

## Ischaemic stroke in hyperthyroidism without cardiac arrhythmia A case report from South East Nigeria.

ONWUEKWE I, MBBS MWACP FWACP, EZE C, MBBS, FWACP  
EKENZE O, MBBS FWACP.

Neurology Unit, Department of Medicine, University of Nigeria Teaching Hospital, Ituku Ozalla, P.M.B. 01129 Enugu, Nigeria

### SUMMARY

**BACKGROUND:** The relationship between hyperthyroidism and stroke is well established in the setting of atrial fibrillation. However there is limited literature for ischaemic stroke occurring in hyperthyroidism without cardiac arrhythmia. No such case had been described in South East Nigeria.

**METHOD:** This report highlights a case of ischaemic lacunar infarction in an elderly Nigerian woman with re-emergent thyrotoxicosis, without atrial fibrillation.

**RESULT:** A 75- year old retired female teacher presented with a painless goiter of 3 years duration and right sided hemiplegia of 2 months duration. She had sub-total thyroidectomy 32 years ago for thyrotoxicosis with subsequent good outcome and had been managed for diabetes mellitus for 13 years with good glycaemic control. She was not a known hypertensive. She was thyrotoxic on examination with a large non- tender goiter. There was sinus tachycardia. She had a right sided facial nerve palsy and ipsilateral spastic hemiplegia. Sensations were spared. Results of investigations confirmed hyperthyroidism while brain CT scan was unremarkable except for cerebral atrophy. She had no other associated risk factor associated with hyperthyroidism. Within two weeks of admission she was stabilized on anti-thyroid and anti-diabetic medications, her motor functions significantly recovered and she was independent. She was discharged to be followed up at the out-patients' clinic.

**CONCLUSION:** Ischaemic stroke may present in hyperthyroid patients without atrial fibrillation. This possibility needs to be entertained despite the absence of cardiac arrhythmia or other well established factors for cardioembolic stroke. There is a need for more studies on this relationship.

**KEY WORDS:** ischaemic stroke, hyperthyroidism, South East Nigeria.

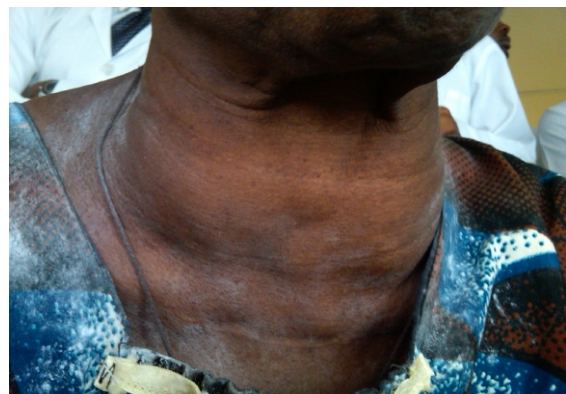
arteritis, and cerebral venous thrombosis. However, only case reports or case series were found in the literature, and the causal relationship between hyperthyroidism and these syndromes cannot be established.<sup>2</sup> In thyrotoxic patients without cardiac arrhythmia, only 7 cases of acute cerebrovascular ischaemic disease have been identified, and even in some of these cases, paroxysmal AF or vasculitis was not excluded entirely.<sup>1</sup> No literature was found from South East Nigeria describing this association.

### CASE SUMMARY

A 75- year old retired female teacher presented to the Neurology Clinic of the University of Nigeria Teaching Hospital Enugu in May 2011 with a painless anterior neck mass and weakness in the right limbs of 3 years and 2 months duration respectively. The neck mass was associated with mild dysphagia, heat intolerance, weight loss, palpitations, tremulousness and anxiety. The weakness on the right limbs was noticed on waking up in the morning and associated with ipsilateral facial weakness. There was no headache, vomiting, impaired sensorium, seizures or preceding head trauma.

She had undergone a sub-total thyroidectomy 32 years previously (1978) for a hyperthyroid goiter with good outcome. She had no record of a histology report on the goitre removed. She was not known to have hypertension but has had diabetes mellitus for 13yrs (since 1998) for which she's been well controlled on oral hypoglycaemic agents (glibenclamide and metformin). Her father died from stroke. She neither took alcohol nor tobacco.

