Topic: Thyroid Eye Disease (TED)
Learning objectives: Introduction etiology, clinical features and management of Thyroid Eye Disease (TED)

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Dysthroid Ophthalmopathy

Graves disease:

- Auto immune disease characterized by excess secretion of thyroid hormones by the entire thyroid gland
- 3rd – 5th decades of life
- Male: female ratio is 8:1
- Most common cause of thyrotoxicosis

- Thyroid Ophthalmology is the most common cause of bilateral as well as unilateral proptosis.

- Proptosis is axial, uninfluenced by treatment of hyperthyroidism and permanent in 70% of cases.

Other causes:

- Toxic nodular goiter, sub-acute thyroiditis, factitious hyperthyroidism
- In 10-25% of cases, thyroid ophthalmopathy occurs in absence of clinical and biochemical evidence of thyroid dysfunction
- In Ophthalmic Graves disease, the Ophthalmic signs of Graves disease occur in a patient who is not clinically hyperthyroid.

Risk factors

- More common in females (M:F 6:1)
- HLA – DR3, HLA – B8 and the genes for CTLA4 and the thyroid stimulating hormone (TSH) receptor
- Smoking
- Personal or family history of autoimmune thyroid disease

Etiology/Pathogenesis of Ophthalmopathy

IgG antibody

Enlargement of extraocular muscles:

- Increase in glycosaminoglycans may enlarge to 8 times their normal size.

Cellular infiltration: of interstitial tissues with lymphocytes, plasma cells, macrophages and mast cells during the congestive stage. Later fibrosis occurs.

Proliferation of orbital fat, connective tissue and lacrimal glands due to retention of fluid and accumulation of glycosaminoglycans.

Clinical Manifestations

- Soft tissue involvement
- Eyelid retraction
- Proptosis
- Optic neuropathy
- Restrictive myopathy

Soft tissue involvement:

Symptoms:

Include grittiness, photophobia, lacrimation and retrobulbar discomfort.

Signs:

Periorbital and lid swelling:

caused by edema and infiltration behind the orbital septum.

Conjunctiva hyperaemia:

is an important sign.

Chemosis:

- Edema of the conjunctiva and caruncle.
- In severe cases, the conjunctiva prolapses over the lower eyelid

