Case 6 – Dysthyroid Optic Neuropathy

Mrs B, a 67 year old female presents with progression of her POAG in the right eye despite treatment. She is currently taking cosopt (dorzolamide 2% and timolol 0.5%) twice daily to both eyes and has had previous right inferior SLT.

Her ocular diagnoses, aside from right POAG, include bilateral LASIK vision correction (previous high myope) and stable thyroid related orbitopathy.

She has no family history of note.

She has an allergy to brimonidine.

Her visual acuity is: RE 6/12 with glasses (6/7.5-2 with pinhole) LE 6/7.5 with glasses.

On testing there is full Ishihara plates in each eye and there is a right RAPD.

IOP are RE 13 and LE 16

CCT RE 494 LE 469

Gonioscopy reveals open anterior chamber angles in both eyes.
Fixation Monitor: Blind Spot
Fixation Target: Central
Fixation Losses: 2/16
False POS Errors: 4%
False NEG Errors: 15%
Test Duration: 06:28
Fovea: 33 dB
Stimulus: Ill White
Background: 31.5 asb
Strategy: SITA Standard
Date: Sep 12, 2017
Time: 9:37 AM
Age: 67

GHT: Outside Normal Limits
VFI: 81%
MD: -6.08 dB P < 0.5%
PSD: 7.73 dB P < 0.5%

Total Deviation
Pattern Deviation

:: P < 5%
:: P < 2%
:: P < 1%
:: P < 0.5%
Q1: Briefly describe the association between hypothyroidism and glaucoma and the evidence for this in the literature.

A number of case reports and case series have found an association with hypothyroidism. However, others have failed to find a significant association between hypothyroidism and glaucoma.

There appears to be a relative lack of consistent evidence for an association between hypothyroidism and glaucoma in the literature.

Q2: Describe a suggested mechanism for the development of glaucoma in hypothyroidism.

Hypothyroidism may lead to deposition of mucopolysaccharides in the trabecular meshwork may act like a surfactant, sticking together adjacent endothelial membranes, which results in increased aqueous outflow resistance thus raising IOP.

Q3: Briefly describe the association between hyperthyroidism/thyroid related orbitopathy/Graves ophthalmopathy and glaucoma and the evidence for this in the literature.

There are variable results in the literature. The prevalence of glaucoma in the general population is around 1.5-2%.

A number of patients have looked at rates of glaucoma in patients with thyroid related orbitopathy. In these studies, the reported prevalence of glaucoma approximately ranged from 2.8% to 13%. However, several studies have shown no increase in the prevalence of POAG between the general population and thyroid related orbitopathy groups.

Q4: Briefly describe the potential mechanisms for raised IOP in thyroid related orbitopathy.

Patients with thyroid eye disease may have elevated IOP in primary gaze, or more commonly, on attempted up gaze. The mechanism for this increase in IOP in thyroid related orbitopathy may be due to the following:

- Hypertrophy of the extraocular muscles may induce orbital congestion and increase in the episcleral venous pressure.
- Restrictive fibrosis of the inferior rectus muscle causes mechanical in the primary gaze position which may lead to increased IOP
- Another possible mechanism is the accumulation of mucopolysaccharides in the trabecular meshwork which would reduce drainage of aqueous humor.
Q5: This patient’s IOP’s were recorded as 13 for the right eye and 16 for the left eye. Utilising this patient’s history and examination findings, please describe a possible reason that the measured IOP’s may not be accurate. Please also state if these are likely to be under or overestimated.

This person has a history LASIK in both eyes. Her central corneal thickness is reduced compared to normal (average corneal thickness is approximately 520 microns) in each eye, as demonstrated by the pachymetry readings.

A decrease in measured IOP by Goldmann applanation tonometry has been found to be correlated with ablation depth, CCT, and baseline IOP. Change in IOP following LASIK has been variable between studies. Some have found minimal change, while others have reported reduction of IOP in excess of 5 mmHg.

One study has reported that thin corneas produce underestimation of the IOP by as much as 4.9mmHg whereas thick corneas produce overestimations by as much as 6.8mmHg. However, it is not possible to accurately make measurement conversions based on CCT readings.

Q6: Please describe the reported adverse reactions from brimonidine.

Ocular adverse reactions associated with α2-adrenergic agonists include hyperamia of the conjunctiva, anaemia conjunctiva, pupil dilation, allergic conjunctivitis, with conjunctival follicles.

