

# Non Atrial Fibrillation related Central Retinal Artery Occlusion (CRAO) in Hyperthyroidism: A Case Report

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## Abstract

We report a case of non AF related Central retinal artery occlusion (CRAO) (Stroke) in untreated & uncontrolled hyperthyroidism. CRAO can be considered as an ocular analogue of stroke or an ocular equivalent of acute myocardial infarction. Generally hyperthyroidism is associated with Stroke (CRAO) because of atrial fibrillation. However, we report a case of uncontrolled hyperthyroidism with CRAO in the absence of atrial fibrillation. It is with an intent to highlight the fact that a hyperthyroid state is not only complicated by AF, but even hyperthyroidism in itself is a potential risk factor in the causation of stroke. We came across only one case report of ischaemic stroke in a hyperthyroid patient without AF. We could not find any case report of hyperthyroidism with AF related CRAO in literature. Hence we report first case of non AF related CRAO in hyperthyroidism & perhaps second case report of non AF related stroke in hyperthyroidism in literature so far. An uncontrolled hyperthyroid state is tantamount to a sustained inflammatory state that results in endothelial dysfunction by causing hypercoagulable state culminating in a small calibre vessel blockage.

**Keywords:** Atrial fibrillation (AF), Central Retinal Artery Occlusion (CRAO), Hyperthyroidism.

## Introduction

Central retinal artery occlusion (CRAO) is a disease of the eye where the flow of blood through the central retinal artery is blocked (occluded). Central retinal artery is a branch of ophthalmic artery which causes sudden, acute, and painless loss of vision in one eye [2]. The most common cause for CRAO is carotid artery atherosclerosis [3]. Hyperthyroidism is a common endocrinal disorder affecting 0.5% to 2% of the population and young adults comprise a sufficient proportion of disorders [4,5]. We came across only one case report of ischaemic stroke in a hyperthyroid patient without AF [1]. We could not find any case report of hyperthyroidism with AF related CRAO in literature. Hence we report first case of non AF related CRAO in hyperthyroidism & perhaps second case report of non AF related stroke in hyperthyroidism in literature so far.

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## Case Report

A 22 years young male diagnosed by ophthalmic surgeon as central retinal artery occlusion (CRAO) was referred to us for evaluation and further management. He presented with sudden, acute, painless loss of vision in right eye since last 24 hours.

There was no headache, vomiting, convulsion or any neurological deficit. He was diagnosed case of hyperthyroidism since 3 years, took treatment for 3 months only and was not on any treatment since then.

On examination, he was conscious, oriented, afebrile with pulse rate of 110/ min, blood pressure of 130/70 mmHg. His peripheral pulsations were well felt, no carotid bruit was heard.

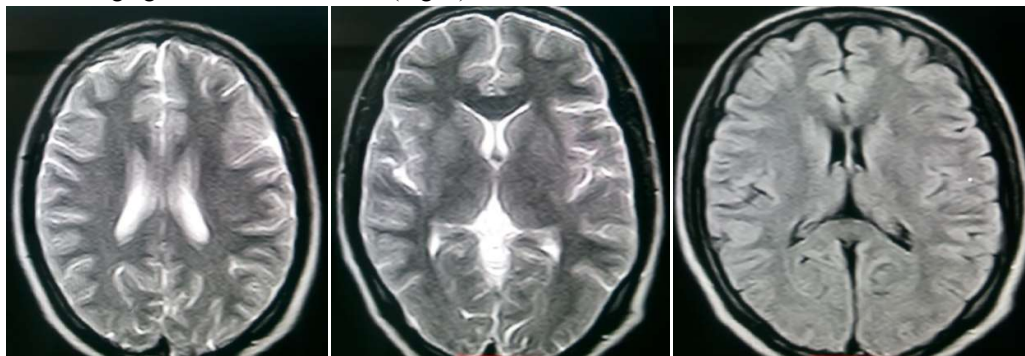
He had all deep tendon reflexes brisk on examination. Rest of the examination was unremarkable.

