Thyrotoxicosis in old age: a different clinical entity?

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Thyrotoxicosis generally presents with classic signs and symptoms in younger people. Among the elderly population atypical presentation is recognized, although this has not been well quantified or characterized. To avoid misdiagnosis or delay in diagnosis, clinical suspicion needs to remain high.

Thyrotoxicosis, a condition producing a raised level of circulating thyroid hormones, is accompanied by a broad array of symptoms and signs, which can differ markedly among individuals. It is often stated, and is the authors' impression, that the clinical features of thyrotoxicosis may be significantly altered in elderly people, so that symptoms and physical findings typical in young persons may be modified, different or absent in this age group. There are, however, few published data.

The diagnosis of thyroid disorders may be further complicated by the normal ageing-associated changes in thyroid physiology (Monzani et al, 1996). The situation is often compounded by the impact of non-thyroidal illnesses, which frequently accompany older people, influencing diagnosis and management. To try and characterize these differences, we reviewed 36 cases of thyrotoxicosis among elderly patients seen in our endocrinology clinic.

METHODS

Thirty-six patients presenting to our endocrinology clinic over 6 years, who were 65 years of age or more at the time of initial diagnosis, were reviewed. Information was collected retrospectively regarding symptoms and their duration, clinical signs, and biochemical results in support of the diagnosis, as well as immunological and radiological reports wherever appropriate.

In all cases attempts were made to find out the aetiological diagnosis (i.e. Graves' disease, toxic multinodular goitre (MNG), toxic adenoma) which included clinical evidence of ophthalmopathy or dermopathy, thyroid microsomal antibodies, ultrasonography and radionucleotide scan of the thyroid gland. In follow-up clinic attendance improvement of symptoms, physical signs and biochemical parameters were noted.

Thyrotoxicosis secondary to over-replacement of thyroxine in cases of primary hypothyroidism and drug-induced thyrotoxicosis (e.g. amiodarone) were excluded from our review.

RESULTS

Patient characteristics

Of the 36 patients, 8 (22%) were male and 28 (78%) were female, with a mean age of 70.3 years (65–85). Mean duration of follow-up was 22.4 months (2–62).

Presentation

Common presenting features are shown in *Table 1,* comparing their frequency of presentation with those in the general population with the same condition (Lersen et al, 1998). The mean duration of symptoms before presentation was 11.3 months with a range of 2–24 months. Nervousness, increased sweating, heat intolerance, palpitations and weight loss, which are considered as typical presenting features, were strikingly less frequent in our elderly patients; 20 (55%) had denied any of these symptoms. In contrast, atrial fibrillation, which is reported in around 10% of younger thyrotoxic patients, was present in 55% of our group. The common clinical signs of tachycardia, tremor and bruit were absent in seven (20%) of our patients.

Atypical features are far more frequent among the older age group. Twenty-two patients (61%) presented with one or more atypical features, among which weight gain and constipation were the most frequent (*Table 2*). One in five patients had nausea, vomiting and

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dizziness, while 27% complained of depression. Sleep disorder was a frequent complaint: six patients (13%) reported increased sleepiness and eight reported insomnia. Other complaints included cold intolerance, decreased appetite and agitation.

One patient (not shown in table) presented as a surgical emergency with abdominal pain, vomiting and high-grade fever. Exploratory laparotomy was negative. She continued to deteriorate, becoming more toxic, pyrexial and confused. Thyrotoxic crisis was eventually diagnosed. She made a rapid full recovery with medical treatment (Bhattacharyya and Wiles, 1997).

Thyroid function tests

Thyroid-stimulating hormone (TSH) was suppressed (<0.06 mu/litre) in all of our patients. Thirty-two (89%) had elevated plasma total thyroxine of 214 nmol/litre (± 37.05) (normal 60–156). The patient with thyrotoxic crisis had a normal total thyroxine level, but her free thyroxine index was high at 181 (normal 65–130). The remaining three patients had triiodothyronine (T3) toxicosis with total plasma T3 levels of 3.8, 3.9 and 4.2 nmol/litre (normal 1.1–2.8), aetiology being toxic adenoma (two) and toxic MNG (one).

Aetiology

Sixteen of the 36 cases (44%) were diagnosed as Graves' disease, 16 (44%) as toxic MNG and four (11%) as toxic adenoma. Of the patients with Graves' disease six had ophthalmopathy, and none had dermopathy. One patient with MNG had retrosternal extension without obstructive features.

