Case Report

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Graves' Disease Presenting with Headache: An Unusual Association

Internal Medicine Section

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ABSTRACT

Headache is a common presenting complaint seen in the general population, with varying causes. However, headache as a primary symptom of thyroid disorders, specifically hyperthyroidism, is not routinely observed. Hyperthyroidism due to Graves' disease presents with typical symptoms such as hyperactivity, palpitations, fatigue and weight loss and can be associated with signs such as tachycardia, tremors and ophthalmopathy. Studies have not shown any definitive association between headache and Graves' disease. Authors hereby, describe a case of a middle-aged female patient who presented with severe bouts of headache. She was using Non Steroidal Anti-Inflammatory Drugs (NSAIDs) and other medications for pain relief, but they had no long-lasting effect. An initial diagnosis of primary headache was made after ruling out other pathologies based on blood investigations, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) studies. Despite starting appropriate therapy, the patient continued to experience persistent headache and tachycardia. Further evaluation revealed hyperthyroidism, which was managed using antithyroid drugs. This, in turn, led to the resolution of her main complaint, which was headache. She required no further pain medication and was symptom-free.

Keywords: Cephalalgia, Hyperthyroidism, Tachycardia, Thyroid antibody

CASE REPORT

A 32-year-old female who came to the Medicine Outpatient Department (OPD) with complaints of bouts of headaches in the left temporal and periorbital regions for the past year, which had increased in severity over the past month. The pain was of a stabbing type and restricted to the left side of the face only. It was episodic, with each episode lasting about one to two hours. The patient reported a history of taking analgesics—Tab Paracetamol 650 mg three times daily initially, followed by Tab Naproxen 500 mg twice daily and Tab Amitriptyline 10 mg at bedtime; she previously experienced mild relief but had no long-lasting relief. She had no history of hypertension, diabetes mellitus, ischaemic heart disease, or any other co-morbidities. There was no history of fever, loss of appetite, weight loss, or night sweats. The patient reported no history of head trauma and denied any alcohol or tobacco use.

Upon presentation, the patient was quite restless, in severe pain, and exhibiting excessive perspiration. Tenderness was elicited in the left temporal and periorbital regions. The vital examination showed tachycardia with a heart rate of 118 beats per minute, a normal blood pressure of 120/70 mmHg, a respiratory rate of 16 cycles per minute, and an oxygen saturation of 97% on room air. On central nervous system examination, the patient was completely conscious and oriented, with a Glasgow Coma Scale score of 15/15, no motor or sensory deficits, and normal reflexes. The ophthalmic examination showed no evidence of papilloedema or any other abnormalities. Initial laboratory parameters were all within normal limits [Table/Fig-1]. An MRI scan of the brain revealed no significant abnormalities.

An initial diagnosis of cluster headache, a primary headache disorder, was made, given the typical history, presentation, and lack of any significant abnormalities in the investigations done. The patient was given subcutaneous sumatriptan 6 mg for acute treatment, and Tab Verapamil 80 mg was started as prophylactic therapy. The patient experienced mild symptomatic relief but still complained of recurrent headaches and persistent tachycardia, with a pulse rate of around 120 beats per minute. Further evaluation of the tachycardia was conducted; the Electrocardiogram (ECG) showed sinus tachycardia. A 2D-ECG revealed a normal study with an ejection fraction of 60%, no regional wall motion abnormalities, or valvular pathologies. A thyroid function test was performed, which revealed elevated T3 (Triiodothyronine) and T4 (Thyroxine) levels, with a suppressed Thyroid Stimulating Hormone (TSH) level, suggestive of primary hyperthyroidism [Table/Fig-2].

