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Mini Atlas

Congenital ocular anomalies in newborns: a practical atlas

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Abstract

All newborns should be examined for ocular structural abnormalities, an essential part of the newborn assessment. Early detection of congenital ocular disorders is important to begin appropriate medical or surgical therapy and to prevent visual problems and blindness, which could deeply affect a child's life. The present review aims to describe the main congenital ocular anomalies in newborns and provide images in order to help the physician in current clinical practice.

Keywords

Congenital ocular anomalies, newborn, anophthalmia, microphthalmia, aniridia, iris coloboma, glaucoma, blepharoptosis, epibulbar dermoids, eyelid haemangioma, hypertelorism, hypotelorism, ankyloblepharon filiforme adnatum, dacryocystitis, dacryostenosis, blepharophimosis, chemosis, blue sclera, corneal opacity.

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Introduction

Congenital ocular malformations (COM) are the result of defective development of ocular tissues during the intrauterine life and they show multifactorial inheritance (genetic, environmental, teratogens or chromosomal factors are involved) [1].

The reported incidence of COM varies from 3.6 to 6.8 per 10,000 newborns [2, 3].

The most frequent COM are anophthalmia/microphthalmia, congenital cataract, coloboma and congenital glaucoma.

Early identification of eye-related pathologies after birth permit prompt treatment and may have an important impact on the prognosis for many ocular disorders [4].

Anophthalmia/microphthalmia

Anophthalmia is a congenital malformation characterized by the total absence of an eyeball due to the lack of formation of optic vesicles during embryogenesis.

It should be distinguished from microphthalmia, an alteration of the ocular shape by reduction of the axial length, which can be associated with anterior or posterior segment dysgenesis.

The etiology of anophthalmia and microphthalmia is multifactorial.

Chromosomal, monogenic (*SOX2*, the major causative gene) and environmental causes (infections in pregnancy, vitamin A deficiency, X-ray exposure, solvents and thalidomide) were described.

Anophthalmia can occur isolated or associated with other malformations in syndromes.

Waardenburg anophthalmia syndrome, or anophthalmia-syndactyly syndrome, is characterized by bilateral anophthalmia or microphthalmia connected with alterations in the limbs and fingers, such as long bone hypoplasia, synostosis, syndactyly, oligodactyly or polydactyly (**Fig. 1** and **Fig. 2**).

This is caused by the mutation of the *SMOC1* gene (SPARC-related modular calcium-binding

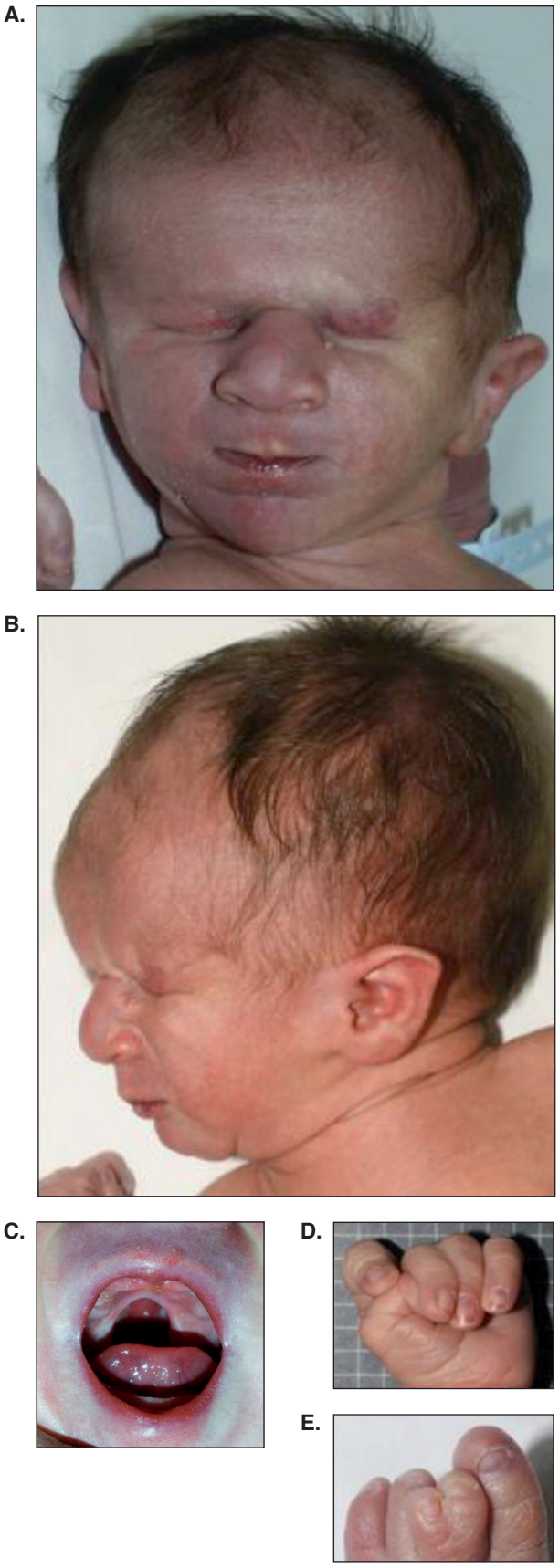


Figure 1. Newborn affected by Waardenburg anophthalmia syndrome. **A, B.** Facial features include flattened midface, short palpebral fissures, sparse eyelashes. **C.** Cleft palate. **D.** Anomalies of fingers position. **E.** Syndactyly of the second and third toes.