TABLE 1.
Presenting features of thyrotoxicosis

		General population*	Older people†
Symptoms (%)	Nervousness	99	33
	Increased sweating	91	19
	Heat intolerance	89	16
	Palpitation	89	19
	Weight loss	85	33
	Dyspnoea	75	42
	Increased appetite	65	14
	Eye complaints	54	14
Signs (%)	Tachycardia	100	67
	Goitre	100	83
	Tremor	97	61
	Bruit	77	55
	Eye sign	71	55
	Atrial fibrillation	10	55
	Splenomegaly	10	0
	Palmar erythema	8	3

* Lersen et al (1998) (*n*=247); † Our patients (*n*=36)

Associated medical problems

Older people often suffer from multiple medical problems (Khaw, 1997). Twenty-six (73%) had other chronic medical problems, predominantly congestive cardiac failure (50%), chronic obstructive airways disease (33%) and ischaemic heart disease (47%).

DISCUSSION

Thyrotoxicosis is a relatively common endocrine disorder affecting predominantly young to middle aged individuals, especially women. Several studies of prevalence indicate the presence of hyperthyroidism in 1–2% of community residing individuals (Ronnov-Jessen and Kirkegaard, 1973; Tunbridge et al, 1977; Kawabe et al, 1986).

In a study population of Whickham, UK, hyperthyroidism was identified in 19 per 1000 women, a prevalence rate 10 times greater than in men. The estimated new cases were 2–3 per 1000 women per year (Tunbridge et al, 1977). The proportion of patients with hyperthyroidism who are over 60 years of age is estimated to be 15–20% (Ronnov-Jessen and Kirkegaard, 1973). The commonest cause of hyperthyroidism in elderly people has been reported as toxic MNG, possibly because MNG itself is common in old age (Denham and Wills, 1980). In our study, the incidence of toxic MNG and Graves' disease was the same (44% each).

TABLE 2.
Atypical presentations of thyrotoxicosis seen in this study

Presentation	%
Weight gain	25
Constipation	27
Nausea/vomiting	22
Dizziness	22
Depression	27
Increased sleepiness	17
Insomnia	22
Cold intolerance	11
Decreased appetite	22
Agitation	17

Clinical presentation

The clinical presentation of thyrotoxicosis in these older patients often differs from the classical description of the disease in younger individuals (Kawabe et al, 1986; Zisselman et al, 1995). Among this older group, only a minority of patients presented with classical features of thyrotoxicosis — tremor, tachycardia, nervousness, exophthalmos, heat intolerance, and weight loss despite increased appetite. Only 33% of our patients presented with nervousness, while it is described in 99% of the general population (Lersen et al, 1998).

More than half of our patients had atrial fibrillation at presentation, which is five times more common than in their younger counterparts. Six of the 20 patients with atrial fibrillation reverted to sinus rhythm while on treatment with carbimazole. In older people, presenting features are frequently atypical (Isley, 1993), two thirds of patients presenting with one or more of fatigue, weakness, changes in mental status, loss of appetite and congestive cardiac failure. Some patients even presented with weight gain, cold intolerance and constipation.

Thyroid changes in old age

Along with structural changes in the thyroid gland, several functional changes have been noted in older people. Radioactive iodine uptake, secretion of thyroid hormones from the gland and peripheral deiodination of thyroxine to produce T3 all decrease in old age (Morley, 1983). Levels of circulating TSH have been reported as showing no change with age (Ordene et al, 1983), but others have shown a high concentration with increasing age (Harman et al, 1984; Parle et al, 1991).

The thyrotropin-releasing hormone test measures the reserve of pituitary TSH and in older subjects it is often blunted, as seen in hyperthyroidism (Morley, 1983; Monzani et al, 1996). Reduced or absent TSH responses to thyrotropin-releasing hormone are particularly common in sick older patients whether they are euthyroid or thyrotoxic. An absence of response is therefore an uncertain marker of thyrotoxicosis in such patients (Davies et al, 1985).

Long-term management

Once the diagnosis of hyperthyroidism is confirmed (*Figure 1*), determination of underlying aetiology is important for long-term management. Beta-blockade remains a useful initial measure for those undergoing investigation for suspected hyperthyroidism, but may be difficult in older people because of the high prevalence of chronic obstructive airways disease and congestive cardiac failure. Carbimazole remains the drug of choice for everybody. All patients or their carers must clearly understand the potential risk of agranulocytosis and know how to react if they develop unresolving infection, particularly sore throat. The incidence of agranulocytosis is very low (Meyer-Gessner et al, 1994; Cooper, 1998), but it may be life-threatening if the drug is not stopped promptly.