Epibublar hyperaemia overlying a horizontal rectus muscle

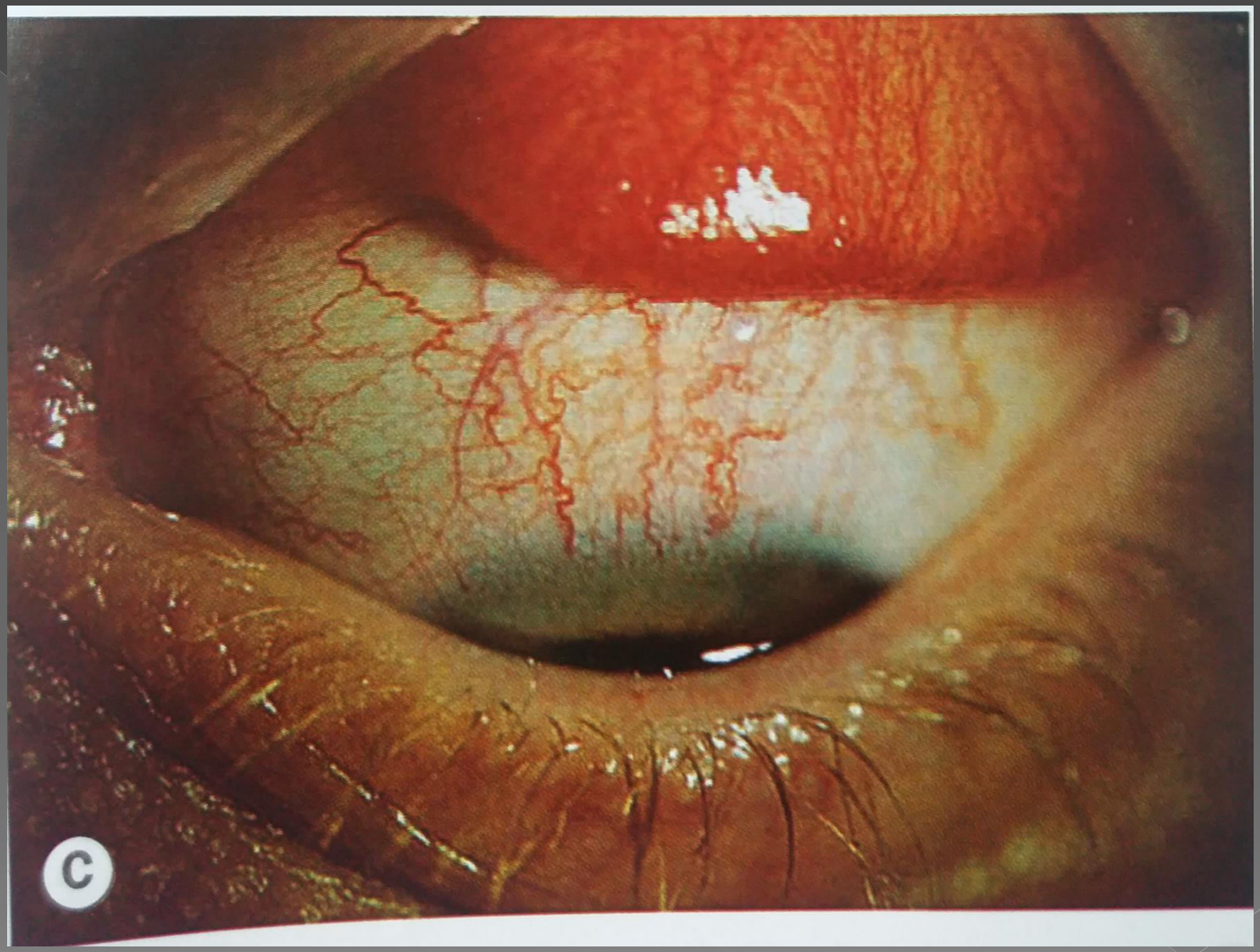
Periorbital oedema, chemosis and prolapse of fat into the eyelids

Superior limbic keratoconjunctivitis:

- Usually bilateral, asymmetrical
- Characterized by papillae on superior bulbar conjunctiva, papillary hypertrophy at the limbus, punctate epitheliopathy and corneal filaments.

Keratoconjunctivitis sicca:

- Secondary to infiltration of lacrimal glands



Superior limbic keratoconjunctivitis

Management

- Topical therapy with lubricants. Artificial tears can be used during day time and ointments during night. Patients with superior limbic K.C may require topical adrenaline 1% and acetylcysteine 5%.

- Head elevation using 3 pillows during sleep.

- Taping of the lids during sleep is specially beneficial in patients with exposure keratopathy

- Diuretics used at the night may reduce the morning accumulation of periorbital edema.

Eyelid retraction

- Retraction of both eyelids occurs in about 50% of patients with Graves disease.
- The postulated mechanisms are:
  - Contraction of the levator muscle associated with fibrosis and adhesions between the levator and overlying orbital tissues.
  - Worse on down gaze in the lower eyelid, fibrosis of inferior rectus may occur.

- Secondary overaction of levator – superior rectus complex in response to the hypophoria induced by fibrosis and tethering of the inferior rectus.
- There is increased lid retraction from down gaze to up gaze.

- Chemically induced over action of Muller muscle as a result of sympathetic over stimulation, secondary to high levels of thyroid hormones.
- In some patients, lid retraction may be reduced by the topical use of the sympatholytic drug Guanethidine.

Mild left lid retraction

Clinical features (Symptoms)

- Staring or bulging eye appearance
- Difficulty closing the eyes and
- Ocular surface symptoms

Signs

- Upper lid margin normally rests 2mm below limbus
- Lid retractiion suspected when the margin is either level with or above superior limbus, allowing sclera to be visible (scleral show)

- The lower eyelid margin normally rests at inferior limbus
- Retraction suspected when sclera shows below limbus
- Dalrymple sign is lid retraction in primary gaze

- Kocher sign describes a staring and frightened appearance of the eyes, marked on attentive fixation

- The Von Graefe sign signifies retarded descent of the upper lid on down gaze

Management

- In 50% of patients, the retraction improves spontaneously.
- Treatment of associated hyperthyroidism may also improve the retraction

- Surgery is considered in patients with marked but stable lid retraction.
- Indications are:
  - Exposure keratopathy
  - Poor cosmesis

- The sequence of surgery in thyroid ophthalmopathy is:
  - Orbital decompression
  - Strabismus surgery
  - Eyelid surgery

Surgical procedures

- Inferior rectus recession of 4mm is done in cases of inferior rectus fibrosis.
- Mullerectomy is done in mild cases.
- Recession of lower lid retractors with a scleral graft, when retraction of lower lid is 2mm or more.