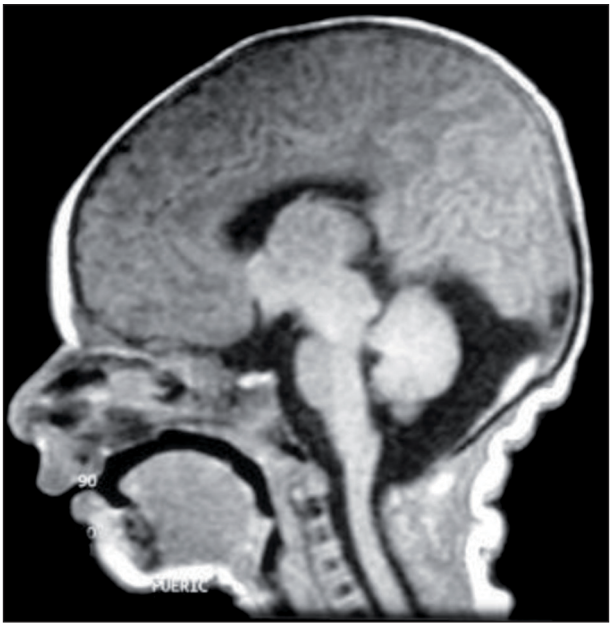
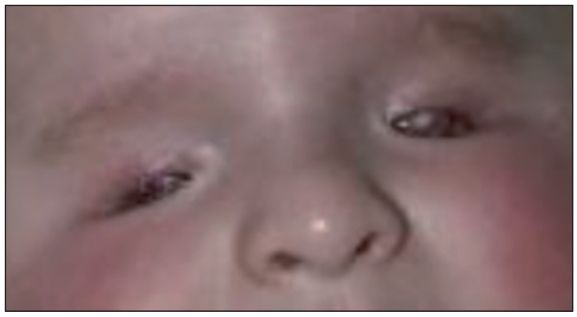


Figure 2. Head Computed Tomography of the patient presented in **Fig. 1** shows total absence of eyeballs.

protein 1) on chromosome 14q24.1, involved in bone development regulation.

Lenz microphthalmia syndrome is an X-linked condition characterized by ocular malformations (anophthalmia or microphthalmia, coloboma, cataract), skeletal and finger anomalies, microcephaly, intellectual disability, facial dysmorphism, genitourinary changes (renal hypoplasia, cryptorchidism) and, rarely, congenital heart disease (**Fig. 3** and **Fig. 4**) [5-7].

A.



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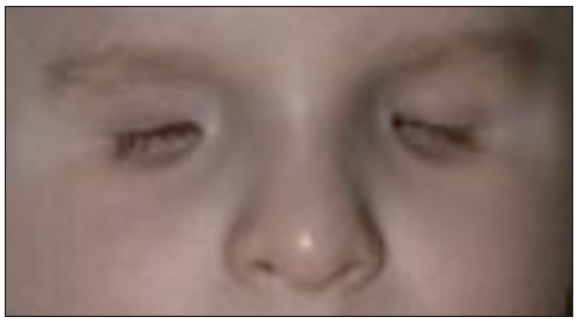
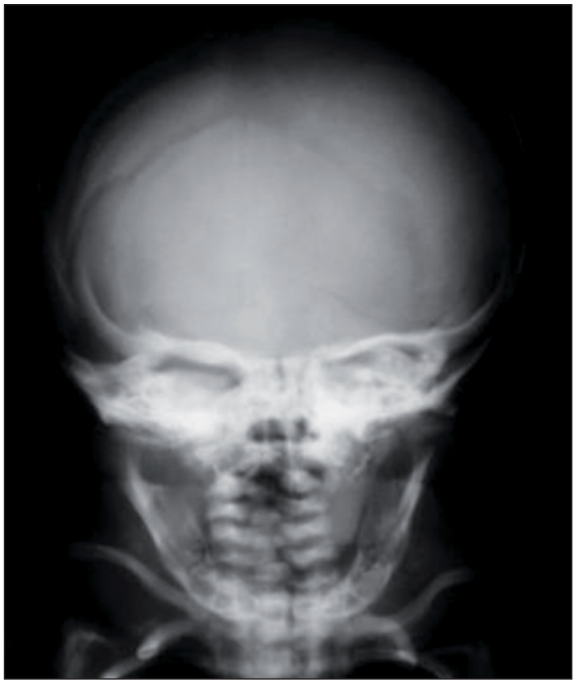


Figure 3. Child affected by Lenz microphthalmia syndrome at different ages.

A.



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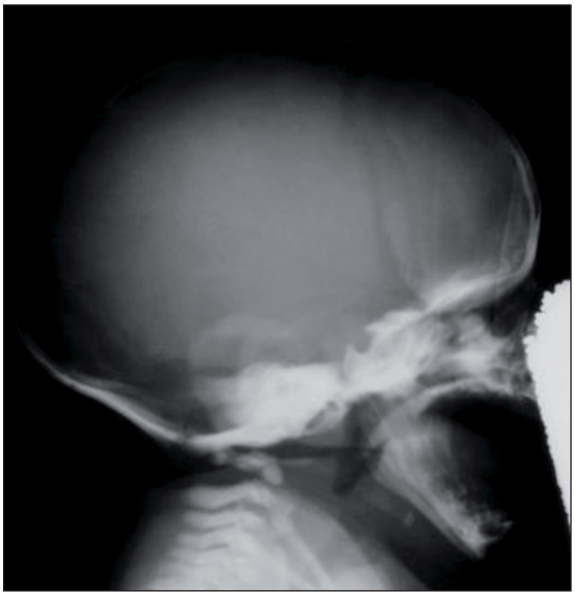

Figure 4. Head radiographies of the patient presented in **Fig. 3** confirm bilateral reduction of the orbital bones.

Aniridia

Aniridia is the partial or total congenital absence of the iris (**Fig. 5**).

It is a rare congenital anomaly caused by the mutation of the *PAX6* gene, located on chromosome 11p13.

This gene is involved in the early development of the eyes, brain and central nervous system.

Aniridia is frequently associated with other ocular abnormalities such as macular hypoplasia or optic nerve, glaucoma, nystagmus and corneal degeneration.

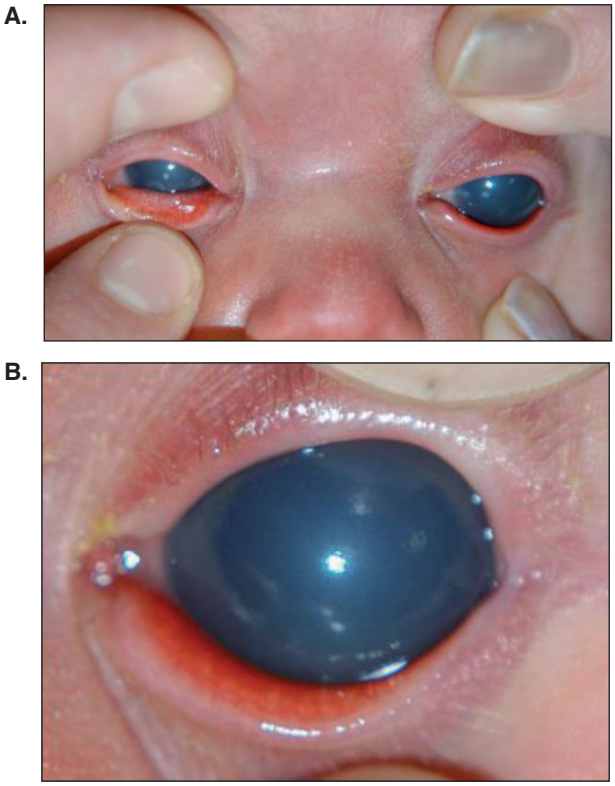

Figure 5. Newborn with bilateral congenital absence of the irises.

