Approach to Structural Eye Anomalies

Developed by Arjan Dhoot and Dr. Michael Wan for PedsCases.com.
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Introduction:

Hi everyone, my name is Arjan Dhoot and I am a 3rd year medical student at the University of Toronto. This podcast will provide an overview and organized approach to anomalies affecting ocular structures. I would like to thank Dr. Michael Wan, staff physician in the Department of Ophthalmology and Vision Sciences at the University of Toronto and SickKids Hospital for his help in developing this podcast.

After listening to this podcast, the learner should be able to:

1) Review anatomy of the eye, ocular muscles, and bony orbit.
2) Identify common structural eye anomalies.
3) Develop an approach to managing an infant presenting with a structural eye anomaly.

Congenital eye disorders are an important causes of childhood blindness. They can be found in isolation, in combination, or as part of a syndrome. In the human embryo, the eyes are formed by a delicate and complex process. Problems in this process can lead to structural eye anomalies.

Before we start, let's review basic anatomy of the eye, ocular muscles, and bony orbit. There are 3 chambers of the eye: anterior chamber (between the iris and cornea), posterior chamber (between the iris and lens), and vitreous chamber (behind the lens). The retina lives behind the vitreous chamber and is responsible for converting light into electrical signals that propagate along the optic nerve, or Cranial nerve II, to the brain for interpretation.

There are six muscles controlled by three cranial nerves that regulate movements of the eye. Cranial nerve VI (Abducens nerve) controls the lateral rectus muscle and abducts the eye. A cranial nerve six palsy should raise suspicion for elevated intracranial pressure. Cranial nerve four (Trochlear nerve) controls the superior oblique muscle and moves the eye down when looking towards the nose as well as internally rotating eyes. Cranial nerve III (oculomotor nerve) controls the remaining muscles of eye movement including the superior rectus muscle, medial rectus muscle, inferior rectus muscle, and inferior oblique muscle. As well, Cranial nerve III is involved in elevation of the eyelid via innervation of the levator palpebrae superioris muscle and constriction of the pupil via parasympathetic innervation of the sphincter pupillae. Dysfunction of Cranial nerve III presents as a "down and out" eye with a dilated pupil and droopy eyelid. When there is a dysfunction of one or more of the extraocular muscles, a misalignment of the eyes can

result. This phenomenon is known as strabismus and is the focus of another podcast available at PedsCases.com.

Next, we will review the bony orbit. The orbit is composed of seven bones forming the orbital roof, floor, medial and lateral walls. The seven bones are the sphenoid, ethmoid, lacrimal, frontal, palatine, maxillary, and zygomatic bones. The orbital roof is composed of the frontal bone and lesser wing of the sphenoid bone, the orbital floor is composed of the maxillary bone, palatine bone, and zygomatic bone. The lateral wall of the orbit is composed of the zygomatic bone and greater wing of the sphenoid bone and the medial wall of the orbit is composed of the maxillary bone, lacrimal bone, ethmoid bone, and lesser wing of the sphenoid bone.

To better understand some of the anomalies of ocular anatomy and how they can present clinically, let's start with a case.

John is a 10-year-old boy that presents to the emergency department of a pediatric hospital with a bulging left eye and increasing difficulty moving this eye for the past 2 weeks. He complains of blurry vision on the left and a left sided headache for the past 3 days. His mother mentions that these symptoms started after he bumped his head while running on a playground and is worried about a head injury.

What is our differential diagnosis? Our differential includes:

- Orbital hematoma
- Orbital cellulitis
- Orbital vascular malformation
- Primary malignancy
- Metastatic tumor

Going back to the case now:

Upon further history, we find that he does not have any nausea, vomiting, seizures, balance issues or mental status changes. He has not had a recent upper respiratory tract infection and does not have a fever. He endorses nighttime sweating and a 15 lb unintentional weight loss in the past 6 weeks. He does not have a past medical history of ocular complaints or otherwise. His mother has a history of tuberous sclerosis.