Systemic adverse reactions associated with this class of medication include reduction in blood pressure, reduced pulse rate, drowsiness, and dry mouth. Allergy to brimonidine is common and allergy rates are reported to be around 9-11.5%.

Q7: Please give a brief overview of the mechanisms of adverse reaction to brimonidine drops.

Glaucoma drops contain the main therapeutic agent along with various additives. Adverse reactions to glaucoma drops may result from the main agent or the additive agents, particularly preservatives. This is a delayed hypersensitivity reaction. Brimonidine is also available with purite as the preservative in Alphagan P. Purite oxidises microbial cellular components but has no significant effect on human ocular tissues.

Most preservatives act as surfactants which destabilise bacterial cell membranes resulting in destruction of the cell membrane and inhibition of cell growth. These effects also occur with the corneal and conjunctival cells resulting in ocular surface disorders.

Q8: This patient has a diagnosis of thyroid related orbitopathy. Give a brief overview of the pathophysiology of dysthyroid optic neuropathy and if this diagnosis could be consistent with the patient’s visual fields and OCT.
Dysthyroid optic neuropathy has mechanical, vascular, and inflammatory components. The annulus of Zinn surrounds the optic nerve at the orbital apex and is the common insertion site for the rectus muscles.

Orbital fibroblast deposition of hyaluronic acid leads to extraocular muscle enlargement, enlargement of orbital fat, and overall increase in vascular congestion. Orbital fibroblasts represent the main effector cells in thyroid eye disease and demonstrate higher levels of TSH receptor expression in this disease in comparison to normal individuals. This is suggestive of a role as a potential autoantigen.

Swelling of these muscles can result in compression of the optic nerve, optic nerve ischaemia or the inhibition of axonal flow. The medial rectus muscle is most proximal to the optic nerve at the apex.

Given the damage that can occur as a result of compression of the optic nerve it is possible for such damage to result in changes consistent with the clinical picture, visual field defect and RNFL thinning seen in this patient.

Q9: This patient is noted to have stable thyroid orbitopathy. Please list the signs and symptoms you would monitor this patient for that represent increasing activity of their thyroid orbitopathy.

- ocular or retrobulbar pain
- pain with eye movement
- eyelid swelling
- eyelid erythema
- conjunctival chemosis
- conjunctival erythema
- caruncle swelling/erythema

Q10: Please describe the role of imaging in a new patient that presents with signs and symptoms consistent with thyroid orbitopathy and what the purpose of this investigation would be.

Orbital imaging techniques such as computer tomography (CT) or magnetic resonance imaging (MRI) will aid in the diagnosis of thyroid eye disease (TED) and dysthyroid optic neuropathy. Imaging is of increased importance for patients with bilateral disease; where RAPD and colour testing are less useful. Orbital imaging will demonstrate muscle enlargement in TED. In cases of dysthyroid optic neuropathy, it will demonstrate apical crowding and extraocular muscle enlargement that is greater than that seen in TED. It may also show orbital fat prolapse through the superior orbital fissure.

Imaging may also demonstrate proptosis. MRI may reveal findings similar to CT but has superior soft tissue imaging.
References:


Case 6 Test

Question 1: Increased IOP in Grave's disease may be due to:

a. Swelling of extraocular muscles which may induce orbital congestion
b. Contraction of extraocular muscles against intraorbital adhesions
c. Autoimmune destruction of the trabecular meshwork
d. a and b
e. a, b, c

Question 2: The following about glaucoma is true:

a. It is a leading cause of blindness worldwide
b. Incidence reduces with age
c. Incidence is higher among African-Americans than most other racial and ethnic groups
d. a and c and correct
e. a, b, c are correct
Question 3: Which statement about thyroid associated orbitopathy is incorrect?

a. It is an autoimmune disease  
b. Hyperthyroidism is the underlying cause in 30-40% of cases  
c. Eyelid retraction is a characteristic feature  
d. Proptosis is a characteristic feature  
e. Restrictive strabismus is a characteristic feature

Question 4: The prevalence of glaucoma in patients with thyroid associated orbitopathy in the literature is approximately:

a. 2.8 - 13%  
b. 3 - 25%  
c. 5 - 12%  
d. 7 - 13%  
e. 10 - 30%

Question 5: Vision loss in dysthyroid optic neuropathy results from an orbital apex syndrome. True or False?