Infants with aniridia have an increased risk of nephroblastoma.

It may be a sign of WAGR syndrome (11p13 chromosomal deletion disease), in which aniridia is associated with Wilms tumor, genitourinary disorders and intellectual disability [8-10].

Coloboma

Ocular coloboma is a congenital malformation of the eye due to failure to close the optical fissure during embryonic life.

This defect is characterized by the absence or incomplete development of ocular tissue that may variably involve iris, crystalline, choroid, retina or optic nerve (**Fig. 6** and **Fig. 7**).

Its prevalence is more than 1/100,000 live births.

It may be associated with other eye changes such as anophthalmia/microphthalmia.

Etiologically, there are many identified causes: viral diseases, toxoplasmosis, gene mutations, such as *SALL2* gene, or syndromes.

For instance, CHARGE syndrome consists of coloboma, cardiac anomalies, choanal atresia, growth retardation, genital hypoplasia and deafness [11-13].

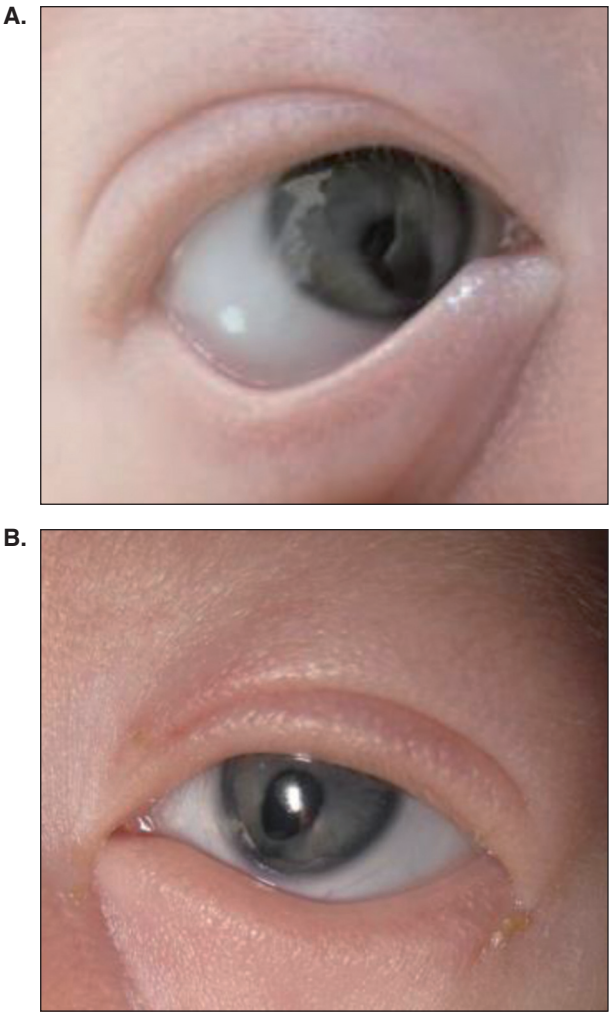

Figure 6. Iris coloboma in term infants.

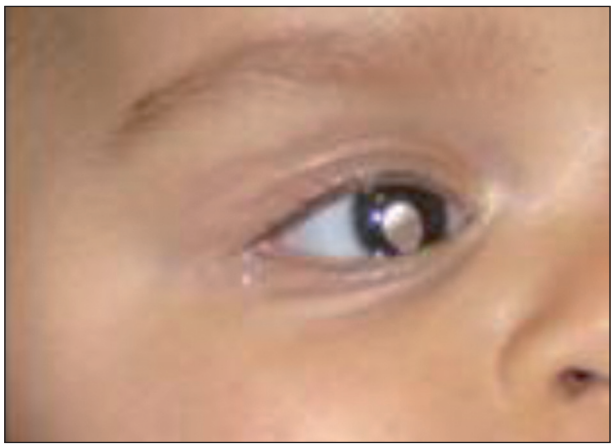

Figure 7. Leukocoria (white pupillary reflex) in a newborn. There is an abnormal white reflection from the retina of the eye due to coloboma of iris.

Glaucoma

Primary congenital glaucoma is a pathology due to agenesis or dysgenesis of the anterior chamber angle.

An anomaly in the development of the iridocorneal angle can occur during the embryonic life, which hinders the outflow of the aqueous humor and increases intraocular pressure.

The reported incidence of glaucoma is 1/100,000.

It is more prevalent in males and typically exhibits bilateral presentation.

Clinically, patients have an increase in the corneal diameter (megalocornea) up to the buftalmo or "bull's eye" (increase in the size of the eyeball), which leads to optic nerve atrophy and corneal opacification (**Fig. 8**).

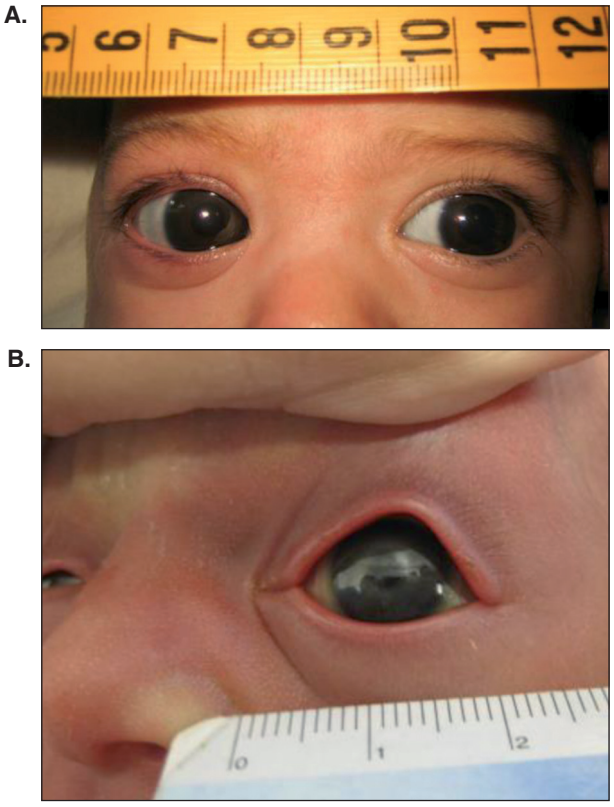

Figure 8. Increase in the size of the eyeball (buftalmo or "bull's eye") in a term infant.