On examination, visual acuity is 20/20 on the right but counting fingers on the left. His extraocular movements are normal on the right but there is an abduction deficit on the left with pain. There is a RAPD on the left. Slit lamp examination reveals eyelid swelling on the left, with a normal cornea, sclera, conjunctiva, anterior chamber, iris, and lens. Dilated fundus examination revealed optic disc edema present on the left. His vital signs were within normal limits.

So what is our working differential now? Our differential includes:

- Malignancy (primary or secondary)
- Orbital cellulitis
- Ocular trauma

What is the next best step?

a) Start empiric antibiotics.
b) Obtain imaging.
c) Follow-up in 2 weeks.
d) Refer to neurosurgery.

Answer: B

This patient needs urgent brain and orbit imaging!

The preferred imaging modality is MRI due to the risk of radiation exposure in children. However, CT is acceptable if MRI is unavailable.

Imaging reveals a large mass in the sphenoid sinus extending superiorly and encasing the left optic nerve and having mass effects on the left superior oblique and medial rectus muscles. The mass is highly suspicious for rhabdomyosarcoma.

Rhabdomyosarcoma (RMS) requires an urgent pediatric ophthalmology referral. RMS comprises 5% of all childhood malignancies (Shields and Shields 2003). The average age of presentation is 8 to 10 years of age. There is a slight male preference and no differences in the prevalence between races. Forty-five percent of all cases of RMS arise in the head and neck. Of these, 25-35% arise in the orbit (Shields and Shields 2003).

RMS is one of the handful of life-threatening diseases that can present as an ocular complaint and should not be missed. A timely diagnosis and initiation of treatment can lead to better outcomes for the patient (Shields *et al.* 2001). The most common presenting symptoms of ocular RMS include: proptosis (80-100% of cases), globe displacement (80% of cases), blepharoptosis (30-50%), conjunctival and eyelid swelling (60% of cases), palpable mass (25% of cases) and pain (10% of cases) (Shields and Shields 2003).

Patients may present to clinic for another reason, such as an ocular trauma as seen in this case, so it is important to always keep RMS in the back of our mind for any patient presenting with these symptoms. Decreased eye movements and decreased visual acuity suggest advanced progression of disease. The initial work-up involves neuroimaging (with CT or MRI) to guide treatment planning. The final diagnosis is confirmed by pathology. The treatment involves a combination of chemotherapy, radiation, and surgery. RMS primarily originating from the orbit has the most favorable prognosis of any anatomic site with a 5-year survival rate of 94% (Shields and Shields 2003).

After treatment, patients should have a comprehensive ocular examination every 3-4 months initially, and then if stable 4-6 months for several years, and then yearly with repeat brain imaging based upon clinical findings.

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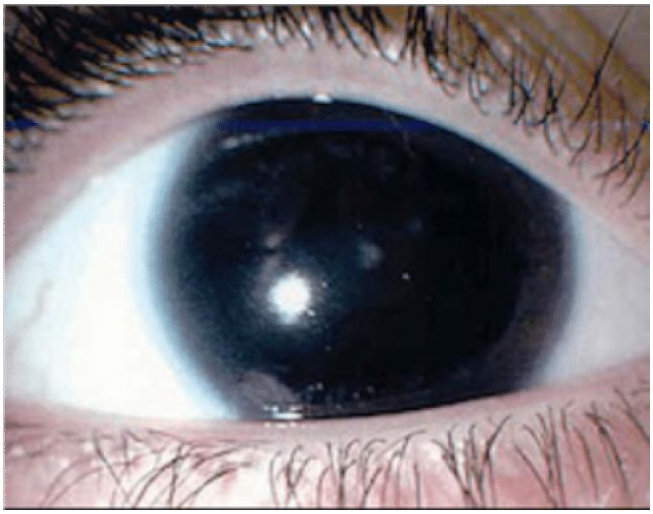
Now, let's move onto another case.

