

ATRIAL FIBRILLATION IN CHILDHOOD WITH FAMILIAL HYPERTHYROIDISM IN AFRO-CARIBBEANS

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ABSTRACT

Atrial fibrillation (AF) associated with familial hyperthyroidism (FH) spanning three generations concomitantly, is rare. The index case was 10 years old when he started having AF secondary to hyperthyroidism, and is the youngest case documented. His mother was diagnosed at 31 years of age, 8 years after giving birth to him; and his maternal grandmother was diagnosed with the same goitre problem, hyperthyroidism, and palpitations at 49 years of age. The index case also has a restrictive perimembranous ventricular septal defect, which makes it a clinically challenging and more interesting case.

Keywords: Atrial fibrillation, hyperthyroidism, goitre, ventricular septal defect, gene.

INTRODUCTION

In 1936, Orgain and Wolf et al.¹ first recorded a familial incidence of atrial fibrillation (AF) and hyperthyroidism after the onset of atrial fibrillation in a patient with a normal heart. Brugada et al.² (1997) and Chen et al.³ (2003) identified Spanish families and Chinese families with atrial fibrillation with a common autosomal dominant chromosomal link on 10q22-24 and 11p15.5 respectively.

The incidence of AF is rare in childhood, and even more so when concomitant hyperthyroidism occurs, as seen in the index case.⁴ Sick Kids Hospital in 1977 noted 35 cases of AF in 22 years. There have also been documented cases of AF in fetuses.^{4,5}

AF can present as, or be the presenting feature with palpitations, syncope, dizziness, fainting, shortness of breath, dyspnoea, chest pain, angina, lethargy, cerebrovascular accident (i.e. stroke), or as myocardial infarction. AF can also present with overt or subclinical hyperthyroidism, valvular heart disease of congenital or rheumatic origin, hypertension, biventricular heart failure, dilated cardiomyopathy, atrial tumours, Thyrotropin (TSH)-secreting pituitary adenoma, carney syndrome and use of specific thyrotoxic drugs like amiodarone, electrolyte disturbance, and carnitine deficiency.¹⁻²²

Drugs associated with AF are highly caffeinated beverages, alcohol, steroids, marijuana and illicit drugs.⁶⁻¹⁵

'Maladie de Roger' perimembranous ventricular septal defects (VSD), have no statistically significant aetiology of AF which the index case has.¹⁶

CASE REPORT

An Afro-Caribbean 10-year-old male presented with goitre (Figure 1), intermittent palpitations, diaphoresis, increased appetite, weight loss, intermittent hand and eyelid tremors, feeling warm, and mood changes for 3 months prior to being seen. There was a complete cessation of symptoms when a course of beta-blocker propranolol and anti-thyroid drug NeoMercazole was started. 2 years later, at 12 years of age, there was a continuation of propranolol but an inadvertent reduction of anti-thyroid NeoMercazole given, from 25 mg three times daily to 10 mg three times daily. Palpitations started on the third day of reduced dosage of the anti-thyroid medication, with complete resolution when the appropriate dosage was recommenced.

The index case was diagnosed at 6 months of age with a small restrictive perimembranous VSD, now partially closed with tricuspid valve tissue as

well as mild pulmonary valve stenosis. At 2 years of age he was diagnosed with autism and mild developmental delay.

He is the second of four children for his mother. All the other siblings, two boys and one girl, aged 14 years, 6 years and 3 months old, born before and after the mother was diagnosed with hyperthyroidism, are normal.

The index case's mother was diagnosed with hyperthyroidism presenting with goitre (Figure 2) and the first palpitations in the family at 31 years of age, when the index case was 8 years old. She is controlled completely on the same beta-blocker and anti-thyroid medication. The maternal grandmother of the index case was diagnosed at 49 years of age, a few months before the index case, with a goitre (Figure 3) and palpitations at a peripheral hospital, and is also controlled with the same medications. There are currently no clinical signs of ophthalmopathy in any of the hyperthyroid family members. There is no other family member with congenital heart disease or electrophysiological disorder, except the index case. There was no history of any medical or illicit drug usage in any family member, except those prescribed.