Photophobia, blepharospasm and excessive tearing are associated signs.

Surgical treatment (goniotomy, trabeculectomy or sclerectomy) is the gold standard, while medical therapy is used to control intraocular hypertension [14, 15].

Blepharoptosis

Blepharoptosis (BPT), or ptosis of the eyelid, is a malformation characterized by reduced palpebral fissure due to upper eyelid weakness (**Fig. 9**).

The most common cause in newborns is a congenital defect of levator palpebrae superioris muscle, which is innervated by the upper branch of the third cranial nerve.

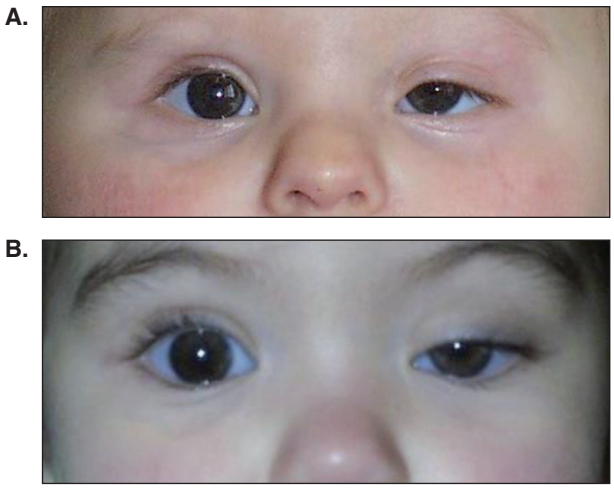

Figure 9. Children affected by left blepharoptosis (BPT) at different ages.

More rarely, it can be caused by birth trauma.

Congenital ptosis is usually unilateral, non-progressive and without any evidence of objective neurological involvement.

It may be familial or related to syndromes such as the retraction syndrome of Duane (oculomotor muscles paralysis, ocular globe retraction and ptosis), blepharophimosis-ptosis-epicanthus inversus syndrome (BPES), Marcus-Gunn and congenital Horner's syndrome. BPT should be corrected early in order to prevent amblyopia [16-19].

Epibulbar dermoids

Epibulbar dermoids (ED) are the most common ocular congenital tumors.

They appear as a white-yellowish, roundish, generally unilateral lesions located in regions of the bulbar conjunctiva, limbus, cornea and caruncles (**Fig. 10**).

ED are choristomas consisting of ecto-mesodermal tissue derived from an embryological anomaly occurring in early gestation (5-10 weeks), resulting in a metaplastic transformation of the mesoblast between the rim of the optic nerve and surface ectoderm.

Although they are benign lesions, they grow, albeit slowly, making surgical removal necessary to avoid complications from mass effects.

They rarely tend to recur. Surgical treatment is more difficult in cases of lipodermoids, lipomatous formations that originate from the back of the bulb and protrude anteriorly to the eyelid line.

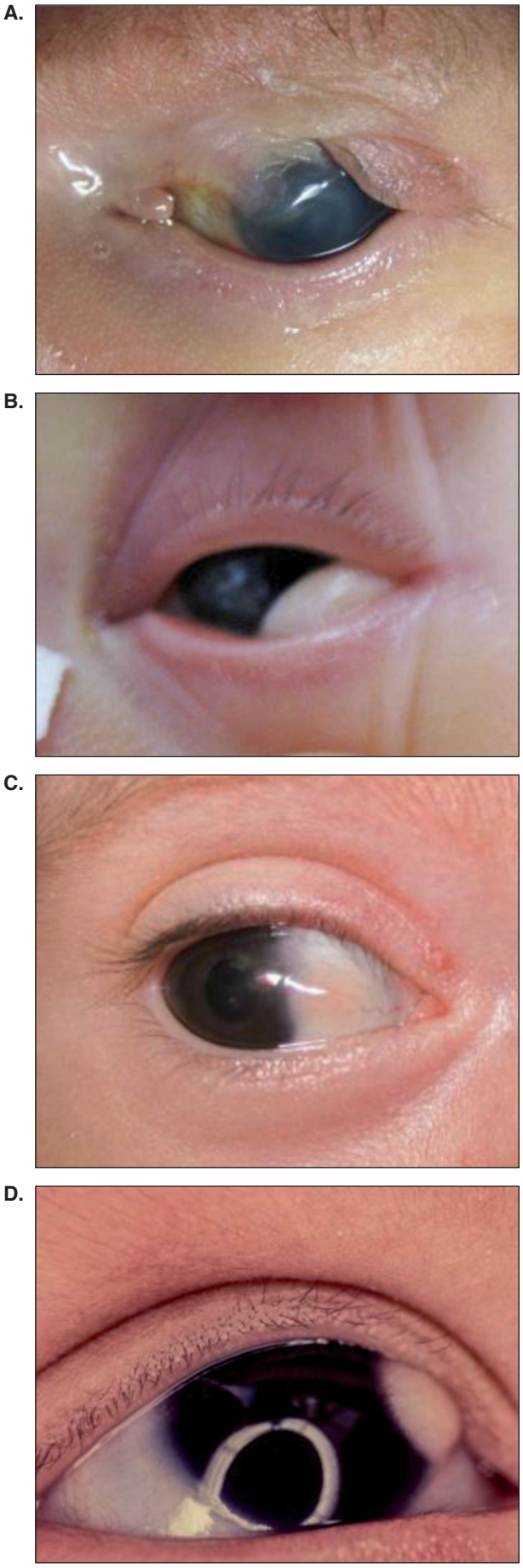

Figure 10. Epibulbar dermoids (ED) in infants.

