retinopathy, optic nerve dysplasia/drusen and choroidal hypoplasia [8] (Fig. 9).

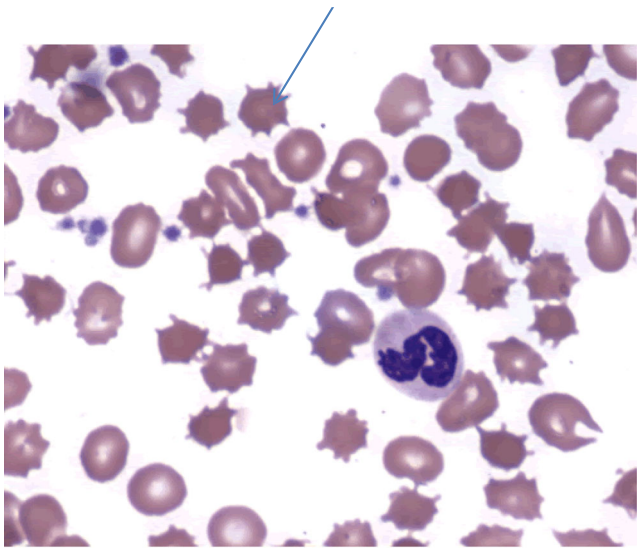

Fig. 5 Acanthocytes

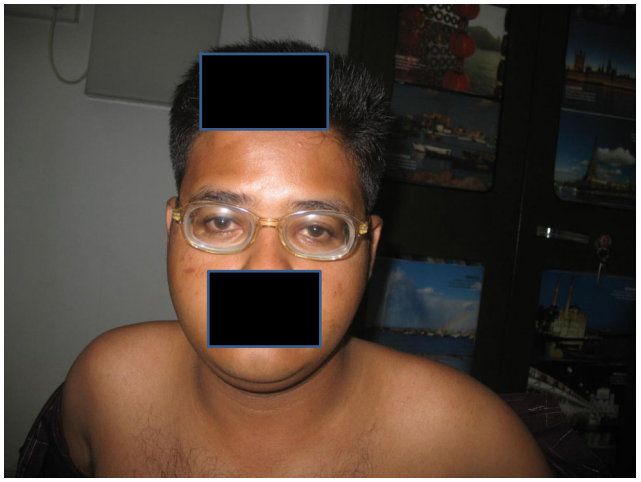

Fig. 6 Cohens syndrome

Chromosomal abnormalities like *Downs syndrome* have associated Brushfields spots (more in Caucasians) cataracts,myopia, nystagmus, strabismus and amblyopia [9].

Phakomatoses

These are a group of disorders, also called neurocutaneous syndromes associated with multiorgan involvement with hamartomas predominantly in the skin, eye and brain. The eye is involved in most of them. They are all autosomal dominant inheritance except Sturge Weber, which is sporadic and Ataxia Telangiectasia, which is autosomal recessive.

Tuberous Sclerosis

Epiloia, Bournevilles disease is characterised by early onset epilepsy, mental retardation and adenoma sebaceum and has characteristic retinal hamartomas called astrocytomas seen in 50% of patients and are bilateral in 1/3rd. They can be a) flat

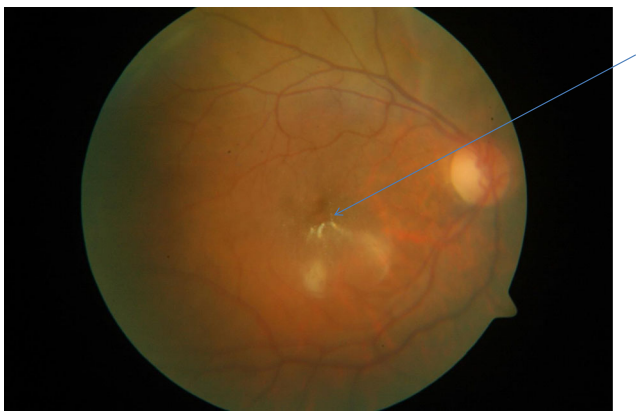

Fig. 7 Sjogren Larsson syndrome has glistening yellow dots at the fovea

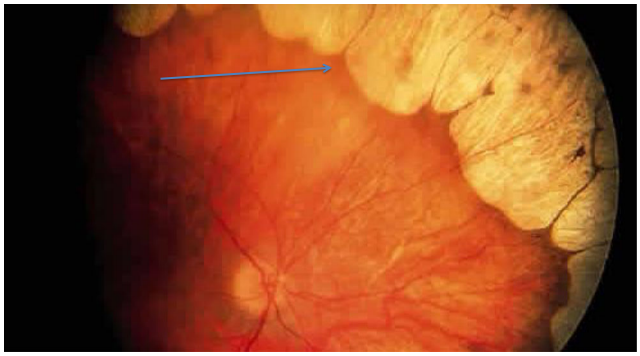

Fig. 8 Gyrate atrophy showing scalloped margins of atrophy

smooth and noncalcified gray translucent lesions (70%) b) elevated multinodular, calcified, opaque mulberry like lesions or c) combination of both. They usually remain static and rarely can cause vitreous hemorrhage. Other retinal findings include chorioretinal, hypopigmented, punched out lesions in the midperiphery in upto 40% patients [10] (Fig. 10).

