Cerebral venous thrombosis with auto-immune hyperthyroidism

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Sudden deterioration of visual functions warrants comprehensive ophthalmic examination with evaluation for systemic association. Cerebral venous thrombosis (CVT) is an uncommon disorder that can present with neurological deficits. We report a young female patient aged 28 years who presented with severe headache and sudden diminution of vision and was subsequently diagnosed with hyperthyroidism and CVT. Management of CVT and hyperthyroidism hastened full recovery of visual functions.

Key words: Auto-immune hyperthyroidism, auto-immune optic neuropathy, cerebral venous thrombosis

Access this article online	
Quick Response Code:	**Website:** www.ijo.in
	DOI: 10.4103/ijo.IJO_23_18

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Manuscript received: 05.01.18; Revision accepted: 13.08.18

Hyperthyroidism is a rare risk factor for cerebral venous thrombosis (CVT). Optic nerve dysfunction can develop in patients without previous diagnosis of thyroid ophthalmopathy and in the absence of classic signs and symptoms of this clinical entity.

Case Report

A 28-year-old female was referred to the ophthalmology department with progressively worsening sudden diminution of vision OD for 15 days prior to presentation. Visual deterioration was preceded by severe frontal headache accompanied with an episode of vomiting. She was 1-year postpartum at presentation and had history of irregular menstrual cycles with menorrhagia for 7 months. There was no history of oral contraceptive drug intake. At presentation, her blood pressure was 118/80 mm Hg; pulse rate was 80 beats/min, regular with good volume and best-corrected visual acuity (BCVA) was hand movements with inaccurate projection of rays (PR) – OD and 6/18 with accurate PR – OS. The rest of the general physical and systemic examination was normal. She had bilateral upper eyelid retraction [Fig. 1], lid lag in down-gaze with decreased convergence and no proptosis. On pupillary examination, right-sided relative afferent pupillary defect (RAPD) was present. Color vision

Cite this article as: Madan S, Chaudhuri Z. Cerebral venous thrombosis with auto-immune hyperthyroidism. Indian J Ophthalmol 2018;66:1649-51.

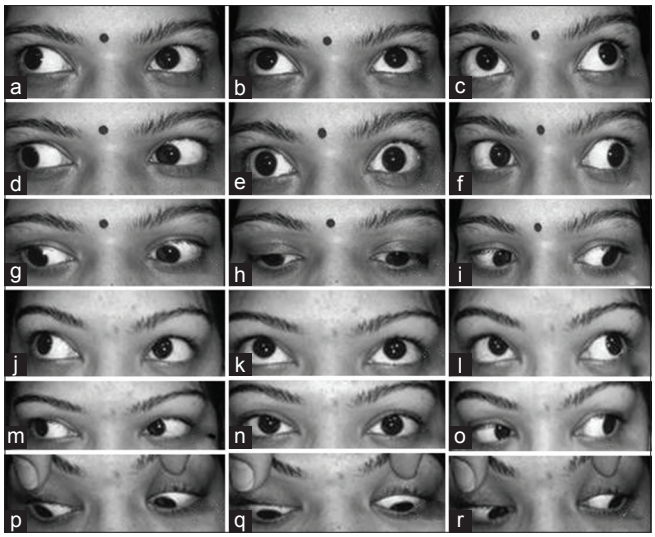

Figure 1: (a–r) Sequential patient photographs. The patient presented with marked bilateral upper eyelid retraction (a–i) and right exotropia with reduced convergence (e). Ocular movements were full in all gazes. (a–i) After 6 weeks of follow up and treatment, the eyelid retraction resolved (j–r), visual functions and ocular alignment were restored