- Blepharoplasty to remove excess fatty tissue and redundant skin.
- Lateral tarsorrhaphy can be done for hiding residual proptosis following lid recession. Tarsorrhaphy should not be done as a primary procedure.

Proptosis

- Thyroid ophthalmopathy is most common cause of bilateral as well as unilateral proptosis.
- Proptosis is axial, uninfluenced by treatment of hyperthyroidism and permanent in 70% of cases.
- If untreated, it may lead to exposure keratopathy.

symmetrical

Asymmetrical

Bacterial keratitis due to severe exposure

Management

- Non – invasive and surgical
- Systemic steroids may be used in patients with rapidly progressive and painful proptosis, provided there is no contraindication such as TB or peptic ulcer.

- Oral prednisolone 80 – 100 mg is given initially. Dose is tapered after 48 hours, over a duration of 2-8 weeks. Addition of cyclosporine permits a lower dosage of prednisolone.

- I.V prednisolone (0.5 gm in 200 ml saline over 30 minutes) which can be repeated after 48 hours.

- Radiotherapy can be considered in patients who have any contraindication to steroids or unresponsive.
- A positive response is evident in 6 weeks, with maximal response in 4 months.
- Surgical decompression:
  - Two – wall decompression
  - Three – wall decompression
  - Four – wall decompression

Optic neuropathy

- Affects about 5% of patients
- Caused either through direct compression of optic nerve or its blood supply at the orbital apex by the enlarged recti.
- Patient presents with slowly progressive impairment of central vision, along with defective red – green color appreciation.

Signs

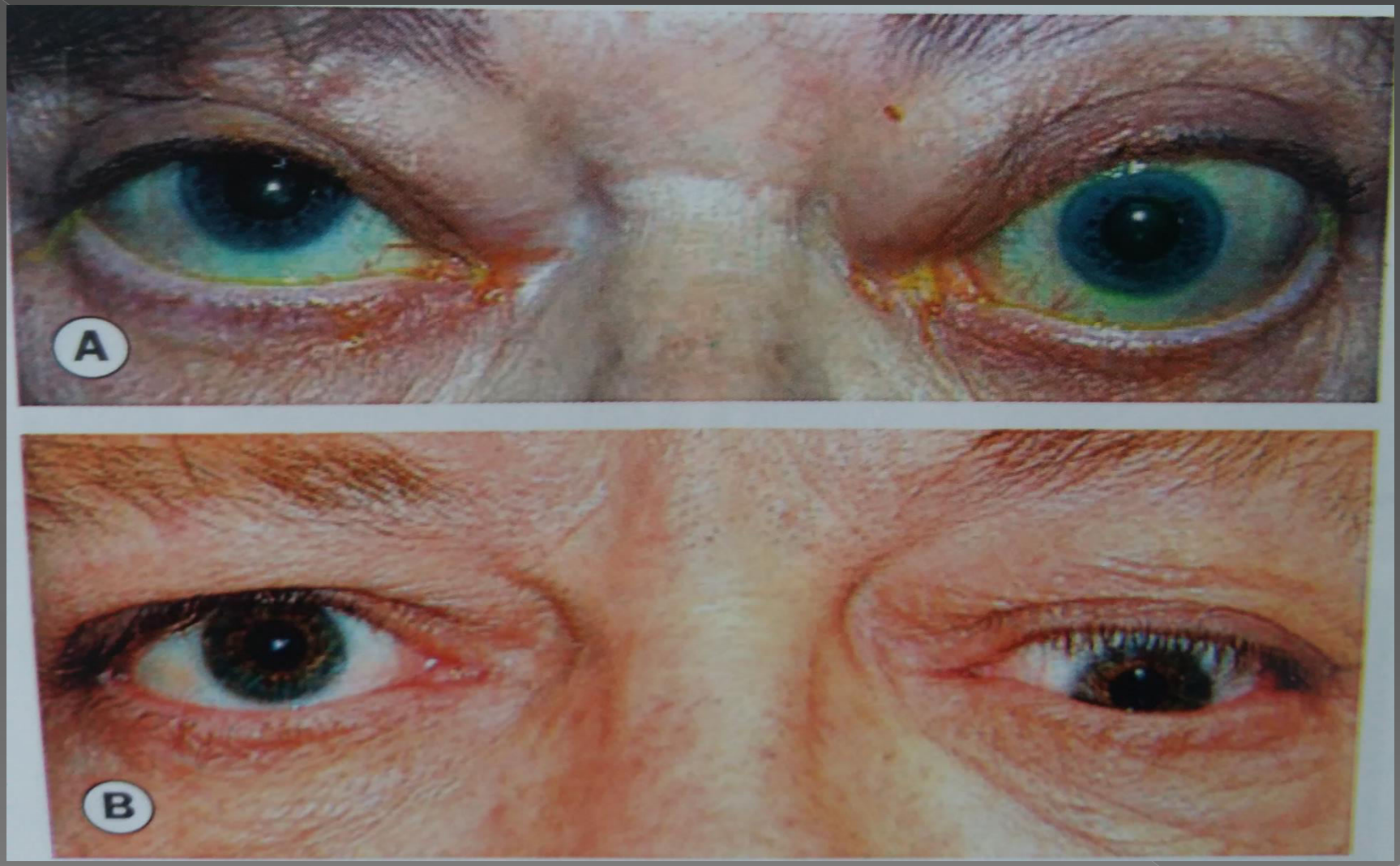
- Diminished VA may be present
- Features of optic nerve dysfunction
- Central or paracentral scotoma which may be combined with nerve fiber bundle defects
- Optic atrophy is present only in very advanced cases.
- Usually the optic nerve appears normal, although it may be swollen.