Physical examination disclosed a conscious and alert woman, anxious, with fine tremors of her hands which were warm. She had a grade 4 goiter with benign features (see figure 1). There were negligible eye signs of hyperthyroidism.



**Date Accepted for Publication:** 19th September, 2012

NigerJMed 2012;458-461

Copyright ©2012. Nigerian Journal of Medicine

### INTRODUCTION

Hyperthyroidism is well-known to be associated with an increased risk of atrial fibrillation (AF) among people aged 60 years or older and there is a high risk for cardioembolic stroke in hyperthyroidism patients with atrial fibrillation.<sup>1</sup> Hyperthyroidism may also be associated with various types or aetiologies of cerebrovascular disease, including Moyamoya disease, antiphospholipid syndrome, giant cell arteritis, Takayasu

There was a right facial nerve palsy (UMN type); a right spastic hemiplegia with exaggerated reflexes and ankle clonus. Fundoscopy showed arteriosclerotic vessels. Visual fields and sensations were normal.

She had a resting tachycardia of 120/min with a normal rhythm and slightly thickened arterial wall; blood pressure was 136/84 mmHg; apex beat was at the 5<sup>th</sup> left interspace and mildly heaving and the heart sounds were normal.

She was admitted into the ward as a case of ischaemic lacunar infarction and hyperthyroidism.

Laboratory investigations done within 4 days of admission confirmed hyperthyroidism with the following values: elevated T<sub>3</sub> at 1.8ng/ml (normal 0.6- 1.6), normal T<sub>4</sub> at 9.6µg/dl (normal 2.5- 12.5), normal free T<sub>4</sub> at 1.2µg/dl (normal 0.8- 2.2), reduced TSH at 0.4µU/ml (normal 0.5- 4.8). Complete blood count, serum lipid profile and electrolytes, blood urea nitrogen and creatinine levels were all within normal range. Fasting blood sugar was elevated at 198mg/dl.

Electrocardiogram showed sinus tachycardia. Chest radiograph was unremarkable. Brain CT scan disclosed only diffuse cerebral atrophy while thyroid ultrasound scan was suggestive of adenomatous goiter.

She was treated with propranolol, insulin, clopidogrel, low dose aspirin, vitamins C and E and carbimazole. She also received physiotherapy and dietary advice. By the second week of admission she was converted to oral anti-diabetic medications. Following progressive improvements in motor functions and relief of thyrotoxic symptoms she was discharged home on her medications. Follow-up at the clinic 3 months after showed her to be very stable.

## DISCUSSION

Stroke is a leading cause of death and long-term disability in adults.<sup>3</sup> Several conditions such as hypertension, atherosclerosis, diabetes mellitus are well established risk factors for ischaemic stroke. Although hyperthyroidism may involve short-term and long-term cardiovascular consequences,<sup>4</sup> data concerning the association between hyperthyroidism and cardiovascular outcomes are inconsistent.<sup>5</sup> Hyperthyroidism is well-known to be associated with an increased risk of atrial fibrillation among people aged 60 years or older,<sup>1</sup> and there is a high risk for cardioembolic stroke in hyperthyroidism patients with atrial fibrillation. Hyperthyroidism may also be associated with various types or etiologies of cerebrovascular disease in the absence of arrhythmia, including Moyamoya disease, antiphospholipid syndrome, giant cell arteritis, Takayasu arteritis, and cerebral venous thrombosis (CVT). However, only case

reports or case series were found in the literature, and the causal relationship between hyperthyroidism and these syndromes cannot be established<sup>1</sup>

In thyrotoxic patients without cardiac arrhythmia, only 7 cases of acute cerebrovascular ischemic disease have been identified, and even in some of these cases, paroxysmal AF or vasculitis was not excluded entirely.<sup>1</sup> This formed the basis for the interest in our case. Because acute cerebral ischaemia is rarer than CVT it has been argued that these case reports do not prove that there is an increased rate in thyrotoxic patients without cardiac arrhythmia.<sup>1</sup> To what extent these factors contribute to the aggravation of stroke-induced injury and neurological deficits is still not clear.<sup>3</sup> Although studies had shown that hyperthyroidism increased stroke mortality in elderly patients<sup>6,7</sup> the risk of stroke did not increase in patients aged 25 to 74 years with hyperthyroidism diagnosed by free thyroxine index measurement.<sup>8</sup>