ED may be associated with other abnormalities such as in the Goldenhar syndrome, or oculo-auricolo-vertebral dysplasia, characterized by craniofacial microsomia, ocular dermoids and spinal anomalies [20-23].

Eyelid haemangioma

Palpebral hemangiomas are vascular tumors of mesodermal origin.

They can present with a flat or raised surfaces and chromatic variability from a bright red to a violet-bluish depending on their depth (**Fig. 11**).

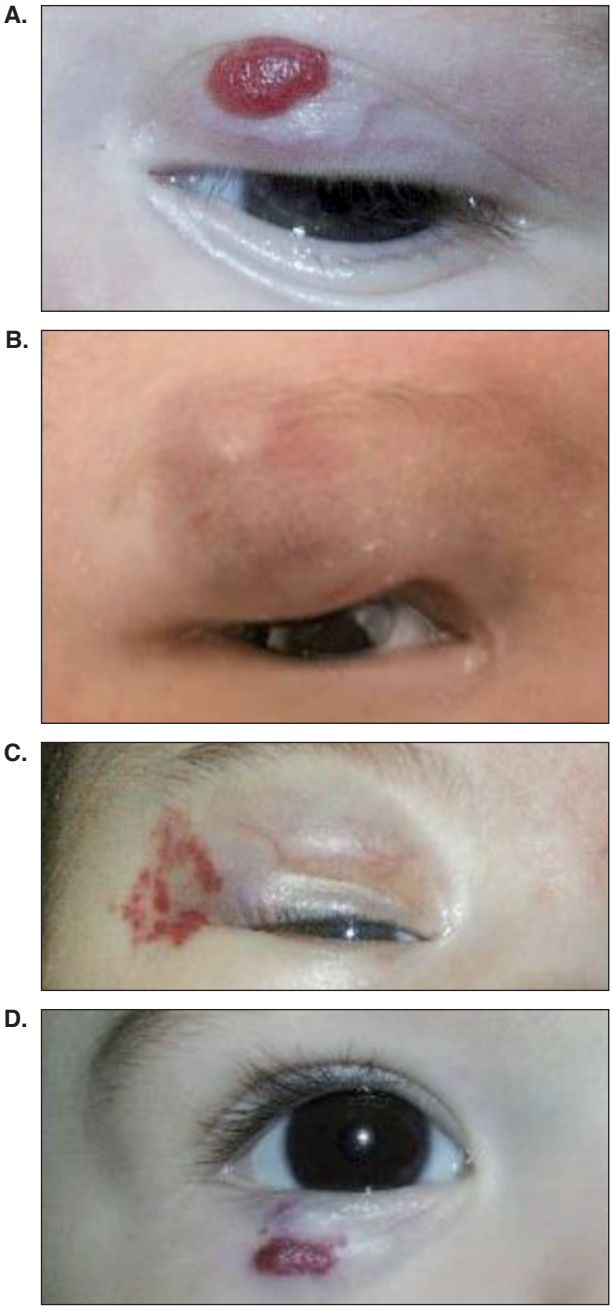

Figure 11. Superficial hemangiomas and deep hemangioma on the upper and lower eyelid.

According to skin characteristics, they can be classified as superficial and deep, localized or segmental.

Basing on localization, they are distinguished in eyelids, extraconal (behind the bony orbit, but outside the extraocular muscles) or intraconal (inside the cone of the extraocular muscles).

Deeper hemangiomas involving the orbit can cause alteration of visual function (amblyopia), compression of the eyeball (astigmatism, myopia) and infiltration of the oculomotor muscles (strabismus).

A segmental vascular alteration in the trigeminal region may be a sign of meningo-facial angiomatosis or Sturge-Weber disease [24, 25].

Hypertelorism

Ocular hypertelorism (OH) is a congenital malformation due to an increase of intercanthal and interpupillary distance (**Fig. 12**).

This alteration is caused by a real increase in the distance between the orbital bones.

It can be unilateral or bilateral, symmetrical or asymmetrical, isolated or associated with a vertical orientation anomaly (orbital dystopia).

It should be distinguished from telecanthus, or pseudohypertelorism, in which inner canthal distance is increased while outer canthal distance and the interpupillary distance are normal (**Fig. 13**).

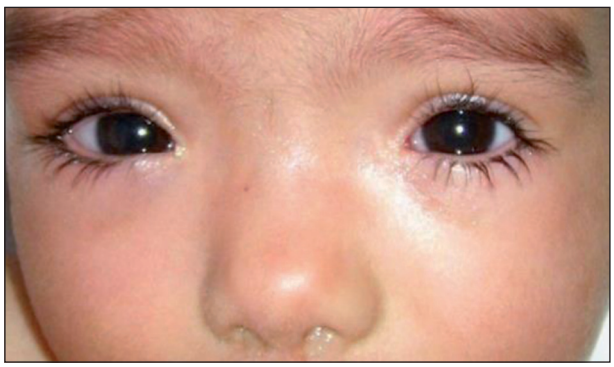

Figure 12. Ocular hypertelorism (OH) in a child, increase in the distance between the orbital bones.

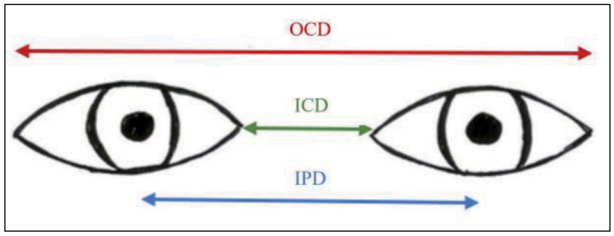

Figure 13. Outer canthal distance (OCD), inner canthal distance (ICD), interpupillary distance (IPD).

OH is not a disease, but the manifestation of a craniofacial deformity.

It can be found in various conditions such as craniofacial dysplasia, encephalocele, dermoid cysts, glial tumors, craniofacial dysostoses (Apert and Crouzon syndrome) and in various syndromes such as Edwards, Turner, Cri du chat, Opitz, DiGeorge, Leopard [26-28].

Hypotelorism

Ocular hypotelorism (OHP) is a congenital anomaly that consists in a decrease of interorbital distance.

The most common cause of OHP is a defect in the migration of germ cells; thus, it is considered a midline migration defect.