Neurofibromatoses

Both types 1 and 2 are associated with ocular findings. In type 1, the pathognomonic eye feature is the iris hamartomas called Lisch nodules that are of diagnostic significance and are seen in almost all affected adults [11]. Other findings include plexiform neurofibromas, sphenoid wing dysplasia,optic nerve gliomas and congenital glaucoma especially in the eye with eyelid hamartoma [12]. NF2 can have presenile posterior subcapsular cataracts and combined retinal and pigment epithelial hamartomas [13] (Fig. 11).

Von Hippel Lindau

Capillary hemangiomas of the retina are the common finding in this syndrome. They are most often seen after

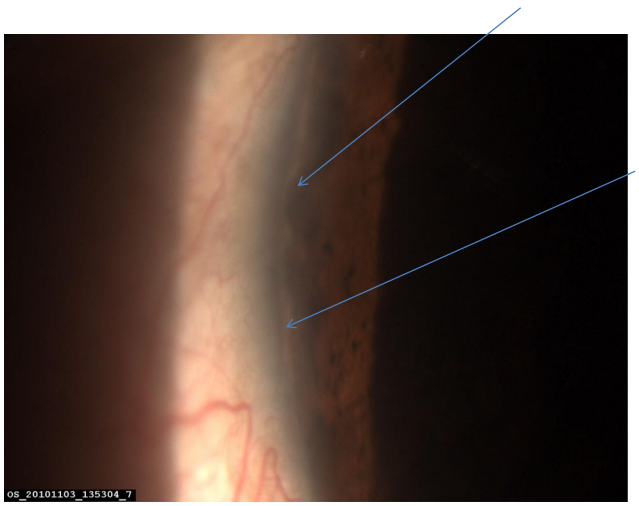

Fig. 9 Posterior embryotoxon

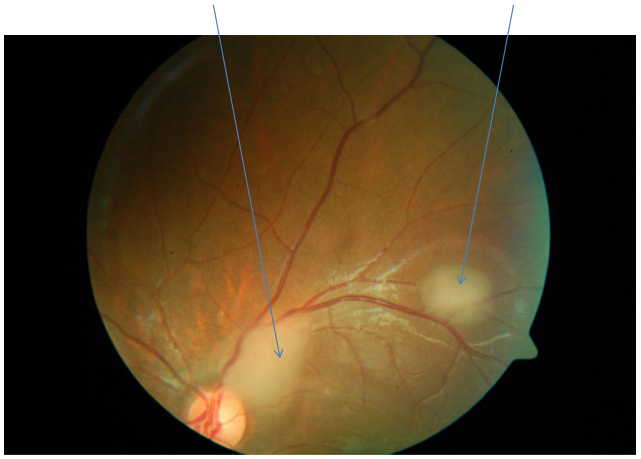

Fig. 10 Retinal astrocytomas

the age of 5 y in the anterior to equator, most commonly in the superotemporal quadrant [14]. They can lead to retinal detachment, exudation and neovascularisation in the late stages. If detected early, they can be treated by laser photocoagulation or cryotherapy (Fig. 12).

Metabolic Disorders

Wilsons Disease

It is an autosomal recessive disorder caused by deficiency of copper transporting ATPase and is characterised by Kayser Flesicher (KF) ring due to deposition of copper in the descemets membrane and subcapsular sunflower cataracts (Fig. 13a).

Galactosemia

These patients develop oil droplet cataracts which are refractive changes in the lens nucleus and look like oil drop – they later progress to lamellar cataracts and then total

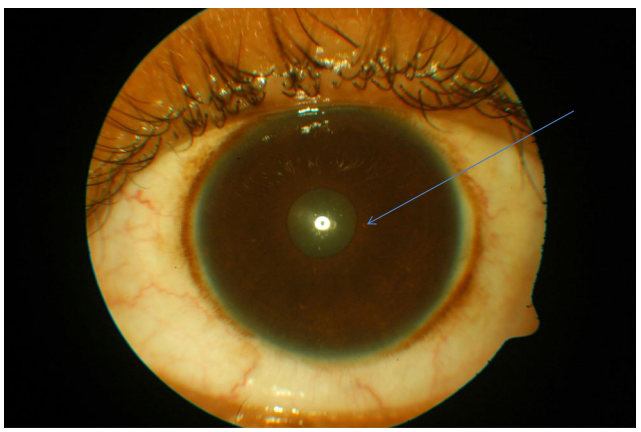

Fig. 11 Lisch nodules

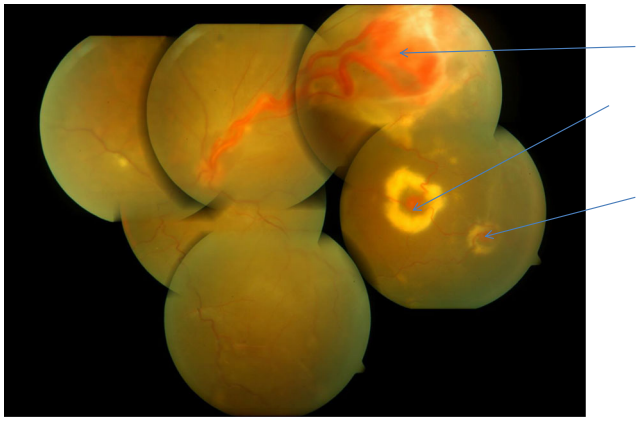

Fig. 12 Capillary angiomas in Von Hippel Lindau with surrounding exudation

cataracts. They maybe reversed if appropriate dietary changes are started [15].