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He had no addiction. Other personal history was insignificant. He had no history of any medications or drugs. His family history was insignificant. His thyroid function tests showed rise in free T3 & T4 with suppressed serum TSH of 0.0004 suggestive of frank hyperthyroidism.

His kidney function tests, liver function tests & lipid profile were normal. His coagulation profile was absolutely normal. His Sr. ANA, ds DNA, and Anti phospholipid antibodies workup was negative & other autoimmune markers were also negative with an ESR of 40 mm.

Also his ANCA panel was negative, including both myeloperoxidase and perinuclear antibodies. Coagulation profile including Protein C, Protein S and antithrombin III were normal. His 2D echo was normal. MRI brain with angiogram too was normal (Fig 1).



**Fig 1: MRI Brain reveals Normal Study**

**Discussion**

We have reported a case which shows that hyperthyroidism itself can cause stroke (central retinal artery occlusion) in the absence of atrial fibrillation.

Retinal artery occlusion (RAO) is a blockade in one of the small arteries that carry blood to the retina. Retinal arteries may become blocked when a blood clot is lodged in the arteries. Clot may travel from other parts of the body and block an artery in the retina. The most common sources of emboli are the heart and carotid artery in the neck i.e. cardioembolism or artery to artery embolism respectively [6]. The retinal artery occlusion may last for only a few seconds or minutes, or it may be permanent. Retinal artery occlusion (RAO) is mostly seen in the elderly with clinical findings suggestive of atheromatous emboli [7]. Von Graefe in 1859 described CRAO in a patient of endocarditis and multiple systemic emboli [8].

Carotid doppler study was also normal. Holter monitoring was done which was reported as normal. In view of all normal reports, except uncontrolled hyperthyroid state, the patient was treated as a case of primary hyperthyroidism with CRAO.

He was put on antithyroid treatment; aspirin & clopidogrel (Dual antiplatelet), statins were started immediately and low molecular weight heparin was given for 5 days. Immediately on 2<sup>nd</sup> day, interventional radiologist posted him for intraarterial thrombolysis but there was no improvement of vision.

Patient was under follow up, his heart rate was normal. He was put on antithyroid treatment, aspirin and low dose statin therapy. In our case there was CRAO in an uncontrolled state of hyperthyroidism in absence of atrial fibrillation.

The commonest cause of CRAO in adults and aged seems to be AF related to hypertension, diabetes, ischaemic heart disease, old age (60-65 years), smoking, endocarditis and atrial myxoma [2]. However the cause of stroke in young is multifactorial [9], most common is hyperhomocystenemia [10], others are hypercoagulable states, hyperviscosity syndromes, vasculitic conditions, connective tissue disorders and sickle cell disease [11]. An estimated 0.85 per 10,000 patients over the age of 40 years are affected [12]. However, RAO is uncommon in the young population [13]. The most common cause of RAO is embolic obstruction, with carotid artery being the commonest source of endogenous emboli. Usually, RAO occurs in the mean age group of 60-65 years and predominantly affects males [14,15]. High plasma lipoprotein concentration is an independent risk factor for atherosclerosis and thrombosis [16]. Impaired

fibrinolysis and atherogenesis induced by lipoprotein-A may play a role in the pathophysiology of CRAO [17]. A study by Brown and associates [8] found 29.6% patients with coagulation disorder while in a study by Greven et al [13]. 9% patients had coagulation disorders. A study by Suvajach et al [18], showed that ocular arterial and venous occlusions were common in patients with antiphospholipid syndrome. CRAO secondary to vasculitis has been encountered in many conditions. A study by Au and O'doy has shown presence of retinal artery occlusion in 4.5% patients of systemic lupus erythematosus (SLE) [19]. There is no proven treatment for vision loss that involves the whole eye (RAO), unless it is caused by an underlying illness that can be treated. Although some studies suggested that there was no correlation between outcome and time to treatment [20], 6-12 hr of time window is generally accepted [21-23]. Visual prognosis is often poor when thrombolysis is administered more than 20 hr after CRAO [21-25].