Treatment

- Initial treatment is either with systemic steroids or radiotherapy
- Orbital decompression is considered if non – surgical treatment is either ineffective or inappropriate.

Restrictive myopathy

- 30-50% of hyperthyroid patients develop ophthalmoplegia
- Diplopia is permanent in 50% of patients
- Ocular motility is restricted by edema during the infiltrative phase and later by fibrosis
- IOP increase in upgaze



(A) Defective elevation of the left eye
(B) Defective depression of the right eye

Four ocular motility defects

1) Elevation defect
2) Abduction defect
3) Depression defect
4) Adduction defect

Treatment

- Indications for surgery:

  Diplopia in the primary or reading positions of gaze.

  The angle of deviation must be stable for at least 6 months.

  No evidence of congestive ophthalmopathy indicative of active disease.

Treatment

- The goals of surgery:

  To achieve binocular single vision in the primary position of gaze and when reading.

The surgical technique:

- The most commonly performed procedure is recession of an inferior rectus and or medial rectus
- Botulinum toxin injection into the involved muscle

Investigations

1. TFTs

   usually TSH and free T4

   Biochemical investigations in TED

TFT	Hyperthyroid	Hypothyroid
TSH	↓	↑
Free T4	↑	↓

2. Thyroid auto antibodies

Immunological investigations in TED

Autoantibody	Association	
Anti – TSH receptor	>95% Graves disease	
Anti – thyroid peroxidase	80% Graves disease	90% Hashimotos thyroiditis
Anti – thyroglobulin	25% Graves disease	55% Hashiwotos thyroidits