Other conditions with congenital cataracts include trisomy 21, Hallermann Streiff syndrome and Lowes syndrome. The latter also has glaucoma associated with it.

Albinism

This heterogenous disorder of melanin metabolism has important ocular manifestations – Poor visual acuity results due to high refractive errors, delayed visual maturation, foveal hypoplasia and increased iris translucency produces a rabbits eye reflex. They also have visual pathway misrouting with crossed asymmetry in the VEP (Visual evoked potential) [16].

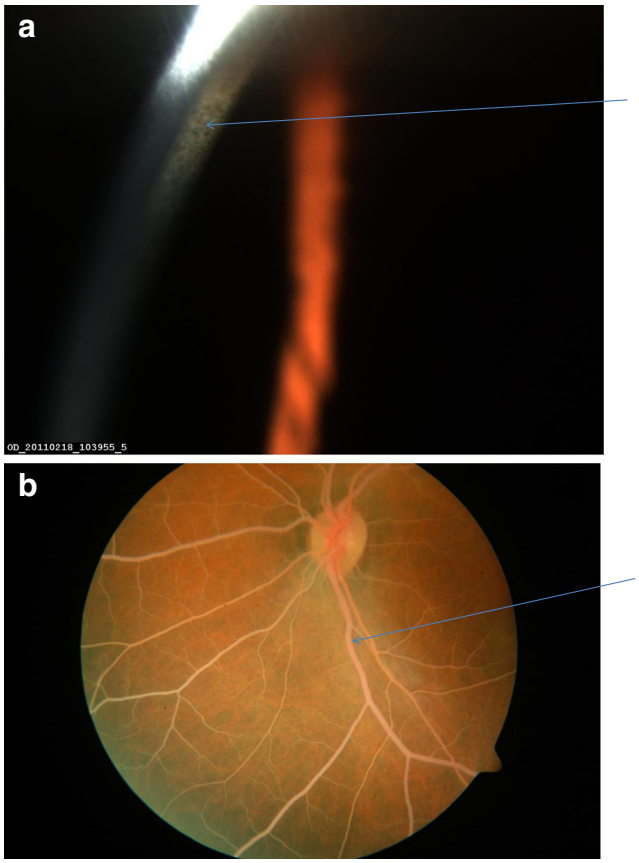

Fig. 13 **a** KF ring. **b** Lipemia retinalis showing the pale pink colored blood vessels

Lipemia Retinalis

A rare retinal manifestation of hypertriglyceridemia-occurs with serum triglyceride levels above 1000–25,000 mg/dl with retinal arteries and veins being creamy white or pale pink in color. The initial changes are seen in the periphery and posterior pole is affected at higher levels. It can be seen in neonates and infants in familial hyperlipoproteinemias I,iii,iv and v and its recognition can help in early detection of the disorder and institution of dietary modification. It does not affect visual acuity (Fig. 13b).

Infectious Diseases

HIV Infection

Incidence of ocular manifestation in HIV is lower in pediatric age group. It can be classified as opportunistic infections like cytomegalovirus (CMV), herpes zoster, toxoplasmosis and non-infectious manifestations [17]. CMV retinitis is usually painless and children can present with advanced retinitis and bilateral involvement. Inflammation is usually minimal unless patient is on highly active antiretroviral therapy (HAART)-then they can develop more inflammatory signs. Toxoplasmosis is the next most common ocular infection in acquired immunodeficiency syndrome (AIDS) [18]. Ocular lesions are commonly due to intrauterine infection or congenital infection. Vitreous inflammation is more common than in CMV retinitis. Other infectious diseases include syphilis, herpes zoster and herpes simplex.

Non infectious manifestations like cotton wool spots and retinal hemorrhages are less common in children less than 8 y. Optic neuropathy, orbital involvement due to malignancies like lymphoma or kaposis sarcoma, infections – bacterial, fungal or parasitic and pseudotumor and cutaneous manifestations like molluscum contagiosum and eyelid verruaccae are also seen [19]. Sjogren like dry eyes, occurs in 2–56% of children and conjunctival and corneal involvement can rarely occur.

Ocular Manifestations of Intrauterine Infections

Rubella

Cataracts are seen in 20–30% of children with congenital rubella syndrome.It is mostly bilateral and rubella virus can be cultured upto four years of age from the cataractous lens. A

pigmentary retinopathy is the most common manifestation which is mottled changes predominantly affecting the posterior pole called salt and pepper appearance. Visual acuity is usually good and ERG and electrooculogram (EOG) are usually normal. Glaucoma is seen in 10% of children [20] (Fig. 14).

Toxoplasmosis

Ocular manifestations of congenital toxoplasmosis include chorioretinitis, microphthalmos, cataracts, panuveitis and optic atrophy. The chorioretinitis is usually bilateral and frequently affects the macula (Fig. 15).

CMV Infection

Ocular manifestations include chorioretinitis, optic atrophy, microphthalmos, and keratitis. It is common among children who were symptomatic at birth than among those who were initially asymptomatic. It is more common among patients born after a primary maternal infection than among those born after a recurrent maternal infection [21].