On examination, at 12 years of age, the index case's weight was 36.8 kg and height was 154 cm. Cardiovascular examination revealed a normal pulse volume and no collapsing pulse. His apex beat was in the fifth left intercostal space in the midclavicular

line, thrusting in character. A pansystolic murmur, grade 4/6, was noted at the mid left sternal border. There were no signs of heart failure or pulmonary hypertension.

Investigations before recommencing the appropriate dose of anti-thyroid medication revealed increased levels of free T4 82.5 pmol/L (normal 10.3-26.0) and free T3 17.0 pg/mL (normal 1.4-4.2), and low level thyroid stimulating hormone 0.1 uIU/mL (normal 0.39-6.82). The erythrocyte sedimentation rate was 2. The only abnormality on the resting electrocardiogram was a heart rate of 104/minute.

A Holter monitor showed sinus tachycardia with a maximum heart rate of 192 bpm. There were intermittent episodes of AF (Figure 4) with 20% supraventricular ectopy. There were four isolated premature ventricular ectopic beats of no clinical significance.

Transthoracic echocardiography showed a restrictive perimembranous VSD partially closed by tricuspid valve tissue. The maximal velocity of the left to right shunt across the VSD was 5.39 m/s. There was mild pulmonary valve stenosis of 1.79 m/s. There were normal ventricular function, right ventricular pressure and pulmonary artery pressure.

Thyroid ultrasound showed a diffusely enlarged, hypoechoic, hypervascular gland. The right lobe measured 28 mls, left lobe 23 mls and isthmus had an anterior-posterior diameter of 1.5 cms. No discrete nodule or cervical lymphadenopathy was noted.