3. Orbital imaging

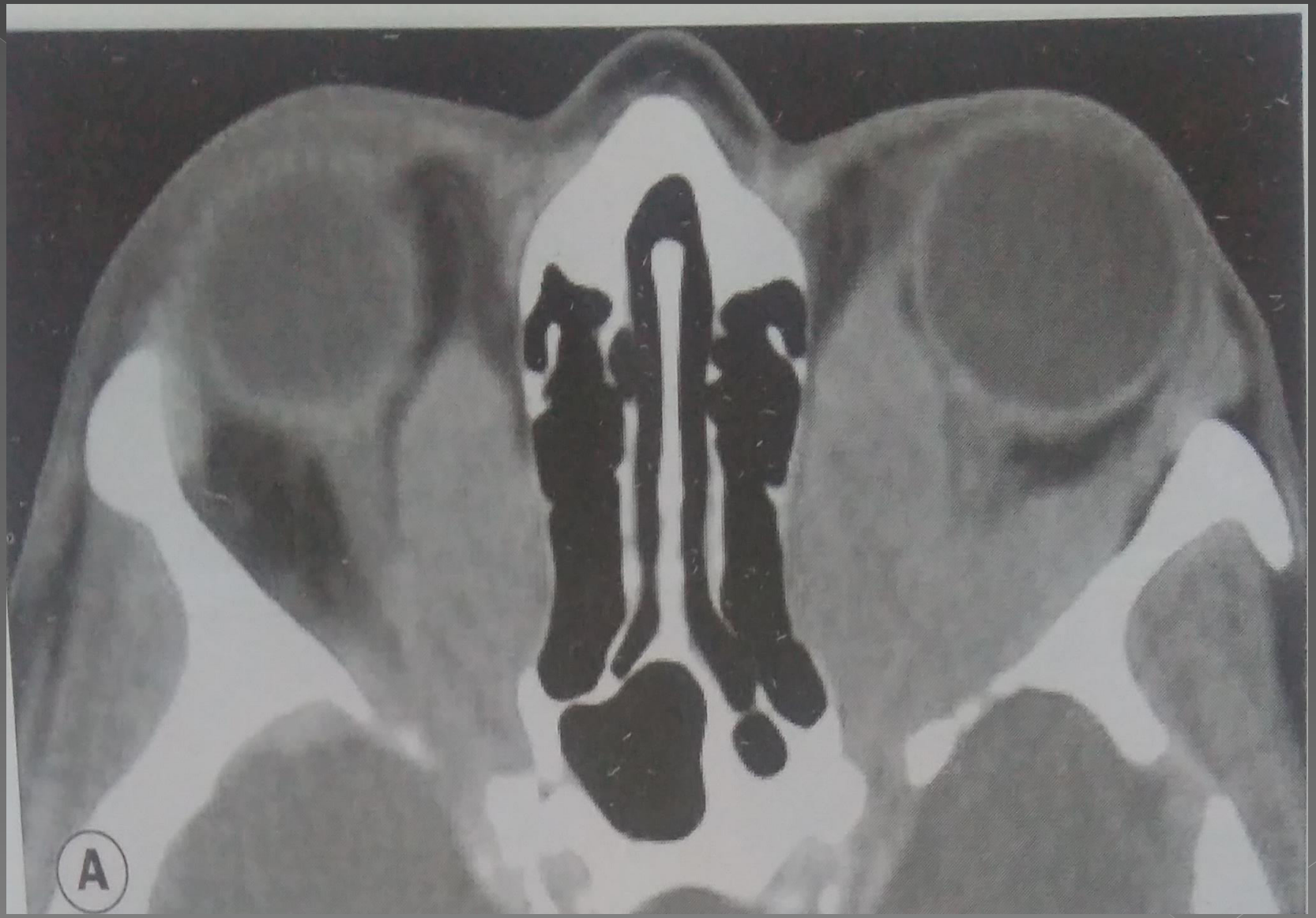
CT orbits – Better bony resolution