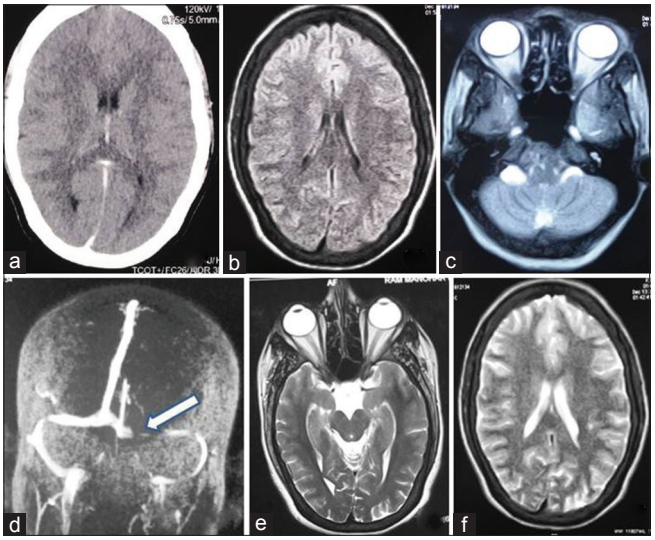

Figure 3: (a–f) Neuroimaging photographs. Axial contrast-enhanced computed tomography (a) and T2 flair magnetic resonance imaging of brain (b) along with T2 axial scan showing orbit and optic nerve (c) was normal. Magnetic resonance venography brain revealed left transverse and sigmoid sinus thrombosis (arrow) with minimal cerebral edema (d). T2 axial magnetic resonance imaging (e and f) at 3 months was normal

and contrast sensitivity were deranged in both the eyes. Bilateral optic discs were hyperemic and swollen with blurred margins, however, macula was normal in both the eyes [Fig. 2a–d]. The visual fields OD were grossly limited on confrontation. Visual field testing OS demonstrated a constricted pattern with a biarcuate type field defect [Fig. 2e]. Intraocular pressure was 14 mm Hg OD and 12 mm Hg OS. Flash visual evoked potential (VEP) waveforms were absent OD and delayed OS (P100: 133 ms). Thyroid stimulating hormone (TSH) was markedly decreased (0.01 μIU/ml)

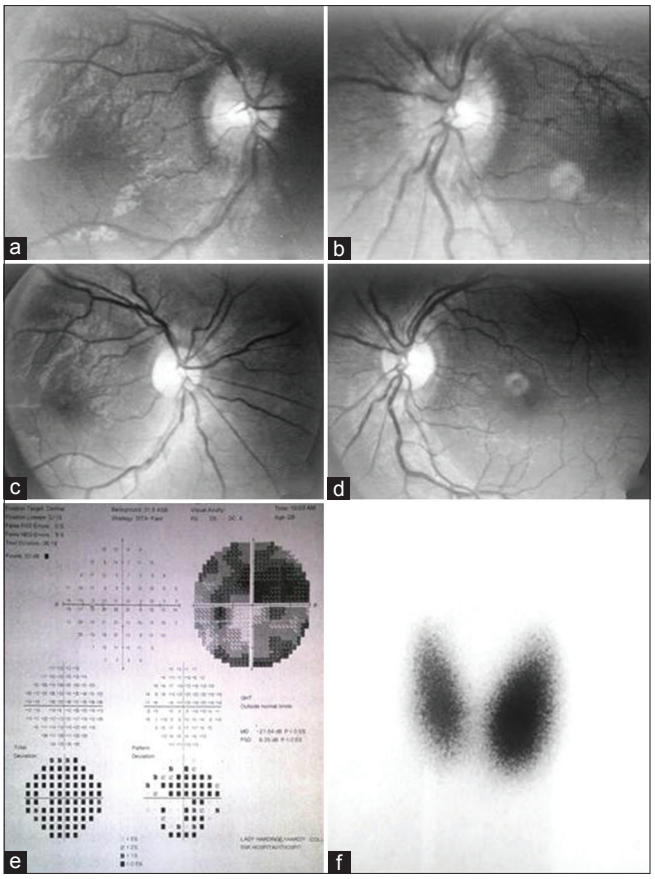

Figure 2: (a-f) Fundus, visual fields, and thyroid scan photographs. At presentation, bilateral optic discs were hyperemic, swollen with blurred margins (a and b) which resolved after treatment (c and d). Visual field charting in the left eye on presentation revealed arcuate type of field defect (e). Thyroid scan revealed features of diffuse toxic goiter (f)