Craniofacial Anomalies

Crouzon's Syndrome

This syndrome consists of premature craniosynostosis, midfacial hypoplasia and exophthalmos. Exophthalmos is mostly due to orbital shallowing. Orbits are also widely separated with laterally rotated axes. Other facial abnormalities include a flattened nasal bridge, prominent lower jaw and high palatal arch. Exophthalmos may result in corneal exposure. Other ocular associations include spontaneous prolapse of the globe, optic nerve complications, raised intracranial hypertension and V pattern exotropia. Iris coloboma, aniridia, corectopia,

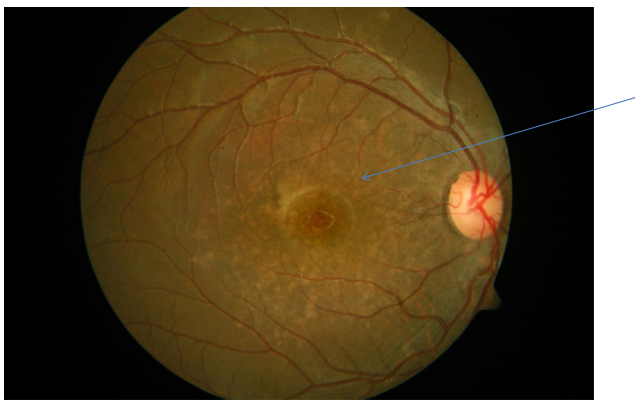

Fig. 14 Rubella retinopathy-salt and pepper changes in the fundus

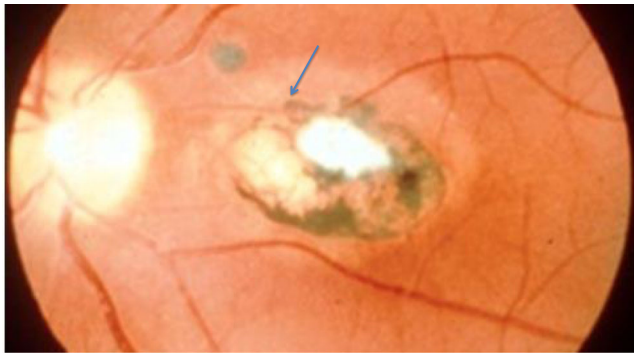

Fig. 15 Congenital toxoplasmosis-punched out scar

microcornea, megalocornea, cataract, Ectopia lentis, blue sclera, glaucoma and nystagmus have also been reported (Fig. 16).

Apert's Syndrome

This condition closely resembles Crouzon's, but is characterised by craniosynostosis, broad thumbs and great toes, symmetrical syndactyly involving the second to fourth or fifth fingers and toes, with fusion of the corresponding nails.The ophthalmic features in Apert's syndrome include proptosis and hypertelorism, but in a milder form as compared to Crouzon's [22]. The palpebral fissures may have an antimongoloid slant. Rare associations that have been reported include keratoconus, ectopia lentis and glaucoma. Optic atrophy may be present (Fig. 17).

Goldenhaar Syndrome

This is a type of clefting syndrome also known as hemifacial microsomia. The expanded Goldenhaar complex includes vertebral, cardiac, renal, an central nervous system abnormalities with severe hydrocephalous and mental retardation. Ocular

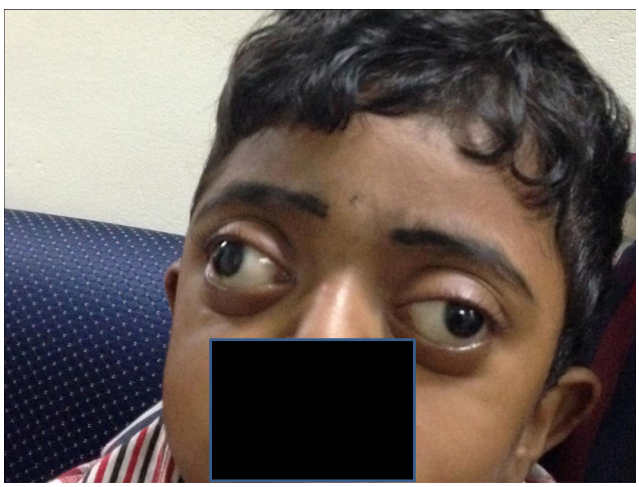

Fig. 16 Crouzons showing proptosis and squint

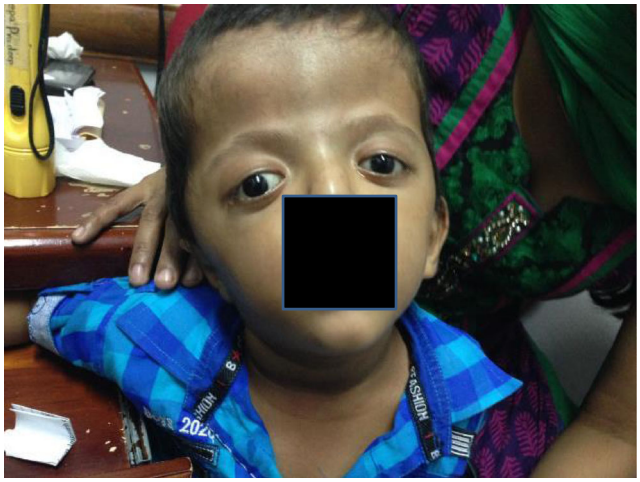

Fig. 17 Aperts showing the antimongloid slant and squint

findings include ptosis, nasolacrimal duct obstruction or fistula and coloboma of the middle third of the upper eyelid which is associated with an epibulbar lesion on the ipsilateral eye. Dermoids are seen commonly, most common site of which is the inferotemporal limbus. Ocular motility syndromes are also common with Duanes syndrome, esotropia and exotropia are commonly seen [23] (Fig. 18).

