CLINICAL RESEARCH

Graves' disease and atrial fibrillation: the case for even higher doses of therapeutic iodine-131

G R SCOTT, J C FORFAR, A D TOFT

Abstract

Seventy five consecutive patients with Graves' disease complicated by atrial fibrillation were given a large single therapeutic dose of 600 MBq (16.2 mCi) iodine-131 in an effort to control their hyperthyroidism rapidly and thus restore sinus rhythm. Patients were initially followed up every three months after treatment and then at yearly intervals. The mean period of follow up was 3.1 years.

A total of 44 of the patients became hypothyroid and 31 euthyroid, and 33 (75%) and 14 (45%) of these patients, respectively, reverted to sinus rhythm ($p < 0.01$). Of the 33 who became hypothyroid and reverted to sinus rhythm, 30 had developed the hypothyroidism within six months after treatment.

These results are a strong case for increasing the dose of radioiodine in patients with Graves' disease complicated by atrial fibrillation in an effort to speed the onset of thyroid failure and thus maximise the rate of reversion to sinus rhythm.

Introduction

Atrial fibrillation is a well recognised complication of hyperthyroidism, although it is rare in patients under 40. In our clinic, however, the arrhythmia occurs in more than 40% of men over 60 presenting with Graves' disease. Although sinus rhythm is restored spontaneously in some 60% of patients given effective antithyroid treatment, there is an appreciable morbidity and a worrying number of deaths from systemic

embolisation, mainly to cerebral arteries, while the arrhythmia persists. This complication affects roughly 10% of all patients in whom atrial fibrillation has been induced by thyrotoxicosis.¹ In recent years our policy has been to employ a large dose of iodine-131 (600 MBq; 16.2 mCi) in these patients in the belief that rapid control of hyperthyroidism is most conducive to restoring sinus rhythm.² This paper reviews the results of such a policy and illustrates the need for an even more aggressive approach with radioiodine.

Patients and methods

We studied 75 patients (52 women, 23 men) with Graves' disease and atrial fibrillation proved by electrocardiography. The patients had presented consecutively to the endocrine clinic between 1978 and 1982 and been treated effectively with a single dose of ¹³¹I. Their mean age was 62.7 years (range 38-81). Graves' disease was diagnosed clinically and on the basis of a technetium-99m or ¹³¹I thyroid scan showing a diffuse uptake of isotope. In each case hyperthyroidism was confirmed by finding a lack of plasma thyrotrophin response to thyrotrophin releasing hormone, associated in all but three patients with raised concentrations of plasma total thyroxine (T₄) and triiodothyronine (T₃). Concentrations of thyroid hormone in these three patients were in the upper normal range.

All patients were treated with 600 MBq ¹³¹I and reviewed three, six, nine, and 12 months later and yearly thereafter. The mean period of follow up was 3.1 years (range 10 months to six years). In addition to clinical examination on each occasion, blood was withdrawn for estimation of plasma total T₄, T₃, and thyrotrophin concentrations. Restoration to sinus rhythm was confirmed by electrocardiography. Post-treatment hypothyroidism was defined on the basis of a low plasma total T₄ value (< 60 nmol/l; 4.7 μ g/100 ml) and a raised plasma thyrotrophin concentration (> 5.7 mU/l).

Results

Thirty one patients became euthyroid after treatment and 44 developed hypothyroidism. There was no difference in mean pre-treatment four hour uptake of ¹³¹I by the thyroid between these two groups (51% *v* 52%). In no patient did hyperthyroidism persist beyond the third month after treatment. Spontaneous reversion to sinus rhythm occurred in significantly more of the patients who

University Department of Medicine, Royal Infirmary, Edinburgh EH3 9YW

G R SCOTT, MB, CHB, registrar

J C FORFAR, MRCP, lecturer

A D TOFT, MD, FRCP, senior lecturer

Correspondence and requests for reprints to: Dr A D Toft.

Relation between thyroid state and cardiac rhythm in 75 patients with Graves' disease and atrial fibrillation treated with 600 MBq ¹³¹I

Thyroid state after treatment	Reversion to sinus rhythm	Persisting atrial fibrillation	Total
Euthyroid	14	17	31
Hypothyroid	33	11	44

became hypothyroid (75% v 45%; $p < 0.01$; χ^2 analysis) (table). Of the 33 patients who developed thyroid failure and reverted to sinus rhythm, 30 became hypothyroid within six months of treatment, two at nine months, and the remaining patient at five years. Only six of the 11 patients rendered hypothyroid but remaining in atrial fibrillation developed thyroid failure within six months. There was no difference in the use of digoxin or β adrenoceptor antagonists between those reverting to sinus rhythm and those remaining in atrial fibrillation.