Other side-effects include skin rash, arthralgia, myalgia, alopecia, neuritis, hepatitis, and loss of taste sensation and lymphadenopathy. These are usually self-limiting and settle with withdrawal of the drug. Propylthiouracil may have similar side-effects but can be cautiously substituted in patients experiencing adverse reactions with carbimazole. Giving the drug once daily may reduce any problem with compliance in this age group. There is no reported evidence of increase in side-effects to antithyroid drugs in older people. Fortunately there is no significant drug interaction with antithyroid drugs.

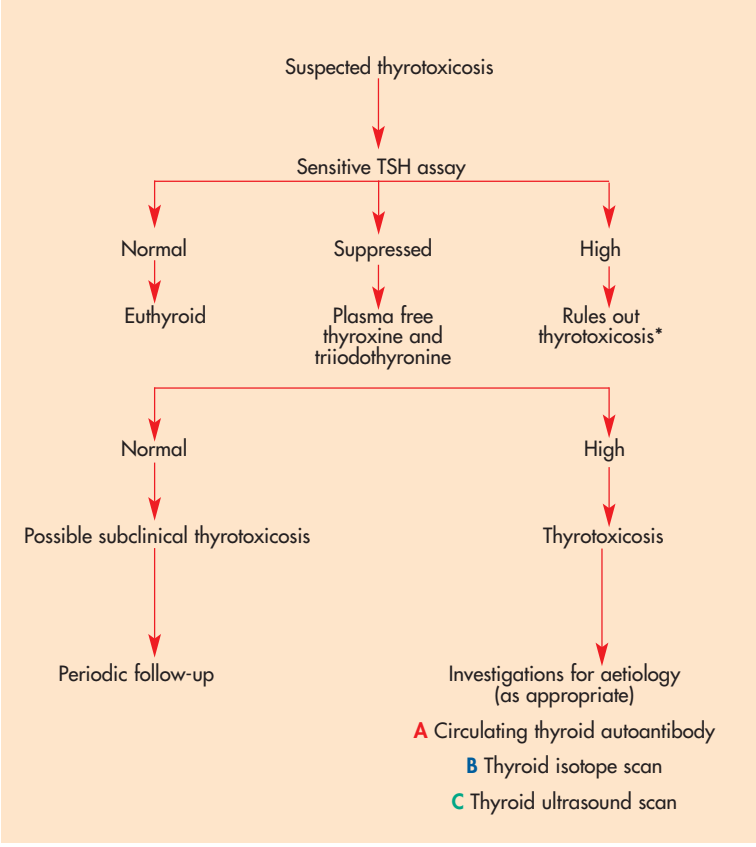

Figure 1. Diagnostic algorithm for thyrotoxicosis. TSH = thyroid-stimulating hormone. *Except for extremely rare TSH-producing pituitary tumours.

In case of toxic MNG or toxic adenoma the desired definitive therapy is to ablate the toxic nodules with radioactive iodine or surgery. Incidences of hypothyroidism after radioactive iodine treatment in such cases are low, as the underactive areas of the thyroid gland regain normal thyroid function following ablation of autonomous hyperactive nodules. A central question in Graves' disease is how long the treatment is to continue with antithyroid drugs. A straightforward answer is not available.

Certain features such as T3 toxicosis, small goitre or decrease in goitre size with treatment, may serve to indicate the likelihood of long-term remission following withdrawal of therapy (Vitti et al, 1997; Lersen et al, 1998). Our present policy is to continue antithyroid drugs for 12–18 months in those who refuse radioactive iodine treatment (Gittoes and Franklyn, 1998).

Surgery is not usually recommended as a primary choice of treatment in older people, unless the goitre is huge or obstructive features are present. The coincident presence of other disorders including cardiac, pulmonary and central nervous system disease may put the patient at increased operative risk.

CONCLUSIONS

Hyperthyroidism is readily amenable to effective treatment that can improve the quality of life. The clinical suspicion of this disease should always be high and exclusion of this diagnosis should be pursued, particularly in older people where features are frequently atypical. A quality standard should be to check thyroid function in any older patient with unexplained chronic signs and symptoms and even in patients with unexplained acute toxic pyrexial illness. TSH assays are quick, relatively easy and inexpensive to perform and should be used as an effective first-line test. If suppressed the tests should be extended to measure FT4 and FT3 to confirm the diagnosis of thyrotoxicosis and later tests to elicit the aetiology of the condition. **HM**

KEY POINTS

- Thyrotoxicosis in old people often presents without classical features such as tachycardia, weight loss, diarrhoea, increased sweating or tremor.
- Atypical presenting features noted in our study were weight gain, constipation, vomiting, dizziness, depression.
- To avoid misdiagnosis or delay in diagnosis, clinical suspicion needs to remain high.
- Thyroid function should be checked in all elderly patients with unexplained chronic symptoms and signs.
- Treatment of thyrotoxicosis is usually straightforward and easy.

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