Isolated OHP is extremely rare and it is highly associated with holoprosencephaly, a spectrum of brain and facial structural malformations resulting from incomplete cleavage of the prosencephalon into two separate hemispheres (**Fig. 14**).

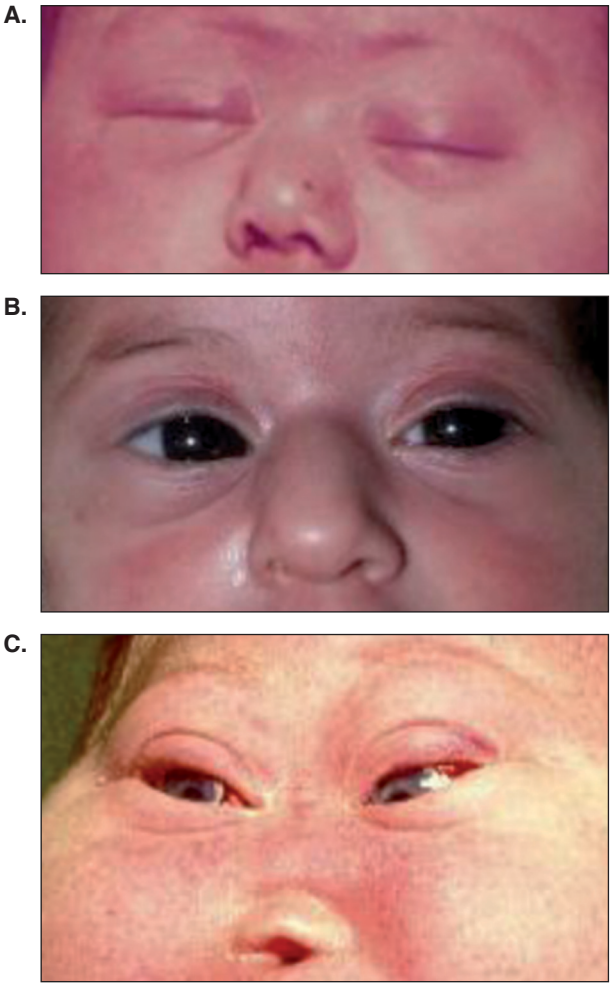

Figure 14. Ocular hypotelorism (OHP) associated with holoprosencephaly: from milder (**A, B**) to the most severe forms (**C**).

The most extreme form of holoprosencephaly is the cyclopia, condition characterized by a single eye or a partially divided eye.

It can also be a sign of other condition, like maternal phenylketonuria, and chromosomal syndromes, such as trisomy 13, microcephaly, Coffin-Siris, Schilbach-Rott, Meckel-Gruber, Williams, 20p syndrome [29-34].

Ankyloblepharon filiforme adnatum

Ankyloblepharon filiforme adnatum (AFA) is a rare congenital anomaly consisting of a partial or complete fusion of the eyelid margins characterized by slender connective tissue flaps, single or multiple, that connect the eyelids to each other in a bridge (**Fig. 15**).

This defect is generally isolated and sporadic, but it can have a familial inheritance and can be associated with other ocular anomalies (iridogoniodysgenesis with juvenile glaucoma) or systemic anomalies (cleft lip and palate), ectodermal dysplasia syndromes, popliteal pterygium syndrome, CHANDS syndrome (curly hair, ankyloblefaron, ungual dysplasia), and Edwards syndrome.

From the functional point of view, AFA can prevent the complete eye opening. Surgical correction should be promptly performed to avoid the risk of amblyopia [35-37].

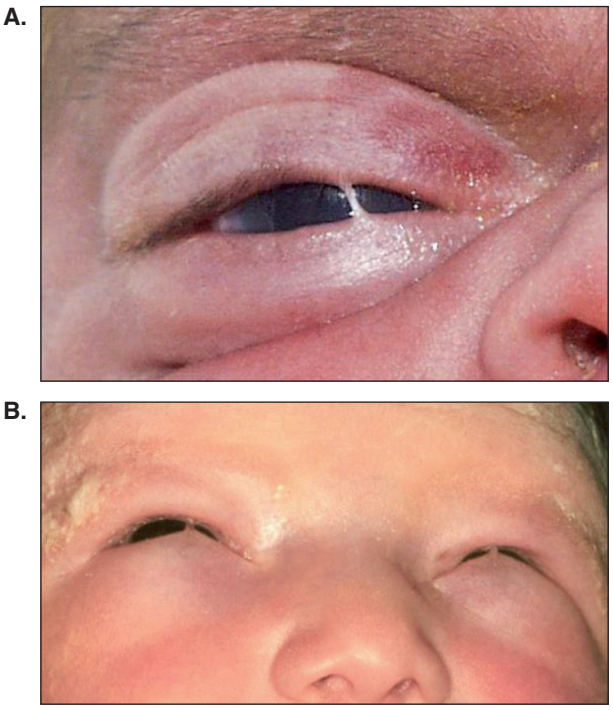

Figure 15. Unilateral (**A**) and bilateral (**B**) ankyloblepharon filiforme adnatum (AFA) in newborns. Note the slender connective tissue flaps that connect the eyelids to each other in a bridge.

Dacryocystitis and dacryostenosis

Acute dacryocystitis (AD) is an inflammation of the lacrimal sac and perisaccal tissues. It is clinically characterized by rapid onset of pain, swelling of the lower eyelid at the inner corner of the eye, eyelid edema and epiphora (**Fig. 16**).

The age of onset is usually in the neonatal period with a female preponderance. AD occurs mostly as a complication of congenital nasolacrimal duct obstruction (dacryostenosis), which causes the blockage of lacrimal outflow (**Fig. 17**).

It is a pediatric medical urgency due to the risk of evolution into lacrimal abscess, orbital cellulitis and meningitis. In most cases, duct obstruction resolves spontaneously in the first 6-10 months of life, while two-thirds of persistent cases resolve with medical therapy in the first year of life.