Treacher Collins Syndrome

Ocular manifestations include antimongloid slant, lower lid colobomas, canthal dystopia, nasolacrimal duct obstruction, and limbal dermoids [24].

Muscular Disorders

Mitochondrial Myopathy [25]

The four most common neurophthalmic abnormalities seen in mitochondrial disorders are bilateral optic neuropathy, ophthalmoplegia and ptosis, pigmentary retinopathy and retro chiasmal visual loss.

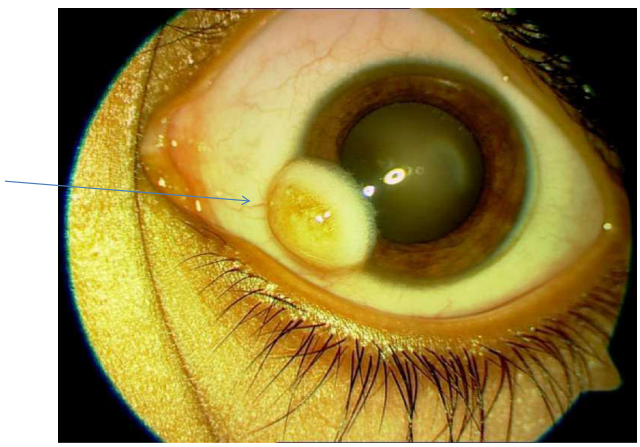

Fig. 18 Epibulbar dermoid just growing into the limbus

Chronic Progressive Ophthalmoplegia (CPEO)

It is the most common ophthalmic manifestation of mitochondrial myopathies. It is characterized by slowly progressive bilateral ocular immobility associated with ptosis. Associated ocular features include optic atrophy, pigmentary retinopathy, corneal changes and cataracts. Kearns-sayre (KSS) syndrome is a subset of CPEO [26].

Pigmentary Retinopathy

Pigmentary changes in the retina may occur in patients with mitochondrial disease. Pigmentary retinopathy is one of the diagnostic criteria in KSS. Pigmentary retinopathy can also occur in patients with mitochondrial disease who does not have CPEO such as MELAS (Mitochondrial Encephalopathy, Lactic Acidosis Stroke) and Leigh syndromes [27].

Retro-chiasmal Visual Loss

Patients with mitochondrial disease may have visual loss not attributable to optic nerve or retinal dysfunctions, but rather due to disruption of the retro-chiasmal visual pathways, thereby resulting in homonymous hemianopic field defects or cortical blindness. The mitochondrial disease most consistently associated with retro-chiasmal visual loss is MELAS.

Myotonic Dystrophy

Extra ocular movement assessment shows Ophthalmoplegia and extraocular myotonia. The ophthalmoplegia consists of limited adduction, described as “pseudo-internuclear ophthalmoplegia.” Extraocular mytonia manifests as slowed and disconjugate saccades. The abnormalities consist of a reduction in saccade peak velocity and increased saccade duration primarily if the eye is fixed on an object for a longer period of time (long interstimulus interval), thus highlighting the phenomenon of myotonia. Pupils show miosis and are slowly responsive to light. Intraocular pressure is usually low and is possibly due to ciliary body detachment. The lids show blepharoptosis and there maybe brow ptosis. Cataract with fine dust like opacities on the outer layers of the lens that are highly colored and iridescent, are seen and are described as a “Christmas Tree” appearance. A peripheral pigmentary retinopathy can also be seen [28].

Inflammatory Disorders

Sarcoidosis

Ocular sarcoidosis can be seen in up to 25–50% of the patients with systemic disease. Bilateral granulomatous uveitis sometimes can be the only sarcoid related pathology. Bilateral ocular involvement is the most common ocular pattern occurring in 30–70% of the cases. The International Workshop on Ocular Sarcoidosis (IWOS) has identified seven signs "suggestive" for the diagnosis of ocular sarcoidosis. These include mutton-fat/granulomatous keratic precipitates and/or iris nodules (Koeppe/Busacca), trabecular meshwork nodules and/or tent-shaped peripheral anterior synechiae, snowballs/string of pearls vitreous opacities, multiple chorioretinal peripheral lesions (active and/or atrophic), nodular and/or segmental periphlebitis (+/− candlewax drippings) and/or retinal macroaneurysm in an inflamed eye, optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule, and bilaterality. Keratoconjunctivitis sicca (KCS) is the second most common ocular manifestation followed by adnexal granulomas. Adnexal granulomas most commonly affect the conjunctiva followed by eyelid. Rarely lacrimal gland and orbital granulomas are also seen [29–31] (Fig. 19).

Behçet's Disease

Bilateral panuveitis is the most common ocular manifestation with relapses, hypopyon, large retinal vein occlusions and retinitis. Conjunctivitis,episcleritis and optic nerve involvement by optic neuropathy can occur [32].