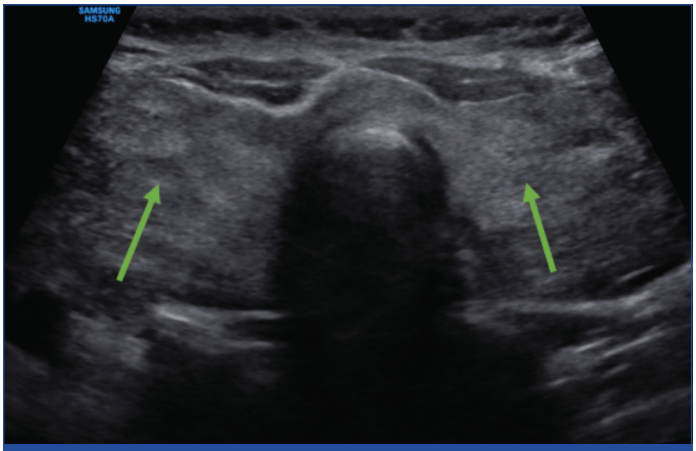
Based on these reports, a sonography of the neck [Table/Fig-3,4] was conducted, which showed mildly enlarged thyroid lobes and isthmus with heterogeneous echotexture and increased vascularity on colour Doppler, suggestive of thyroiditis. TSH receptor antibody immunoassay, antithyroglobulin antibody immunoassay, and anti-

Parameters	Observed value	Reference range
Haemoglobin (g/dL)	14.2	11.6-15
Total leukocyte count (/µL)	8500	4000-10000
Platelet (/µL)	273000	150000-410000
Bilirubin (total) (mg/dL)	1	0.22-1.22
Bilirubin (direct) (mg/dL)	0.30	≤0.5
Bilirubin (indirect) (mg/dL)	0.70	0.1-1
SGOT (U/L)	26	8-43
SGPT (U/L)	20	7-45
ALP (U/L)	103	25-104
Protein (total) (g/dL)	7.2	6.4-8.3
Albumin (g/dL)	4.2	3.5-5.2
Urea (mg/dL)	26	17-49
Creatinine (mg/dL)	0.44	0.6-1.2
Na^+ (mmol/L)	136	136-145
K^+ (mmol/L)	4.13	3.5-5.10
Ca^{2+} (mg/dL)	9.1	8.6-10.2
Mg^{2+} (mg/dL)	1.83	1.8-2.40

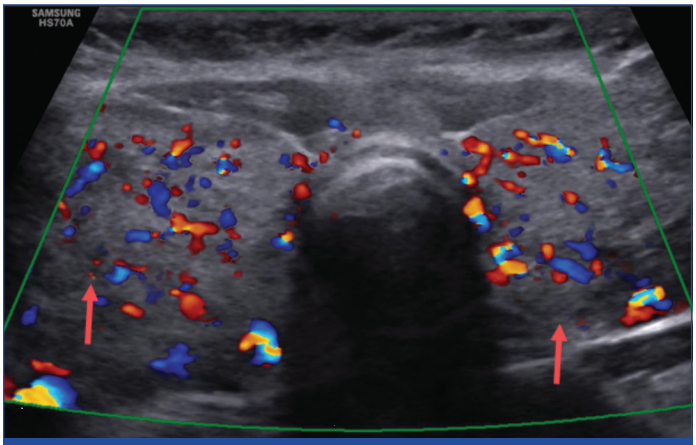
[Table/Fig-1]: Laboratory investigation on presentation.
SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamate pyruvate transaminase; ALP: Alkaline phosphatase; Na^+: Sodium; K^+: Potassium; Ca^{2+}: Calcium; Mg^{2+}: Magnesium; g/dL: grams per deciliter; µL: microliter; mg/dL: milligrams per deciliter; U/L: units per liter; mmol/L: millimoles per liter

Parameter	Observed value	Reference range
T3 (ng/mL)	2.23	0.64-1.52
T4 (µg/dL)	>24	4.87-11.72
TSH (ultrasensitive) (µIU/mL)	<0.01	0.35-4.94

[Table/Fig-2]: Thyroid function tests.
T3: triiodothyronine; T4: thyroxine; TSH: thyroid stimulating hormone; ng/mL: nanograms per milliliter; µg/dL: micrograms per deciliter; µIU/mL: micro international units per milliliter



[Table/Fig-3]: Sonography of neck showing mildly enlarged lobes of thyroid with heterogenous echotexture (green arrow).