Question 6: The following about adverse reactions with eye drops is incorrect:

a. The majority of glaucoma medications contain the preservative sodium chlorite  
b. Adverse reactions can be to the preservative effects  
c. Adverse reactions can be due to a delayed hypersensitivity reaction  
d. Adverse reactions can occur both locally (the eye) and systemically  
e. Side effects of timolol drops may include reduced heart rate and reduced cardiac contractility

Question 7: Which of the following is not a potential ocular adverse reaction for prostaglandin analogues?

a. Conjunctival hyperaemia  
b. Hypertrichiasis  
c. Iris pigmentation  
d. Corneal verticillata  
e. Eyelid pigmentation

Question 8: The following about brimonidine is correct?

a. Brimonidine is primarily an $\alpha_1$-agonist  
b. Brimonidine is not known to have systemic adverse reactions  
c. Brimonidine reduces aqueous humor production  
d. Brimonidine does not increase uveoscleral outflow  
e. Brimonidine has not been associated with hyperaemia conjunctivae

Question 9: Which of the following about preservatives in eye drops is correct?
a. Have a bacteriostatic effect
b. Act as surfactants
c. Cause the destruction of cell membranes
d. Can cause corneal epithelial erosion
e. All of the above

Question 10: Surgical orbital decompression for dysthyroid optic neuropathy is often required when it is refractory to medical treatment. True or False?

Question 11: The following signs may be observed in thyroid associated orbitopathy:

   a. Increased IOP in upgaze
   b. Restricted extraocular muscle movements
   c. Eyelid retraction
   d. Proptosis
   e. All are correct

Question 12: The following signs are shared by both thyroid associated orbitopathy and POAG except?

   a. Elevated IOP
   b. Ocular discomfort
   c. Visual field defects
   d. a and b
   e. a and c

Question 13: Goldmann applanation tonometry readings may be affected by which of the following?

   a. History of photorefractive keratectomy
   b. Corneal thickness
   c. History of LASIK surgery
   d. b and c
   e. All of the above

Question 14: Normal central cornea thickness is approximately:

   a. 460 micrometers
   b. 480 micrometers
   c. 500 micrometers
   d. 520 micrometers
   e. 550 micrometers

Question 15: Optic nerve function is not a useful clinical assessment to differentiate patients with dysthyroid optic neuropathy compared to TED. True or False?
Question 16: Which of the following about corneal thickness and its relation to IOP is correct:

a. Thick corneas underestimate IOP
b. Thin corneas overestimate IOP
c. Peripheral corneal IOP measurement has been reported to have increased accuracy following LASIK
d. There is no change in IOP with change in corneal thickness
e. There are currently 2 reliable correction formulas for corneal thickness and IOP readings

Question 17: LASIK may change IOP measurement accuracy by which of the following mechanisms?

a. Change in corneal thickness
b. Alteration in corneal curvature
c. Alteration in corneal rigidity
d. a and b are correct
e. a, b and c are correct

Question 18: Which of the following about IOP measurements is correct?

a. Peripheral IOP is generally less than the central IOP measurement as the cornea is thicker
b. Peripheral IOP is generally greater than the central IOP measurement as the cornea is thinner
c. The change in IOP measurements following LASIK is less in the peripheral cornea compared to the centre
d. The ablated corneal depth in LASIK does not change the IOP measurements
e. All of the above

Question 19: The number of people with Grave's disease who will develop TED is approximately:

a. 7%
b. 0%
c. 15%
d. 25%
e. 50%

Question 20: Timolol targets both $\beta_1$ and $\beta_2$ receptors. True or False?

Question 21: The pathogenesis of dysthyroid optic neuropathy involves all the following except?

a. Orbital fibroblast deposition of hyaluronic acid
b. Extraocular muscle enlargement
c. Vascular congestion
d. Inflammation and swelling of the endocranium
e. Optic nerve ischaemia from compression

Question 22: The following may be used to aid in grading the severity of TED except?

   a. Retrobulbar pain
   b. Pain on eye movement
   c. Eyelid pigmentation
   d. Conjunctival erythema
   e. Swelling of the caruncle

Question 23: The following examination findings would assist in differentiating TED from unilateral dysthyroid optic neuropathy except?

   a. RAPD
   b. Ishihara plate testing
   c. Orbital imaging
   d. Visual field testing
   e. Eye movements

Question 24: Treatments for dysthyroid optic neuropathy include which of the following?

   a. Corticosteroids
   b. Radiation therapy
   c. Immunosuppressive agents (steroid sparing)
   d. Surgical decompression
   e. All of the above

Question 25: CT has advantages over MRI for the imaging of soft tissues. True or False?