Systemic Lupus Erythematosus

Ocular manifestations may occur later in the disease and are less commonly observed in the juvenile form of SLE (jSLE) with prevalence of 5%. Similar to adult-onset disease, the most common ocular finding is keratoconjunctivitis sicca (KCS) while the most visually devastating sequelae occur secondary to optic nerve involvement and retinal vaso-occlusion. Vasoocclusion is more prevalent in the presence of anticardiolipin antibodies and this may precede development of SLE by several years. Lupus retinopathy characterized by retinal hemorrhages and cotton wool spots is due to fibrinoid necrosis of small arteries, arterioles and capillaries [33] (Fig. 20).

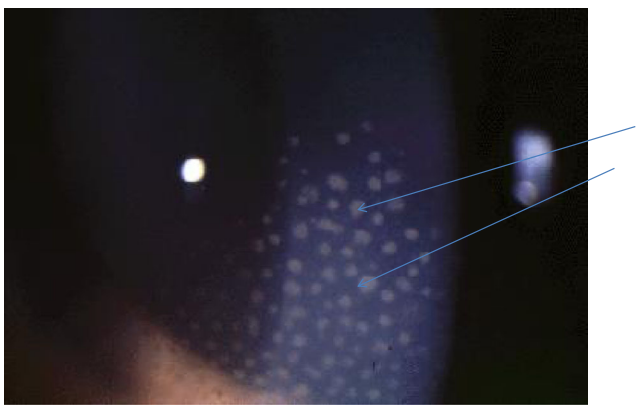

Fig. 19 Granulomatous uveitis showing mutton fat keratic precipitates

Antineutrophil Cytoplasmic Antibody-Associated Vasculitides

Of these vasculitides, ocular involvement is most commonly seen in Wegeners Granulomatoses. In general, ocular findings are less common and affect only 37% at presentation. In children, conjunctival involvement occurs most frequently followed by episcleral/scleral and orbital disease. The sclera can also be involved and necrotizing scleritis portends a poor ocular and systemic prognosis. Orbital involvement can include periorbital edema, panniculitis, myositis, dacryoadenitis, and dacryocystitis/canaliculitis and is highly associated with nasal sinus involvement. Because orbital tissues are frequently involved, a tissue diagnosis of GPA may be achieved *via* an orbital biopsy [29].

Sjogren's Syndrome

Primary Sjogren's syndrome (pSS) in childhood is rare with a recent review identifying only 145 cases with 66.4% having ocular involvement. The mean age at diagnosis was 9.8 y with a 7:1 female predominance. The most common clinical manifestations are bilateral parotid swelling and recurrent parotitis. Sicca-related diseases (KCS and xerostomia) are common presenting symptoms in adults, but occurs later in children possibly secondary to underreporting if patients are not severely affected. A Schirmer test measurement less than 5 mm is typical of KCS. Ocular surface staining can be done with fluorescein, lissamine green or rose bengal dye. Diffuse

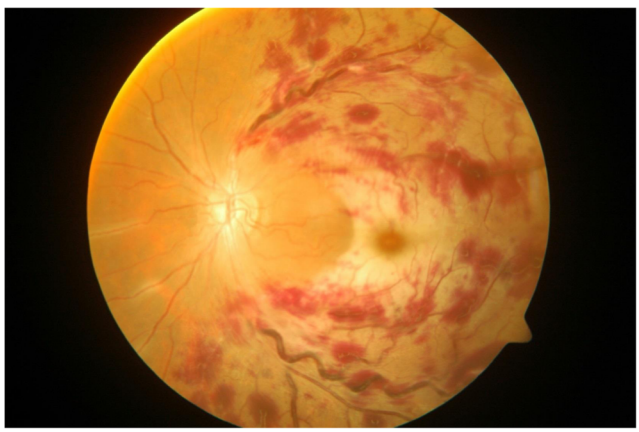

Fig. 20 SLE showing vaso-occlusive vasculitis-arterial and venous occlusion

punctate staining, especially in the interpalpebral region, is characteristic of KCS. Secondary Sjogren's syndrome (sSS) in childhood appears to be more common [30].

Kawasaki Disease

The most common ocular finding is a bilateral non-exudative conjunctivitis involving only the bulbar conjunctiva. Symptoms include tearing, irritation, and mild photophobia. Corneal involvement tends to be mild and is usually in the form of punctate epitheliopathy. However, severe disease such as disciform keratitis has been reported. A mild bilateral non-granulomatous anterior uveitis is also commonly present early in the acute phase of the disease. The intraocular inflammation generally presents in the first week and usually has a self-limited course. Most cases resolve within 2–8 wk and patients rarely have ocular sequelae. However, topical corticosteroids have been successfully used to treat inflammation. Rarely, posterior segment abnormalities have been associated including papillitis, vitreous opacities, and retinal vasculitis [30].

Juvenile Idiopathic Arthritis

More than 75% of cases of pediatric anterior uveitis are associated with JIA. A non-granulomatous anterior uveitis, occurs in up to 80% of children. It may develop before, along with or after the onset of arthritis. The risk factors for uveitis are female gender, oligoarticular subtype, younger age, anti-nuclear antibody (ANA) positivity, and RF negativity.