Fig. 1

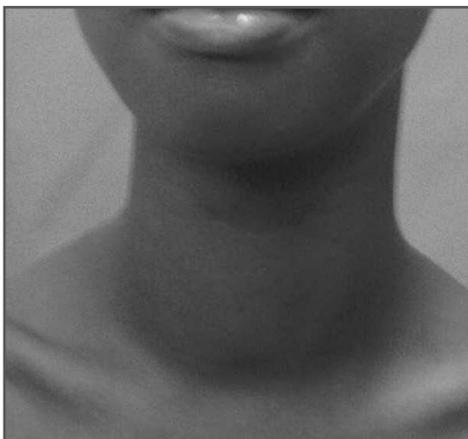


Fig. 2

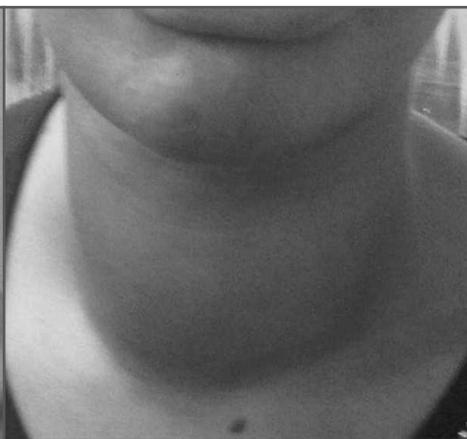


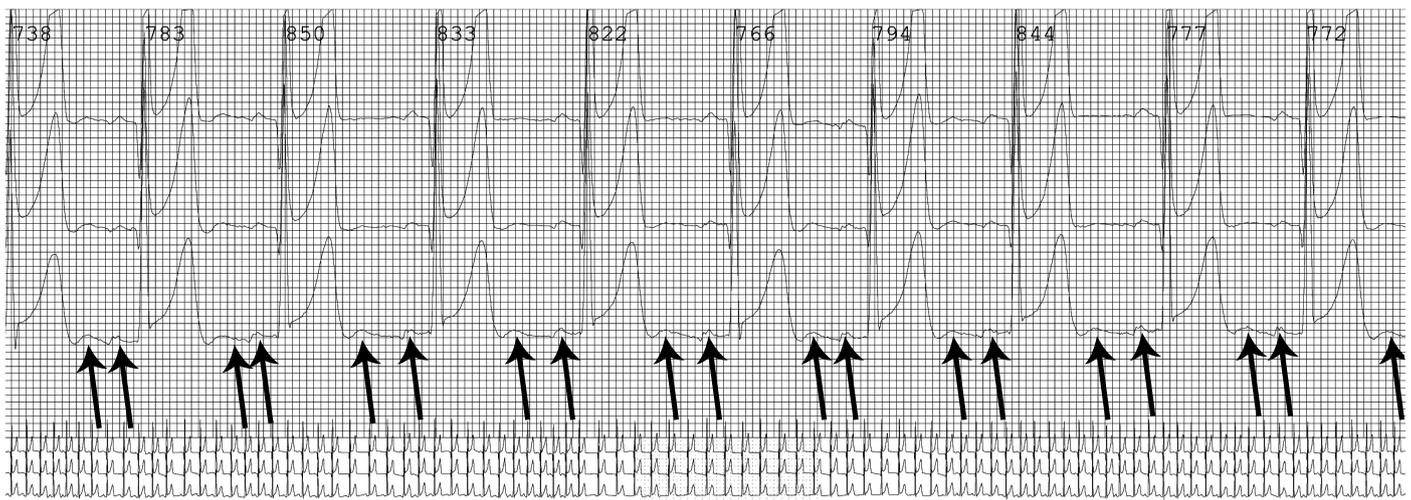
Fig. 3



Figure 1. Goiter 12-year-old male patient.

Figure 2. Goiter 34-year-old mother of patient.

Figure 3. Goiter 49-year-old maternal grandmother.



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Figure 4. Holter monitor reading with intermittent episodes of atrial fibrillation with 20% supraventricular ectopy.

DISCUSSION

The incidence of AF in hyperthyroidism is between 10% to 54.7%, noted by Traube et al.⁶ Bielecka-Dabrowa et al.⁹ and Donatelli et al.,⁷ as compared to 4% of the population. Takasugi et al.¹⁷ and Perry et al.¹⁸ documented the youngest cases of AF associated with hyperthyroidism at 14 years of age.

The effect of hyperthyroid states on the heart predisposing it to AF has been documented to be at various levels by varied researchers, and can be genetic and non-genetic (i.e. mechanical) via dilatation of the atria.¹⁹ Chen et al.²⁰ proved that thyroid hormones have been shown to cause electrophysiological changes in the pulmonary vein cardiomyocytes. Bielecka-Dabrowa et al.⁹ noted a chronotropic, dromotropic effect in the development of AF, ultimately postulating that it leads to an increased heart rate, multiple ectopic foci and, shortening of the refractory period, leading to re-entry phenomenon.^{6,15,19}

Thyroid hormones have an effect on the calcium-activated ATPase and phospholamban, leading to an increase in myocardial contraction. New advances have indicated that the genome alteration affects the ionic transfer of potassium, and the calcium channel is affected in cases of hyperthyroid atrial myocytes. Activation of the renin angiotensin system, peripheral vasodilatation by triiodothyronine, and metabolic increases, leads to an increased cardiac output.^{6,9,15,19} There have been documented abnormalities in the fibrinogen levels (factor VIII and

factor X) with decrease in partial thromboplastin time and increased fibrinogen levels, suggesting susceptibility to thromboembolic phenomenon, in hyperthyroidism. There are documented cases of AF in children who have had a stroke and pulmonary embolism.^{6,9,23-25}

For the past 180 years, the medical literature has been replete with documented genes e.g. LMNA and SCNRA, and chromosomes, which can be autosomal dominant e.g. 10q22-24, and autosomal recessive e.g. 5p13, and ways that hyperthyroid states may affect the heart. These data point to multifactorial reasons, indicating the need for more chromosomal and genetic studies, especially in patients who are familial, to further elucidate the specific reasons which will facilitate optimum management and treatment.^{2-4,6,9,15,19}

The phenotypic presentation of the index case's family members supports an autosomal dominant gene with variable expression.¹⁻⁵ A genetic study of this Afro-Caribbean family would be groundbreaking.

This case report identifies an index family who have made history with the onset of AF secondary to FH at 10 years of age, the youngest case documented, and the concomitant occurrence in three generations of an Afro-Caribbean family, which has also never been documented before, in the English medical literature.

One consistent finding is that a return to an euthyroid state leads to cessation of AF associated with hyperthyroidism, as demonstrated in this index case. The literature is not consistent in the need for

anticoagulation in hyperthyroid patients with AF, with no useful studies focusing on anticoagulants in childhood. Use of anticoagulation in the index patient was deferred following a discussion with the family, until it had been confirmed the risk of stroke

in the index case, with a CHA₂DS₂-VASc score of 0, is considered statistically significant in this group, warranting the risk associated with anticoagulants in an active teenager.

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