Our patient had sub-total thyroidectomy 32 years ago for a hyperthyroid goiter. She did not have hypothyroidism subsequently and was stable clinically till the recurrence of her thyrotoxic symptoms 3 months prior to presentation. Primary hyperthyroidism is suggested by her low TSH level. Also she developed type 2 diabetes mellitus about 20 years after the onset of hyperthyroidism. Circulating thyroid hormone (TH) levels seem to modulate the outcome of ischaemic-reperfusion (IR) injury and hypothyroidism is known to be neuroprotective in the animal stroke model as well as in stroke patients.<sup>9,10,11</sup> In contrast, thyrotoxicosis causes oxidative damage in various tissues such as the liver, heart, and brain of the rat.<sup>12</sup> The risk of dementia and Alzheimer's disease is greater in hyperthyroid patients.<sup>13,14</sup> In thyrotoxicosis, atrial fibrillation and cardioembolic stroke can precipitate acute cerebral ischemia, and oxidative stress along with lipid peroxidation damage have been suggested as plausible mechanisms.<sup>1</sup>

In a clinical-experimental study, chronic thyrotoxicosis in patients has been reported to aggravate the symptoms of hypertensive disease and increased oxygen consumption by tissues, slowed down the electron transport from the respiratory chain, and increased the content of iodine and protein.<sup>15</sup> Though cross-sectional studies in elderly populations are not able to ascertain a clear relationship between thyrotoxicosis, hypertension and strokes<sup>8,16,17,18</sup> clinical case reports suggest that thyrotoxicosis aggravates neurological damage subsequent to cerebral ischaemia.<sup>19,20,21,22</sup> In a case of Grave's disease with frequent episodic transient left hemiparesis and mild slurred speech lasting for a few minutes to 2? hours, the recurrence was prevented by treatment with propylthiouracil and aspirin.<sup>8</sup> The

pathophysiological relationship between thyrotoxicosis and aggravation of ischaemia-induced cerebral damage is not clear. Also cerebral venous thrombosis (CVT) has been reported in patient with thyrotoxicosis. Possible predisposing factors for the development of CVT in patients with thyrotoxicosis are also in line with Charcot's triad. Hypercoagulability, stasis of venous blood flow from the goitre and the hyperdynamic circulation are all contributory for causing CVT.<sup>1</sup>

Our patient neither had clinical nor laboratory evidence for atrial fibrillation, cardioembolism (though an echocardiogram could not be obtained) or CVT. It is known that lacunar infarcts may not be visible on CT but her clinical features were in keeping with a diagnosis of lacunar infarction. The patient's stroke has a strong temporal relationship with the resurgence of a hyperthyroid goitre. The raised blood sugar obtained at admission could be explained via several mechanisms including (i) reactive hyperglycaemia of stroke (Claude-Bernard syndrome), (ii) an acute exacerbation of her diabetes mellitus, despite good adherence to anti-diabetic medications and (iii) hyperglycaemia as a direct complication of hyperthyroidism. Unfortunately HbA1c was unavailable at the hospital at the time in question.

It is our postulation that her case adds to the body of data which emphasizes the need for large, multicentre longitudinal studies to further clarify and define the association between ischaemic stroke and hyperthyroidism especially in patients without cardiac arrhythmia.