Tyler is a newborn infant is seen in clinic for his first well child visit at 1 week of life. He was born at 38 weeks gestational age to a 36yo G3P3 mom who received appropriate prenatal care. The pregnancy was uncomplicated. There is no significant family history and the boy's siblings are healthy. On examination, the child's growth parameters plot symmetrically at the 50th percentile. You cannot appreciate an iris on examination of his eyes. Cardiorespiratory and abdominal examinations are unremarkable. The neurologic examination is appropriate for his age.



So, where is Tyler's iris? Aniridia (a-nr-i-dee-uh) (literally means "absence of the iris." However, in most cases of aniridia, there is a rudimentary stump of iris tissue. It is associated with various systemic disorders and multiple ocular morbidities. Aniridia can be either congenital or acquired after surgery or traumatic injuries to the eye and can be unilateral or bilateral in nature (Tripathy, 2021). Aniridia is noted in around 1.8 out of every 100,000 births and affects males and females equally (Berlin, 1981). Patients with aniridia can have a multitude of ocular findings including nystagmus, decreased visual acuity, photophobia, myopia, and amblyopia.

What are some causes and associations of aniridia? Some of these include:

1) WAGR syndrome
2) Coloboma
3) Traumatic eye injury
4) Ocular surgery
5) Congenital Infection (TORCH)
6) Idiopathic aniridia

Now back to the case. On further examination, you notice that the right testis is not present, and he has bilateral flank masses. What is the most likely diagnosis?

WAGR syndrome is a rare genetic condition characterised by Wilms' tumor, Aniridia, Genitourinary abnormalities and mental Retardation. Congenital aniridia is caused by mutations

to the PAX6 gene on chromosome 11. Congenital aniridia can occur in isolation (inherited in an autosomal dominant fashion) or as part of the WAGR syndrome because the WT1 gene responsible for the other findings in WAGR syndrome is adjacent to PAX6.

Children with WAGR deletions require renal ultrasound examinations every three months until 5 years of age, every 6 months between 5 and 10 years of age, and every 12 months between 10-to-16-year years of age (Tripathy, 2021) Ocular management of congenital aniridia (with or without WAGR syndrome) involves regular eye exams to assess and screen for refractive error, glaucoma, and cataract development. Glaucoma can be treated medically with eye drops but may require surgical intervention. Cataracts can be treated with surgical removal of the cataract and implantation of an intraocular lens.

When examining patients with congenital iris disorders, it is also important to think about coloboma. Coloboma occurs when there is tissue missing in the structures that form the eye. This can present as notches in the iris. Coloboma occurs in approximately 1 in 10,000 people. Since coloboma may not affect vision or eye appearance, some people with this condition are often undiagnosed. Individuals with coloboma commonly also have a condition called microphthalmia. In this condition, one or both eyeballs are abnormally small and disorganized. In some affected individuals, the eyeball may appear to be completely missing; however, even in these cases some eye tissue is generally present. Microphthalmia is associated with glaucoma, cataract formation, hyperopia, and nystagmus. (Medlineplus.gov. 2021)

Before concluding, we wanted to go over our objectives for this podcast. By now, the learner should be able to

1) Understand the anatomy of the eye, ocular muscles, their functions and innervations, and the composition of the bony orbit. In summary, are 6 muscles controlled by 3 cranial nerves and there are 7 bones forming the bony orbit.
2) Rhabdomyosarcoma can present with proptosis and eyelid swelling. RMS is the most common primary orbital malignancy in children and an urgent referral to a pediatric ophthalmology service is crucial, as timely diagnosis and treatment can lead to favorable outcomes.
3) Aniridia is commonly, but not exclusively, associated with WAGR syndrome and patients require routine screening with abdominal ultrasounds and regular eye exams. Congenital aniridia is associated with several ocular findings, including glaucoma and cataracts, and requires regular ophthalmology follow-up.
4) Coloboma presents as missing structures in the eye and is associated with many ocular conditions, including microphthalmia.

Thank you for listening to our podcast and for your attention!

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