Chronic anterior uveitis is the most common presentation. The uveitis is asymptomatic and may not be recognized until decreased visual acuity is detected on routine screening. The chronicity of the inflammation causes more visual damage than the severity of the inflammation. Hence, it is the children who have longer period of uveitis who have a worse outcome. Although the mean age of presentation is between 4 and 9 y, the inflammation usually has been present for some period before diagnosis. Hence, the American Academy of Pediatrics Sections of Rheumatology and Ophthalmology created screening guidelines to detect this asymptomatic disease. Children who are at higher risk (pauci- or polyarticular JIA subtype, ANA (+), short duration of arthritis, and young at arthritis onset) require slit lamp examinations every 3–4 mo. Intermediate, posterior and panuveitis are relatively less common. Symptoms can include pain, redness, photophobia, pupil irregularity, and loss of vision. Band keratopathy (metastatic calcification of the cornea), posterior synechiae (adhesions between the iris and lens), cataract, and ocular hypertension are the complications that decrease visual acuity [30, 34] (Fig. 21).

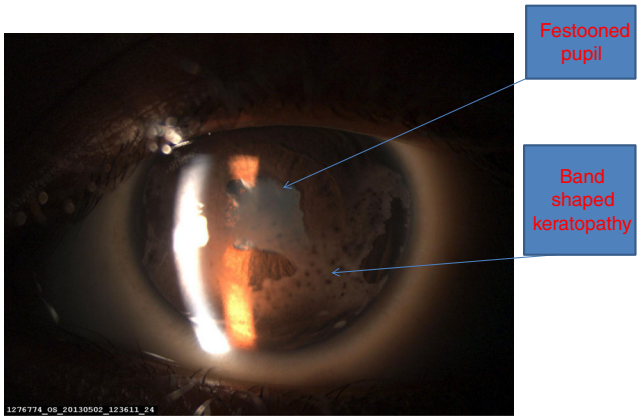

Fig. 21 JIA uveitis with festooned pupil and band shaped keratopathy

Juvenile Spondyloarthropathies [31]

Juvenile spondyloarthropathy (JSA) is a group of arthritides with a prevalence of 7.4% for enthesitis-related arthritis (ERA), 6.3% for psoriatic arthritis, and 19.7% undifferentiated arthritis. Inflammatory back pain (sacroiliitis) is more common in adults whereas peripheral and hip arthritis are more frequent in children. Patients generally present with an acute, unilateral non-granulomatous uveitis. Bilateral ocular involvement is common but usually does not occur simultaneously. Children with spondyloarthropathy may develop pain, photophobia, and redness that differs from asymptomatic disease seen in oligoarticular JIA. Hypopyon may also be observed in children, similar to adults. The *HLA-B27* is a genetic risk marker associated with 80–90% of patients with spondyloarthropathy.

Reactive Arthritis

Reactive arthritis is another inflammatory disorder that can follow an infection. It is associated with HLA-B27 positivity and was earlier known as Reiter's syndrome. In adults, the triad of urethritis, conjunctivitis and peripheral arthritis characterizes it. *Chlamydia trachomatis* is implicated in older children, whereas *Yersinia enterocolitica* and *Shigella flexneri* are

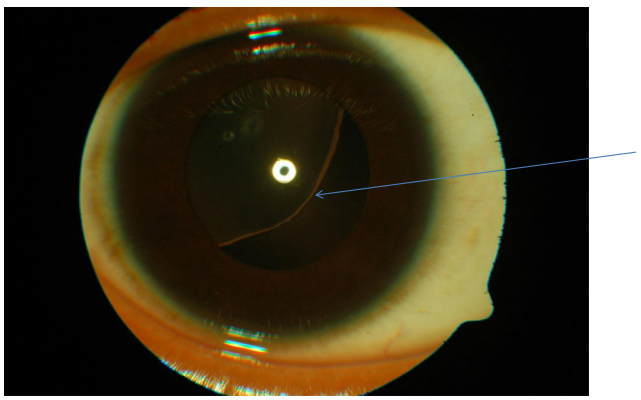

Fig. 22 Subluxated lens

more common in younger children. Seventy-five to 90% of cases are HLA-B27 positive. Age of onset peaks between 8 and 12 y. The ocular disease progresses over the first few weeks after the disease starts. Over 75% of children have eye involvement, most commonly mucopurulent bilateral conjunctivitis in 50% of cases. It often resolves within 1–2 wk. Bilateral non-granulomatous anterior uveitis may be the initial presentation especially in the HLA-B27 positive group. Other entities seen are keratitis, scleritis, papillitis, intermediate/posterior uveitis, cataract, and glaucoma [34].

Miscellaneous

Ectopia lentis or lens subluxation is an ocular finding that occurs in various disorders that affect the fibrillin in the zonules. These include Marfans syndrome, Homocysteinuria and Weil Marchesani syndrome. In Marfans syndrome, the subluxation occurs in 60% [35] and the lens is commonly subluxated upwards while in homocysteinuria, it occurs in 90% and is usually downwards [36]. Microspherophakia is seen in Weil Marchesani and can cause pupillary block glaucoma by anterior subluxation (Fig. 22).

Acknowledgements Dr. Pradeep Venkatesh for his constant help in preparing this manuscript.

Contributions NR for getting the images and writing the manuscript. GSP for editing the final review and is the guarantor for this paper.