## REFERENCE

1. Squizzato A, Gerdes VEA, Brandjes DP, Bullar HR, Stam J. Thyroid diseases and cerebrovascular disease. *Stroke*. 2005;36:2302 - 2310.
2. Jau-Jiuan Sheu, Jiunn-Horng Kang, Hsiu-Chen Liu, Heng-Ching Liu. Hyperthyroidism and risk of ischaemic stroke in young adults a 5 year follow-up study. *Stroke*. 2010;41:961 - 966.
3. Leena Rastogi, Sushil Gupta, Madan Godspole. Pathophysiological basis for thyrotoxicosis as an aggravating factor in post-ischemic brain injury in rats. *J Endocrinol*. 2008;196:335-341.
4. Osman F, Gammage MD, Franklyn JA. Thyroid disease and its treatment: short-term and long-term cardiovascular consequences. *Curr Opin Pharmacology*. 2001;1: 620 -631.
5. Frost L, Vestergaard P, Mosekilde L. Hyperthyroidism and risk of atrial fibrillation or flutter: a population based study. *Arch Intern Med*. 2004;164:1675 -1678.
6. Metso S, Jaatinen P, Huhtala A, Auvinen A, Oksala H, Salmi J. Increased cardiovascular and cancer mortality after radioiodine treatment for hyperthyroidism. *J Clin Endocrinol Metab*. 2007;92:2190 - 2196.
7. Franklyn JA, Maisonneuve P, Sheppard MC, Betteridge J, Boyle P. Mortality after the treatment of hyperthyroidism with radioactive iodine. *N Engl J Med*. 1998;338:712- 718.
8. Qureshi AI, Suri FK, Nasar A, Kirmani JF, Divanni AA, Giles WH. Free thyroxine index and risk of stroke: results from the National Health and Nutrition Examination Survey Follow-up Study. *Med Sci Monit*. 2006;12:CR501 - Cr506.
9. Shuaib A, Ijaz S, Hemmings S. Decreased glutamate release during hypothyroidism may contribute to protection in ischemia. *Exper Neurol*. 1994;128:261 - 265
10. Alevizaki M, Synetou M, Xynous K, Alevizaki CC, Vemmos KN. Hypothyroidism as a protective factor in acute stroke patients. *Clin Endocrinol*. 2006; 65:369 - 372.
11. Rastogi L, Godspole MM, Ray M, Rathore P, Pradhan S, Gupta SK, Pandey CM. Reduction in oxidative stress and cell death explains hypothyroidism induced neuroprotection subsequent to ischemia/reperfusion insult. *Exper Neurol*. 2006; 200:290 - 300.
12. Adamo AM, Llesuy SF, Pasquini JM, Bovers A. Brain chemiluminescence and oxidative stress in hyperthyroid rats. *Biochem J*. 1989; 263:273 - 277.
13. Kalmijn S. Subclinical hyperthyroidism and risk of Dementia. The Rotterdam study. *Clin Endocrinol*. 2000; 53:733 - 737.
14. Kapaki E, Paraskevas GP, Montzou E, Papapostolou A, Alevizaki M, Vassilopoulos D. Thyroid function in patient with Alzheimer disease: implication to anticholinesterase treatment. *Alzh Dis Assoc Disord*. 2006;20: 242 - 247.
15. Beutlin E, Duron O, Kelly BM. Improved method for estimation of blood glutathione. *J Lab Clin Med*. 1969;61: 882 - 887.
16. Völzke H, Alte D, Dörr M, Wallaschofski H, John U, Felix SB, Rettig R. The association between subclinical hyperthyroidism and blood pressure in a population-based study. *J Hypertens* 2006; 24: 1947 - 1953.
17. Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PJ, Feddema P, Michelangeli V. Subclinical thyroid dysfunction and blood pressure: a community-based study. *Clin Endocrinol*. 2006; 65: 486 - 491.
18. Wilson S, Parle JV, Roberts LM, Roalfe AK, Hobbs FD, Clark P, Sheppard MC et al. Birmingham Elderly Thyroid Study Team Prevalence of subclinical thyroid dysfunction and its relation to socioeconomic deprivation in the elderly: a community-based cross-sectional survey. *J Clin Endocrinol Metab*. 2006;91: 4809 - 4816.
19. Smith CD, Ain KD, Ryan S, Ngai BC. Systemic embolism in thyrotoxicosis without cardiac arrhythmia. *Thyroid* 1994; 4: 209 - 211.
20. Rocha MS, Brucki SM, Ferraz AC. Cerebral

- vasculitis and Basedow-Grave's disease: report of two cases. *Arquivos de Neuro-Psiquiatria* 2001; 59: 948-953.
21. Mouton S, Nighoghossian N, Berruyer M, Derex L, Philippeau F et al. Hyperthyroidism and cerebral venous thrombosis. *Europ Neurol.* 2005; 54: 78-80.
22. Tsai MH, Tan TY, Kuo YL, Chang KC. Multiple intracranial arterial stenosis in association with thyrotoxicosis: a case report. *Acta Neurol Taiwan.* 2006; 15: 105-108.