Discussion

Our findings show that patients with Graves' disease and atrial fibrillation who become hypothyroid within six months of receiving a therapeutic dose of ¹³¹I are more likely to revert to sinus rhythm than are those who are rendered euthyroid during this period. The different cardiac responses appear to be related to the degree and to the rate of lowering of thyroid hormone concentrations. Although thyrotrophin releasing hormone tests were not performed routinely after treatment, conceivably in some of the euthyroid patients "normal" concentrations of total T4 and T3 were associated with an absent thyrotrophin response. This combination of results

(often referred to as subclinical hyperthyroidism) has been implicated in the development of atrial fibrillation.³ Evidence suggests that the longer a patient is in atrial fibrillation the less likely he is to revert to sinus rhythm after successful antithyroid treatment.⁴ Nevertheless, it is extremely difficult to date the onset of the arrhythmia, and we did not attempt to correlate these uncertain data with eventual outcome of cardiac rhythm.

Although we intended to induce hypothyroidism with 600 MBq (16.2 mCi) ¹³¹I—a dose previously considered ablative⁵—thyroid failure developed in only 36 (48%) of our patients within the first six months. Hence in order to increase the incidence of early hypothyroidism and thereby maximise the rate of spontaneous reversion to sinus rhythm there is now a case for administering a larger dose—say, 900-1200 MBq (24.3-32.4 mCi)—to patients with Graves' disease complicated by atrial fibrillation.

We are indebted to our colleagues at Bangour General Hospital, West Lothian; Peel Hospital, Galashiels; Milesmark Hospital, Dunfermline; and the Victoria Hospital, Kirkcaldy for allowing us access to their patients' records.

References

- Staffurth J, Gibberd MD, Tang Fui SNG. Arterial embolism in thyrotoxicosis with atrial fibrillation. *Br Med J* 1977;ii:688-90.
- Irvine WJ, Toft AD. The diagnosis and treatment of thyrotoxicosis. *Clin Endocrinol (Oxf)* 1976;5:687-707.
- Forfar JC, Miller HC, Toft AD. Occult thyrotoxicosis: a correctable cause of "idiopathic" atrial fibrillation. *Am J Cardiol* 1979;44:9-12.
- Nakazawa HK, Sakurai K, Hamada M, Momotani N, Ito K. Management of atrial fibrillation in the post-thyrotoxic state. *Am J Med* 1982;72:903-6.
- Wise PH, Ahmad A, Burnet RB, Harding PE. Intentional radioiodine ablation in Graves' disease. *Lancet* 1975;iii:1231-3.

(Accepted 17 May 1984)

Deposition of eosinophil cationic protein in granulomas in allergic granulomatosis and vasculitis: the Churg-Strauss syndrome

PO-CHUN TAI, MARY E HOLT, PAUL DENNY, ALAN R GIBBS, BRYAN D WILLIAMS, CHRISTOPHER J F SPRY

Abstract

Biopsy specimens and tissues obtained at necropsy from two women who died after developing the Churg-Strauss syndrome were analysed to see whether granulomas in these patients contained activated eosinophils or secreted eosinophil cationic proteins, or both. Immunocytochemical studies with monoclonal antibody EG2 showed large

amounts of eosinophil cationic protein and eosinophil protein-X (which are toxic for heart cells and other tissues) in the granulomas. Many activated and degranulating eosinophils were seen to be migrating from the blood into these areas.

Eosinophils may play a central part in the development of lesions in the heart and other tissues in the Churg-Strauss syndrome.

Introduction

Granulomatous and vasculitic diseases have a wide range of clinical features, which have been classified into several named disorders and syndromes. One of these is allergic granulomatosis and angiitis or the Churg-Strauss syndrome.¹ The classical description and analysis of 14 patients by Churg and Strauss in 1951 showed that most patients were young women with a history of asthma and very high blood eosinophil counts.² Necrotising and granulomatous lesions rich in eosinophils were present in the heart, lungs, muscles, kidneys, nervous system, spleen,

Department of Immunology, Royal Postgraduate Medical School, London W12 0HS

PO-CHUN TAI, PHD, research fellow
PAUL DENNY, BSC, research assistant
CHRISTOPHER J F SPRY, FRCP, DPHIL, senior lecturer

Welsh National School of Medicine, Cardiff CF4 4XN

MARY E HOLT, MRCP, senior registrar, department of medicine
ALAN R GIBBS, MRCPATH, senior lecturer, department of pathology
BRYAN D WILLIAMS, MSc, MRCP, senior lecturer, department of medicine

Correspondence to: Dr C J F Spry.