Preferred for planning decompression

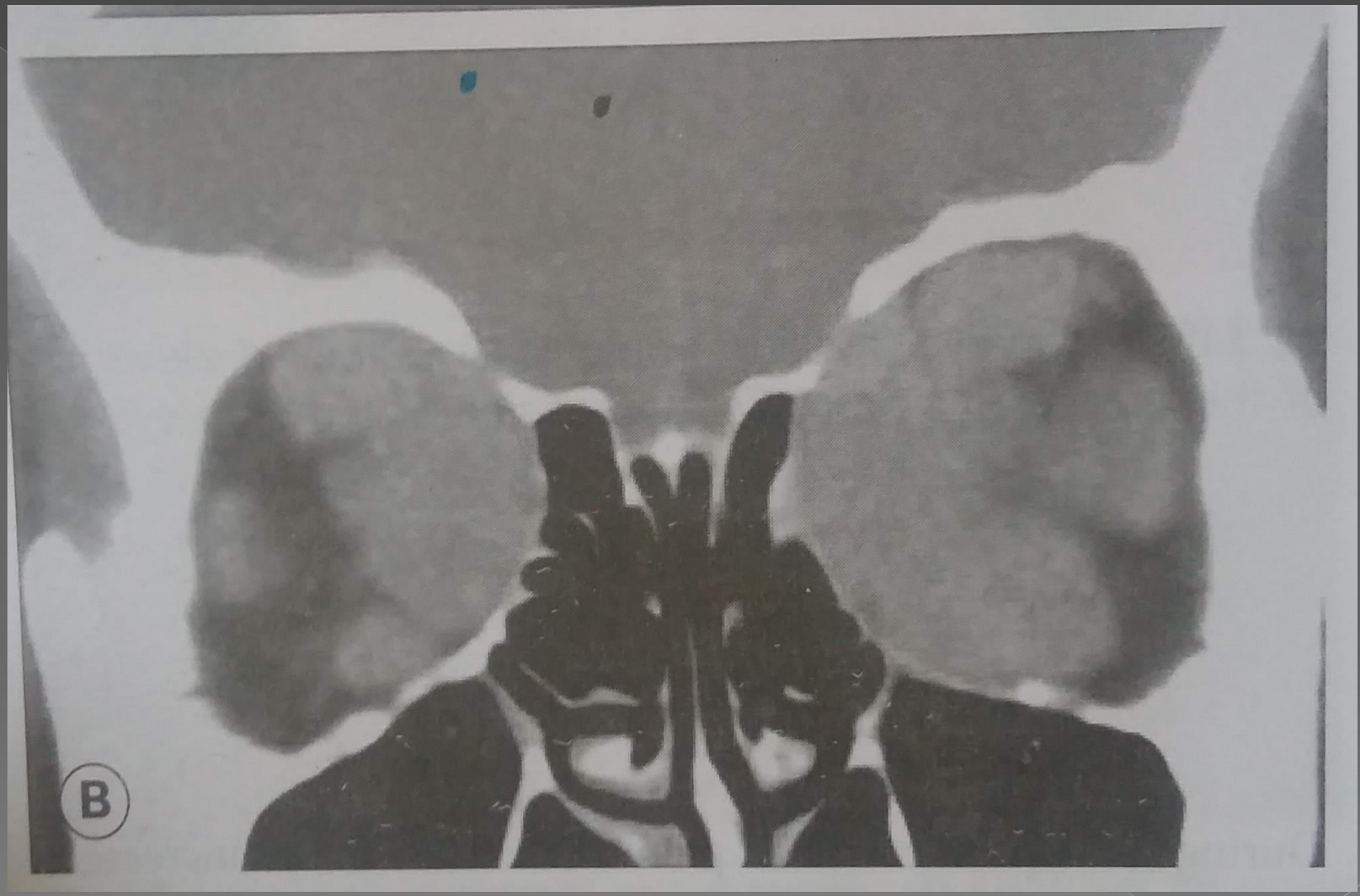
MRI (T2 – weighted & STIR)