Hyperthyroidism is well known to be associated with an increased risk of atrial fibrillation among the people aged 60 years or older [26], and there is a high risk for cardioembolic stroke in hyperthyroidism patients with atrial fibrillation [27]. The mechanism of thyroid hormone – induced dysfunction is multifactorial. The heart rate increases due to increased sinoatrial activity, a lower threshold for atrial activity and shortened atrial repolarization [28,29]. These last 2 factors also create a favourable substrate for the generation of AF, and a similar effect on ventricular myocardium has been linked with ventricular arrhythmias [30]. Volume preload increases due to activation of renin angiotensin system [31]. Contractility increases due to increased metabolic demand and the direct effect of triiodothyronine on cardiac muscle [32] and systemic vascular resistance decreases because of triiodothyronine – induced peripheral vasodilation [33].

Thyroid hormone has numerous effects on coagulation. Studies indicate that hyperthyroidism is associated with increased thrombotic risk [34]. Coagulation abnormalities such as shortened activated partial thromboplastin time, increased fibrinogen levels and increased factor VIII and factor X activity [35] and clinical sequelae such as stroke [36] are seen frequently in patients in sinus rhythm with thyrotoxicosis. Hyperthyroidism is associated with prominent cardiovascular events such as systolic hypertension, which may contribute to vascular morbidity and mortality [37]. Increased stiffness and intima media thickness, the two indices of atherosclerosis, are found in the carotid artery

in patient with hyperthyroidism, which are attributable to harmful effects of increased cardiac output and widened pulse pressure [38,39]. Hypercoagulable state observed in hyperthyroidism, includes increase in blood volume, increased levels of acute phase reactants, thrombin and fibrinogen activity [40]. An increase in Van Willebrand factor level in patient with hyperthyroidism indicates endothelial dysfunction and is associated with enhanced platelet plug formation [41,42].

Atrial fibrillation is a cardiac complication of hyperthyroidism, occurring in an estimated 10% to 25% of overtly hyperthyroid patients. The prevalence of AF in both population increases with age [43]. It is more common in men than in women [44]. High normal thyroid levels or subclinical hyperthyroidism is also associated with an increased risk of developing AF [45].

In patients with hyperthyroidism, AF is frequently of acute onset and will spontaneously revert to sinus rhythm without associated side effects often referred to as silent transient AF of thyrotoxicosis. The prevalence of AF thyrotoxicosis in patients with AF is 2% to 5% [46]. In subclinical hyperthyroidism with serum TSH level <0.1 mIU/L, the incidence of AF is increased, and in overt hyperthyroidism, cardioembolic stroke is clearly associated to thyrotoxic AF.

According to the trial of Org. 10172 an Acute stroke treatment criteria, [47] previous studies have found that strokes of other determined etiologies explained ~ 25% of ischemic strokes in young people, including dissection, antiphospholipid syndrome, moyamoya disease, SLE, migraine related stroke, and coagulopathy [48,49]. A study by shoe et al [50]. suggested that thyrotoxic patients (without AF), as compared to euthyroid individuals, are at increased risk for ischemic strokes with a hazard ratio of 1.44.

## Conclusion

Generally there is high risk of stroke in hyperthyroid patients with atrial fibrillation. However in our case report, hyperthyroidism itself caused stroke (CRAO) without occurrence of atrial fibrillation. There were no other acquired risk factors of stroke or inherited risk factor in our case. Hence, it appears that hyperthyroidism itself by the way of continuous and sustained inflammatory stress, inducement of procoagulation state and endothelial dysfunction may have caused small caliber artery i.e. CRAO stroke. Very few cases of stroke & lesser even of CRAO cases are reported in literature in

hyperthyroidism in absence of AF. We report this case to highlight the fact that uncontrolled hyperthyroidism even without atrial fibrillation can cause stroke of small caliber artery like CRAO.

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