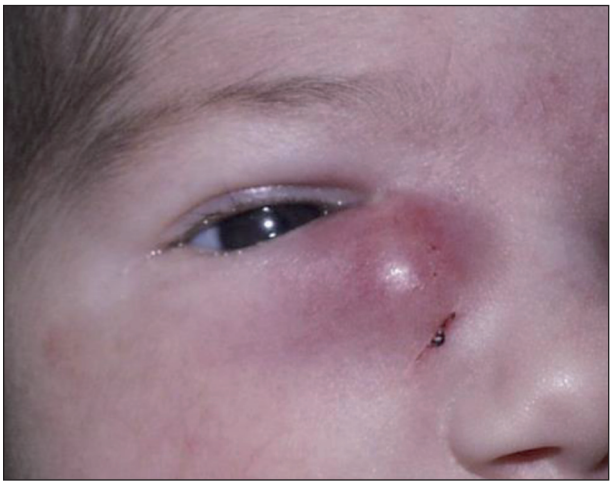

Figure 16. Acute dacryocystitis (AD) in an infant.

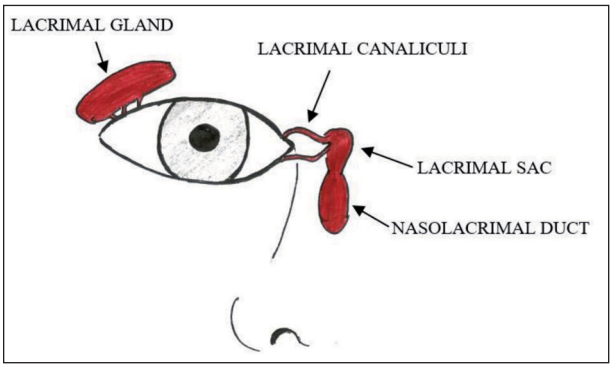

Figure 17. Anatomy of the lacrimal drainage system apparatus: lacrimal gland, canaliculi, lacrimal sac, and nasolacrimal duct.

Medical therapy consists of the compression and massage of the lacrimal sac (Crigler technique) and antibiotic therapy in case of infection.

The massage of the bag may break the membranous obstruction at the level of the Hasner valve restoring tear flow.

If medical therapy fails, probing or intubation of the canaliculi and nasolacrimal duct can be performed [38-40].

Blepharophimosis-ptosis-epicanthus inversus syndrome

BPES is a rare disorder characterized by reduced eyelid opening (blepharophimosis), reduced palpebral fissure (ptosis), increased inner canthal corners (telecanthus) and inverted skin fold which rises from the lower lashes and partially covers the inner canthus (inverse epicanthus) (**Fig. 18** and **Fig. 19**).

Other ocular manifestations may occur, such as lacrimal duct abnormalities, amblyopia and strabismus.

The causative gene is *FOXL2* on chromosome 3q23.

It is an autosomal dominant inherited disease, although sporadic forms, due to *de novo* mutations, are frequent.

Forms caused by translocation or chromosomal microdeletion have also been described.

There are two types of BPES: type I, in which ocular anomalies are associated with an early ovarian insufficiency in women, and type II, in which they are isolated [41, 42].

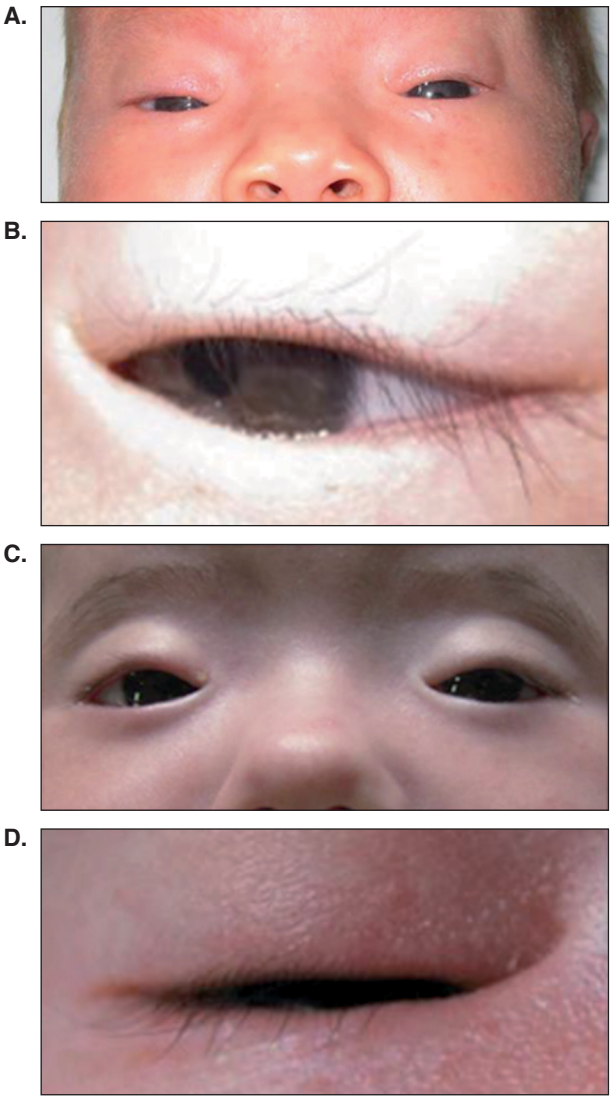

Figure 18. Blepharophimosis-ptosis-epicanthus inversus syndrome (BPES) in infants: reduced eyelid opening, reduced palpebral fissure, increased inner canthal corners and inverted skin fold which rises from the lower lashes and partially covers the inner canthus.

Chemosis

Chemosis (from the Greek χήμη, "shell") is the swelling of the conjunctiva (**Fig. 20**).

It is due to an edematous collection of the tissue that lines the eyelids.

In the newborn, it is usually an ophthalmia neonatorum sign.

This can be caused by bacterial infections, viral infections or chemical agents used in the same prophylaxis (silver nitrate, erythromycin, tetatricicline), which induce a self-limited chemical conjunctivitis in the first 24 hours of life.

Chemosis and prolapse of the conjunctiva can also occur secondarily to the venous stasis that occurs during childbirth, which can cause eyelid eversion [43-45].