with significantly increased levels of free T3 (15.18 pg/ml), free T4 (3.65 ng/dl), and anti-thyroid peroxidase autoantibody (anti-TPO, 217.17 IU/ml). Thyroid scan revealed features of diffuse toxic goiter [Fig. 2f]. Coagulation profile, D – dimer, serum homocysteine levels, contrast-enhanced computed tomography (CT) of the brain [Fig. 3a], and magnetic resonance imaging (MRI) of the brain, also showing the orbital structures and optic nerve [Fig. 3b and c] were normal. There were no radiological features suggestive of thyroid orbitopathy. Magnetic resonance venography (MRV) of the brain demonstrated dural venous thrombosis involving left transverse and sigmoid sinus with minimal cerebral edema [Fig. 3d]. In view of sudden onset diminution of vision, RAPD, severe headache and neuroimaging findings, a working diagnosis of CVT, papilledema, and auto-immune hyperthyroidism was made. Treatment with mannitol [100 ml, intravenous (IV) three times a day (TDS)], oral glycerol [four teaspoonful four times a day (QID)], oral acetazolamide (250 mg QID), enoxaparin 0.6 ml subcutaneously twice a day (BD), oral warfarin 5 mg once a day (OD), oral carbimazole 20 mg TDS, and oral cholecalciferol 60,000 U once a week, was initiated. After 1 week of initiation of this treatment, oral prednisolone in a dose of 40 mg was added and gradually tapered as documented in Table 1. Table 1 demonstrates the sequential follow-up of the patient on treatment.

Table 1: Sequential post-treatment follow-up of the patient

Baseline treatment initiated	Duration after which assessed	Clinical parameters
Mannitol, glycerol, acetazolamide, enoxaparin, warfarin (5 mg), carbimazole, cholecalciferol	1 week	Hand movements OD with accurate projection (improvement from inaccurate projection); 6/12 OS (1 line improvement)
Oral prednisolone 40 mg OD added to above treatment at 2 weeks. Oral prednisolone and oral warfarin gradually tapered to 30 mg and 3 mg, respectively, after 1 week of initiation	3 weeks	Finger counting close to face OD with accurate projection and 6/6 OS (−0.75 DS/−1 DC at 180°)
Oral prednisolone tapered to 20 mg and stopped in 4 weeks. Carbimazole 20 mg TDS tapered to BD dosage and warfarin 3 mg tapered to 2 mg OD at 5 weeks	6 weeks	BCVA of 6/9 OD (−2 DC at 10°) and 6/6 OS (−0.75 DS/−1 DC at 180°)

Repeat MRI of the brain at 12 weeks was normal [Fig. 3e and f]. BCVA remained 6/9 OD and 6/6 OS at subsequent follow-up, the last being at 15 months after the initial presentation [Fig. 1]. The optic disc swelling decreased over time [Fig. 2c and d]. The free T3 and T4 levels gradually normalized over a period of 1 year, oral carbimazole was stopped after 14 months, oral warfarin continued at 1.5 mg for 8 months and the patient was advised periodic monitoring of her thyroid function tests and coagulation profile under the supervision of an endocrinologist.

Discussion

Acquired hematological, inflammatory, infectious, hormonal, and immunologic causes along with malignancy account for nearly 85% of the cases of CVT where the patient is predisposed to a pro-thrombotic state.[1] About 15% of the cases are idiopathic.[1] Grave's disease and thyroid storm have been noted to have an association with acute CVT, however, definitive cause is not elucidated.[2] Increased levels of fibrinogen, von Willebrand factor (VWF), plasminogen activator inhibitor 1 (PAI-1), coagulation factors IX and X, and free T4 induced increase in factor VIII have been observed in patients with hyperthyroidism along with shorter activated partial thromboplastin time (APTT) that could account for a hypercoagulable state, thus predisposing to CVT.[2] A reduction in fibrinolysis and this hypercoagulable state in hyperthyroid patients is thyroxine dependent.[2] Thyroid swelling can result in mechanical compression of veins in the neck leading to CVT, however, this pathophysiological mechanism did not play significant role in our patient. As this patient was 1-year postpartum, we cannot exclude the possibility that she would be thrombogenic as well besides hyperthyroidism.

Conclusion

Bilateral optic nerve edema may be a presenting initial manifestation of thyroid eye disease.[3] Thyroid eye disease is usually self-limiting and the patients can be observed for signs of recovery. When indicated, steroids, both oral and intravenous are the medications of choice in patients with compromised optic nerve functions due to optic neuropathy.[4] CVT, optic neuropathy with auto-immune hyperthyroidism as seen in this case is unusual.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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