Compliance with Ethical Standards

Conflict of Interest None.

References

1. Cantor LB, Lyons CJ, Cioffi GA. Retina and vitreous, basic and clinical science course. USA: American Academy of Ophthalmology; 2015-2016. p. 251.
2. Cleary M, Morris A, Taylor D. Inborn errors of metabolism and eye. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 684–713.
3. Bowling B. Kanski's Clinical Ophthalmology, 8thed. Online by Wolters Kluver India Pvt Ltd: Elsevier; 2016. p. 680.
4. Pruett RC. Retinitis pigmentosa: clinical observations and correlations. Trans Am Ophthalmol Soc. 1983;81:693–735.
5. Boughman J, Vernon M, Shaver K. Usher syndrome: definition and estimate of prevalence from two high-risk populations. J Chronic Dis. 1983;36:595–603.
6. Russell-Eggitt IM, Morris AAM. Usher syndrome. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 563.
7. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. J Med Genet. 1999;36:437–46.
8. Russell-Eggitt IM, Morris AAM. Retinal distrophies with systemic association. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 564.
9. Lambert SR. Retinal distrophies with systemic association. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 441.
10. Rowley SA, O Gallagher FJ, Osborne JP. Ophthalmic manifestations of tuberous sclerosis – a population based study. Br J Ophthalmol. 2001;85:420–3.
11. Ragge NK, Falk R, Cohen WE, et al. Images of Lisch nodules across the spectrum. Eye. 1993;7:95–101.
12. Grant WM, Walton DS. Distinctive gonioscopic findings in glaucoma due to neurofibromatosis. Arch Ophthalmol. 1968;79:127–34.
13. Lyons CJ, Rootman J. Neurofibromatosis. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 308–9.
14. Maher E, Moore A. Von Hippel-Lindau disease. Br J Ophthalmol. 1992;76:743–5.
15. Lambert SR. Retinal dystrophies with systemic association. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 444.
16. Morland AB, Hoffman MB, Neven M, et al. Abnormal visual projection in a human albino studied with functional MRI and VEP. J Neurol Neurosensory Psychiatry. 2002;72:523–6.
17. Brezin AP, Thulliez P, Couvreur J, NobnR, Mc Leod R, Mets MB. Ophthalmic outcomes after prenatal and postnatal treatment of congenital toxoplasmosis**.** Am J Ophthalmol. 2003;35:779–84.
18. De Sa LCF, Soriano DS. Systemic infections and the eye: AIDS. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 188.
19. Pelaez CA, Gurbindo MD, Cortis C, Fernadez MM. A molluscum contagiosum involving upper eyelid in a child infected with HIV. Pediatr AIDS HIV Infect. 1996;7:43–6.
20. Lambert SR. Ocular manifestations of intrauterine infections. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 139.
21. Anderson KS, Amos CS, Boppana S, Pass R. Ocular abnormalities in congenital cytomegalovirus infection. J Am Optom Assoc. 1996;67:273–8.
22. Hanieh A, David D. Apert's syndrome. Child's Nervous System. 1993;9:289–91.
23. Gorlin RJ, Cohen MM Jr, Hennekam RCM. Syndromes of the head and neck. Oxford: Oxford University Press; 2001.
24. Wang FM, Mellman AL, Sidoti PA, et al. Ocular findings in Treacher Collins syndrome. Am J O. 1990;110:280–6.
25. Al-Enezi M, Nasser M. Mitochondrial disorders with significant ophthalmic manifestations. Middle East Afr J Ophthalmol. 2008;15:81–6.
26. Souh H, Sahashi K, Ibi T, et al. Progressive external ophthalmoplegia and myositis. Intern Med. 1993;32:319–22.
27. Schoser BG, Pongratz D. Extraocular mitochondrial myopathies and their differential diagnosis. Strabismus. 2006;14:107–13.
28. Burian HM, Burns CA. Ocular changes in myotonic dystrophy. Am J Ophthalmol. 1967;63:22–34.
29. Choudhary MM, Hajj-Ali RA, Lowder CY. Gender and ocular manifestations of connective tissue diseases and systemic vasculitides. J Ophthalmol. 2014;2014:403042.
30. Palejwala NV, Yeh S, Angeles-Han ST. Current perspectives on ophthalmic manifestations of childhood rheumatic diseases. Curr Rheumatol Rep. 2013;15:341.
31. Reiff A. Ocular complications of childhood rheumatic diseases: nonuveitic inflammatory eye diseases. Curr Rheumatol Rep. 2009;11:226–32.
32. Kang EH, Kim JY, Takeuchi F, et al. Associations between the HLA-A polymorphism and the clinical manifestations of Behcet's disease. Arth Res Ther. 2011;13:R49.

33. Edelsten C. Uveitis. In: Taylor D, Hoyt CS, editors. Pediatric Ophthalmology and Strabismus, 3rd ed. Philadelphia: Elsevier; 2005. p. 420.
34. Lim HW, Oh SY. Ocular manifestations of pediatric systemic disease. Hanyang Med Rev. 2016;36:182–5.
35. Maumenee IH. The eye in Marfans syndrome. Trans Am Ophthalmol Soc. 1981;79:684–733.
36. Cross HE, Jensen AD. Ocular manifestations in the marfans syndrome and homocystinuria. Am J Ophthalmol. 1973;75:405–20.