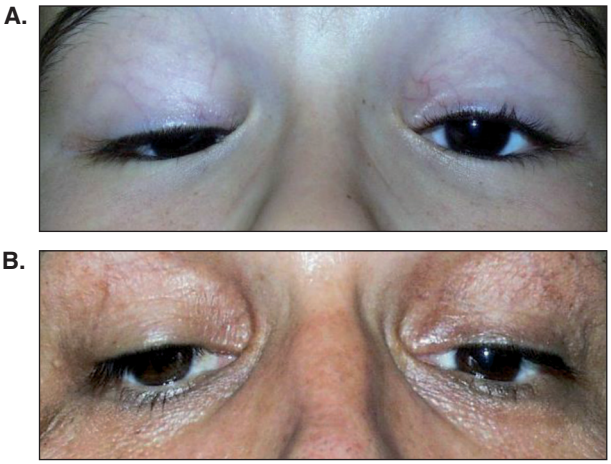

Figure 19. Clinical presentation of blepharophimosis-ptosis-epicanthus inversus syndrome (BPES) in a child (**A**) and in an adult (**B**).

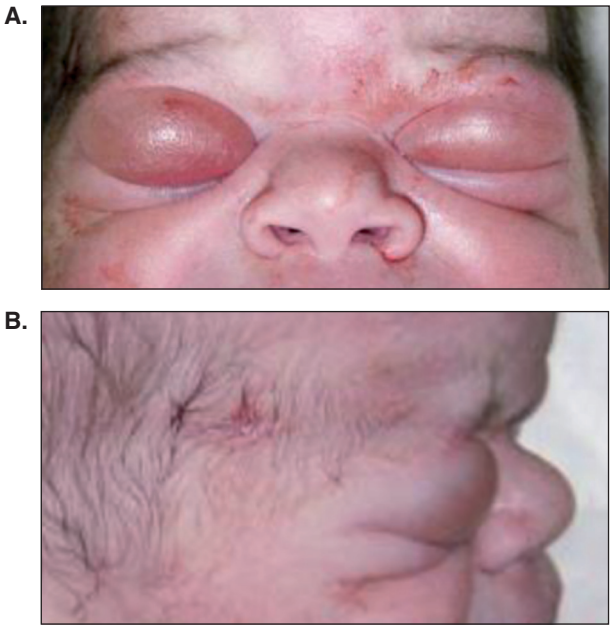

Figure 20. Chemosis occurs during childbirth, note the prominent swelling of the conjunctiva.

Blue sclera

Blue sclera (BS) is a condition characterized by a bluish coloration of the sclera, which normally appears as the white part of the eyes (**Fig. 21**).

The etiology is related to collagen defects that lead to thinness and transparency of the scleral fibers, resulting in a blue to blue-gray appearance imparted by the subjacent vascularity of the uvea.

BS may be an isolated finding in healthy newborns in which usually disappears by 6 months of age with the onset of normal scleral thickening, or may be a sign of various systemic diseases, in particular connective tissue disorders, such as osteogenesis imperfecta (OI).

OI is a heterogeneous group of genetic disorders caused by quantitative or qualitative defects in type 1 collagen. In the majority of cases, mutations are in the *COL1A1* and *COL1A2* genes.

The clinical spectrum of OI range from mild to severe form, which is lethal perinatally.

Bone fragility, skeletal deformities (kyphoscoliosis, chest wall deformities, acetabular protrusion, bowing of long bones) and growth retardation are the main signs of OI.

BS is not pathognomonic for OI; other 66 genetic syndromes have been described with BS, including Marfan's syndrome, Ehlers-Danlos, pseudoxanthoma elasticum, hyperhomocysteinemia, Willems De Vries, Hallermann-Streiff, Kabuki, POEMS, Laron, Caplan, Loeys-Dietz type 1, and Marshall-Smith syndromes [46-49].

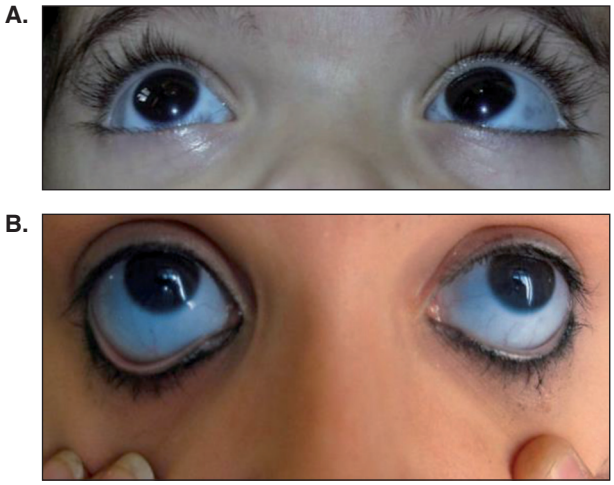

Figure 21. Blue sclerae (BS) in a child (**A**) and in an adult (**B**) affected by osteogenesis imperfecta (OI).

Corneal opacity

Congenital corneal opacities (CCO) are the loss of transparency of the corneal tissue present in newborns at birth (**Fig. 22**).

They are uncommon disorders with the prevalence estimated at 3/100,000 newborns. The etiology of CCO are various.

Several factors (genetic, infectious, traumatic, toxic) may affect development between the 6th and 16th weeks of gestation, when differentiation of the anterior segment occurs.

The differential diagnosis includes: anterior segment dysgenesis disorders (Peters' anomaly [PS], sclerocornea, congenital anterior staphyloma) corneal dystrophies, posterior corneal defects (posterior keratoconus), metabolic disorders (mucopolysaccharidoses, mucolipidoses), corneal dermoids, birth trauma (forceps), infections (congenital rubella, herpes simplex, bacterial infections), and congenital glaucoma.

PS is the most common presentation of OCC. It is distinguished into two types, both characterized by a central corneal opacity, thinning of posterior corneal stroma and absence of Descemet's membrane.

Figure 22. Ocular opacity and sensorineural deafness in a child affected by congenital rubella syndrome.

PS type II, in addition, will have lens abnormalities and tend to be bilateral.

Most cases of PS are sporadic and isolated but can be inherited, involving mutation of the *PAX6*, *FOXC1*, *PITX2*, or *CYP1B1* genes, and can be associated with other ocular or systemic abnormalities [50-53].

Conclusion

Several eye disorders, congenital and acquired, can affect newborns. The majority of this condition have signs that are detectable on a screening eye examination. All newborns should be examined for ocular structural abnormalities, an essential part of the newborn assessment for early detection and prompt intervention. This may have an important impact on the prognosis for many ocular disorders.

Acknowledgements

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Declaration of interest

The Authors declare that there is no conflict of interest.

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