Gives better soft tissue resolution

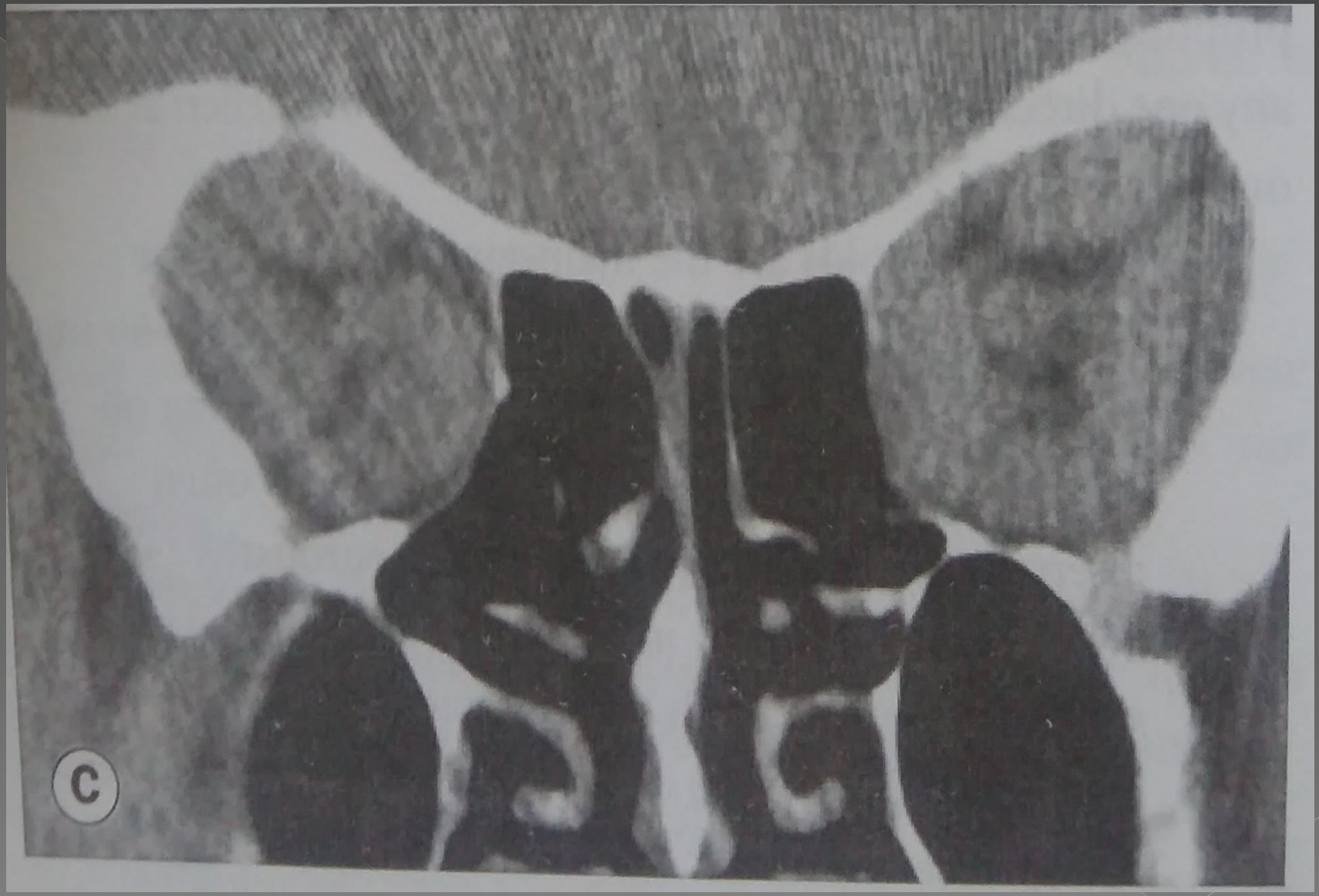
Bellies of muscles show enlargement and inflammation. Tendons spared



Axial view



Coronal view – note sparing of the right lateral rectus muscle



Coronal view shows crowding at the orbital

4. Orthoptic review

   May include – Field of binocular single vision

   Field of uniocular fixation

   Hess / Less chart

   Visual Field

General principles of management of TED

General

- Multidisciplinary input from Endocrinologist and Orthoptist.
- Supportive: counseling ocular lubricants, tinted glasses, bed head elevation. Prisms for diplopia.
- Smoking cessation

Medical

- Immuno suppression – in active disease
- Usually with systemic steroids, include ciclosporin, methotrexate, azathioprine or rituximab.
- Radiotherapy can be used, but not for sight threatening optic neuropathy.

Surgical

- For acute disease:

  Acute progressive optic neuropathy corneal exposure ➡ Emergency orbital decompression.

- For burn out disease:

  Surgery may improve function and cosmesis

  Decompression ➡ motility ➡ Lid surgery

Treatment of hyperthyroidism

Carbimazole, propylthiouracil ➡ Block production of thyroid hormones

Radioactive Iodine ➡ A single oral dose of 400 or 600MBq is given

Surgical thyroidectomy ➡ Total or subtotal preceded by radio active iodine to shrink the goitre

Treatment of hypothyroidism

- Levothyroxine

  Thyroxine replacement

Selenium and mild TED

- Antioxidant selenium
- Comparatively better quality of life
- Less ophthalmic involvement
- Reduced TED progression
- No adverse side effects.

THANKS