Commentary: Dysthyroid optic neuropathy: A lurking danger in thyroid eye disease

Poonam *et al.*, in their retrospective study, highlighted male gender, hyperthyroidism, and smoking as risk factors of developing dysthyroid optic neuropathy (DON) over four years. They highlighted the potential of recurrence of DON in patients with diabetes.[1]

DON is the most dreaded complication of thyroid eye disease (TED), warranting an urgent intervention. Fortunately, the occurrence of DON is noted only in 5%–7% of TED cases.[2] The diagnosis of established DON is majorly clinical, but the diagnosis of subclinical DON may need detailed ophthalmic examination and imaging. Patients with subclinical DON may not experience a sudden diminution of vision, abnormal pupillary reflexes, and features of orbital inflammation—classical of severe TED.[2]

The risk factors for clinical and subclinical DON include older age, male gender, smoking, diabetes (controlled or uncontrolled), radioisotope therapy, hyperthyroidism or Grave's ophthalmopathy, and high level of thyroid autoantibodies.[1,2] The pathogenesis of DON involves mechanical, inflammatory, and vascular factors causing damage to the nerve cells and axons of the optic nerve.[2] TED patients can be classified as type I (predominantly fat enlargement) or type II disease (predominantly extraocular muscle enlargement). In type II TED, the mechanical compression of optic nerve blood supply and axonal flow at the crowded orbital apex occurs due to enlarged extraocular muscles. The reduced arterial supply to the optic nerve and sluggish outflow of the blood from the superior ophthalmic vein comprises of major vascular insults contributing to the DON.[2] Moreover, these phenomena occurring at the orbital apex do not contribute much to clinical proptosis; hence many remain underdiagnosed.

In ophthalmic examination, relative afferent pupillary defect (RAPD), blue-yellow (Tritan) color deficiency, and

reduced contrast sensitivity in patients of TED are sensitive parameters for detecting DON. Clinical examination of the optic disc and optic disc imaging are important for the monitoring of DON.[2]

Orbital magnetic resonance imaging with or without contrast may provide sufficient details about the extraocular muscles, orbital fat, optic nerve, orbital apex, superior ophthalmic vein, and other essential orbital structures. Apparent diffusion coefficient readings from magnetic resonance imaging (MRI) may provide the activity details in the extraocular muscles. Barrett's muscle index of >60% is considered highly sensitive and specific for DON.[3] It is calculated on coronal computed tomography (CT) or MRI at a mid-point between the posterior globe and the orbital apex. Barrett's index includes two indices, horizontal and vertical, and the larger of the two is taken as significant. Other parameters are extraocular muscle volume/orbital volume (MV/OV) and crowding index (CI) are considered reliable indicators of DON. The 3D MRI-based volumetric analysis showed the larger extraocular muscle volume as the most relevant factor in DON.[4]

Optical coherence tomography angiography (OCTA) has been used to measure retinal nerve fiber layer thickness and peripapillary capillary vessel density (whole image and radial vessel density) as DON parameters. The patients with subclinical DON have shown significantly lower vessel densities as compared to normal individuals.[2,5]

Intravenous steroids and orbital decompression surgery remain the mainstay of treatment in DON patients. The best outcomes for DON patients are provided by combined intravenous methylprednisolone and 3-wall orbital decompression, as vision is successfully preserved in most cases with a reduction in proptosis.[6] The advent of teprotumumab, a targeted insulin-like growth factor 1 (IGF-1) receptor-based therapy, is slowly establishing itself as "medical orbital decompression" therapy. It reduces the levels of thyroid stimulating hormone (TSH) receptors and IGF-1 receptors on fibroblasts and reduces the release of pro-inflammatory cytokines like interleukin (IL)-6, IL-8, and tumor necrosis factor alpha (TNF-α) responsible for severe TED.[2,6]

Hence, an ophthalmologist should be aware of the clinical features of subclinical DON and maintain a low threshold for aggressive treatment. For the holistic management of DON, a multidisciplinary team involving an ophthalmologist, endocrinologist, and otolaryngologist should be working in coordination to avoid blindness.

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