[Table/Fig-4]: Colour doppler showing increased vascularity in both lobes of thyroid (red arrow).

thyroid-peroxidase antibody immunoassay tests were sent, which returned positive for TSH receptor antibody and anti-thyroid-peroxidase antibody [Table/Fig-5].

Parameter	Observed value	Reference range
TSH receptor antibodies (IU/L)	11.31	<=2.58
Antithyroglobulin antibody (IU/mL)	<0.9	<4
Antithyroid-peroxidase antibody (IU/mL)	416.7	<9

[Table/Fig-5]: Antibody tests.
IU/L- international units per liter; IU/mL- international units per milliliter

A diagnosis of Graves' disease was made based on the positive TSH receptor antibody and antithyroid-peroxidase antibody assays. The patient was started on Tab Propranolol 10 mg twice daily for symptomatic management, along with Tab Carbimazole 5 mg twice daily. On follow-up after a month, the patient reported no recurrent episodes of headache.

DISCUSSION

Headaches can be debilitating symptoms for many patients. Due to the large number of potential causes, identifying the exact pathology and its specific management can pose a clinical challenge. Graves' disease is the most common cause of hyperthyroidism, characterised by the presence of TSH receptor antibodies. These antibodies lead to the overproduction of thyroid hormones, which results in common signs and symptoms. In addition to these symptoms, about 25 to 50% of patients with Graves' disease develop ophthalmopathy, presenting with symptoms such as bulging eyes associated with pain and pressure [1].

This case presents a novel iteration of the disease in that the presenting symptom was a severe headache, which has not been previously reported. Initial imaging studies and laboratory investigations ruled out causes of secondary headache, such as meningitis, space-occupying lesions and stroke. The patient had no history of addiction or any risk of toxin exposure. The symptoms and signs were consistent with a diagnosis of a primary headache disorder—cluster headache—for which appropriate treatment was initiated. Recurrent headache episodes and persistent tachycardia necessitated further evaluation. A thyroid profile was subsequently sent, which revealed a hyperthyroid status. The diagnosis of Graves' disease was confirmed by positive TSH receptor and thyroid peroxidase autoantibody tests, reinforced by sonography findings of thyroiditis. Treatment with antithyroid drugs proved beneficial in improving both the tachycardia and, fortunately, the headache as well.

Other cases have been reported that display a relationship between excess thyroid hormone and headaches that do not respond to usual treatment [2,3]. Similarly, in present case, the patient experienced symptom relief only after her thyroid levels were brought under control, thus reinforcing the association. The pathophysiology of headaches due to hyperthyroidism is not well understood due to the rarity of such an association. Several studies have discussed the role of increased intracranial pressure due to hyperthyroidism, leading to increased cerebral blood flow as a possible cause of headaches [3,4]. They also mention the role of oxidative stress due to a reduction in gamma-aminobutyric acid synthesis [2].

Another possible mechanism is vasospasm. One study reports the occurrence of coronary artery disease due to thyroiditis leading to vasospasm. The same mechanism could trigger headaches [5]. The International Classification of Headache Disorders lists hypothyroidism as a cause of headaches but not hyperthyroidism. More studies are required to evaluate the exact pathophysiology [6]. The role of thyroid profile tests in the diagnosis of headaches remains controversial. Some studies report that thyroid diseases are common causes of chronic headaches, which could result from increased oxidative stress in the brain [7-9], whereas other studies report an insignificant role of thyroid function in the management of headaches [10,11].

In present case, the presence of tachycardia prompted us to send a thyroid profile, the management of which was therapeutic for the main presenting complaint.

CONCLUSION(S)

Managing headaches can be a challenging task if the cause is not apparent. Headaches are not usually linked to thyroid disorders; however, in present case, the patient experienced significant relief only after the underlying thyroid disorder was diagnosed and the thyroid levels were controlled. The association between Graves' disease and headaches still requires further research. Nevertheless, authors would like to advocate for the use of thyroid evaluations in patients presenting with headaches that have no apparent cause.

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