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Case Presentation
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Hyperthyroidism in the Elderly: Challenges in Diagnosis and Management

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Abstract

Hyperthyroidism is a common disorder among the elderly. However, for the clinician it is often difficult to confidently make a clinical diagnosis. The excess thyroid hormone affects homeostasis of the heart, leading to high-output heart failure and eventually, dilated cardiomyopathy. The author discussed how hyperthyroidism affects cardiovascular pathophysiology, examine the complications caused by excess thyroid hormone discussed the complications and other available treatment options in the elderly patient.

Keywords: Hyperthyroidism; Cholestatic jaundice; Carbimazole; Lithium

Introduction

Hyperthyroidism is one of the most readily recognized diseases in medicine, as the signs and symptoms make the diagnosis obvious. Hyperthyroidism in the elderly is not uncommon. The clinical feature of hyperthyroidism in the elderly, however; is a typical and diagnosis may be missed. The signs and symptoms of hyperthyroidism are frequently attributed to aging or mimic other commoner diseases, leading to delayed diagnosis and complications. High index of suspicion for thyroid disorders in the elderly is therefore important.

Untreated thyroid dysfunction is associated with significant morbidity in the elderly. The diagnosis can be easily confirmed, and compliance to treatment leads to euthyroid state. Treatment options include medical therapies with radioiodine, antithyroid medications and surgery. Anti thyroid medications are widely used and well tolerated.

The author describes a case that illustrates the non-specificity of symptoms in hyperthyroidism among the elderly patient and her treatment was complicated by severe cholestatic hepatitis. Other available options are less commonly used among the elderly. The author also discussed their potential toxicity and drug interactions. A written signed consent was obtained from the patient for this publication.

Case Presentation

Madam T is an 83-year-old lady, who presented in the emergency room with complaints of fever at 38.8°C, poor appetite and cough productive of whitish sputum. She has a background history of hypertension, hyperlipidemia, Parkinson's disease, Ischemic heart disease with cardiomyopathy which she underwent PCI, Osteoporosis complicated by history of closed intertrochanteric, sacral ala, pubic rami and L5 compression fractures. Madam T has no history of thyroid problems or any family history of thyroid dysfunction.

She experienced intermittent episodes of palpitations for quite some time. She denied weight loss, eye symptoms, neck pain, dysphagia, odynophagia nor any compressive symptoms. She was noted by her daughter to be agitated and had symptoms of paranoia for a month with heat intolerance, and preferred to sit in front of electric fan. She had episodes of loose stools but was mostly constipated and required the use of laxatives. She was on the following medications, Aspirin, Calcium Carbonate and Vitamin D, Clopidogrel, Lactulose, Madopar Capsule/Tablet (Levodopa, Benserazide), Paracetamol PO PRN, Bisoprolol Fumarate, Losartan, Omeprazole and Simvastatin.

On physical examination, she was noted to have fine tremor on outstretched hands, her weight was 45 kg, heart rate was 114 beats per min regular and blood pressure of 140/59 mmHg. There was no exophthalmos, neck has no obvious goiter and neck veins were not engorged. She had basal crepitation of both lung fields and bilateral ankle swelling up to the level of her knees. Neuro exam was unremarkable, other than resting tremor, bradykinesia and rigidity.

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Table 1: Laboratory investigations on admission.

	Reference Range	Results
C- Reactive protein	<3.0 mg/L	22.2
procalcitonin	0.00-0.50 ug/L	<0.06
Troponin	0-9 ng/L	237,296,388
Pro BNP	<125 pg/ml	16,858
FT4	10.00-20.00 pmol/L	49.66
TSH	0.400-4.99 mIU/L	<0.004
Thyroid Receptor antibodies	<2.0 U/L	26
Urea	2.8-7.7 mmo/L	8.4
Creatinine	3.1-7.8 mmol/L	41
Total white cells	150-450 $\times 10^3$/uL	8.8
Hemoglobin	4.0-10.0 $\times 10^3$/uL	10.9
Total bilirubin	5.0-30.0 umol/L	6
Alkaline phosphatase	32-103 U/L	50
Alanine transaminase	10-55 U/L	13

Her chest X-ray showed mild prominence of bilateral upper lobe vasculature with no focal consolidation or pleural effusion. Urinalysis was unremarkable. ECG showed sinus tachycardia with T wave inversion in leads II, III, AVF, V2-V6 and isolated Q waved in lead III with borderline R wave progression. Inflammatory markers were all unremarkable. Free T4 was elevated with low TSH and Thyroid Receptor Antibodies were elevated. Liver and renal function tests were all unremarkable (Table 1). Echocardiography showed left ventricular ejection fraction of 35% with regional wall motion abnormality of the left ventricle, consistent with underlying ischemia/infarct, and moderately impaired (grade II) left ventricular diastolic function and elevated left ventricular filling pressure.

Her diagnoses were:

- Viral upper respiratory tract infection.
- Hyperthyroidism
- NSTEMI
- Heart failure due to myocardial ischemia and possible contribution from high output failure secondary to hyperthyroidism.
- Background ischemic cardiomyopathy

She was managed medically with diuretics, beta blocker, Angiotensin Converting enzyme Inhibitor (ACEI) and nitrates. Carbimazole was initiated for management of hyperthyroidism. She made a full recovery from heart failure and NSTEMI. Physically though, she was weaker. She declined rehabilitation and at discharge, she needed heavy assistance with her ADLs. She was discharged home with Carbimazole 30 mg daily was further reduced to 20 mg daily after one month and was placed on dual anti platelet on top of her maintenance medications.

She was seen in clinic five weeks post discharge and was noted to be deeply jaundiced. She was not aware of her skin discoloration, but she did complain of pruritis. There were no other associated symptoms of abdominal pain or weight loss. Results of her blood investigations are shown in Table 2. She was admitted for work up for painless obstructive jaundice. CT scan of abdomen was unremarkable.

Carbimazole and Simvastatin were stopped, in view of the liver dysfunction. Her liver function took 40 days after stopping Carbimazole to normalize. She was referred for radioiodine treatment, as an alternative. However, while waiting for appointment for radioactive iodine, her T4 was increasing and it was felt that radioactive iodine may induce a thyroid storm, if the T4 was left untreated and continued to climb. The options left included propylthiouracil, cholestyramine and Lithium.

The endocrinologist chose cholestyramine and Lithium in combination while waiting for the radioactive iodine. Madam T wasn't fully compliant with Cholestyramine. She complained of

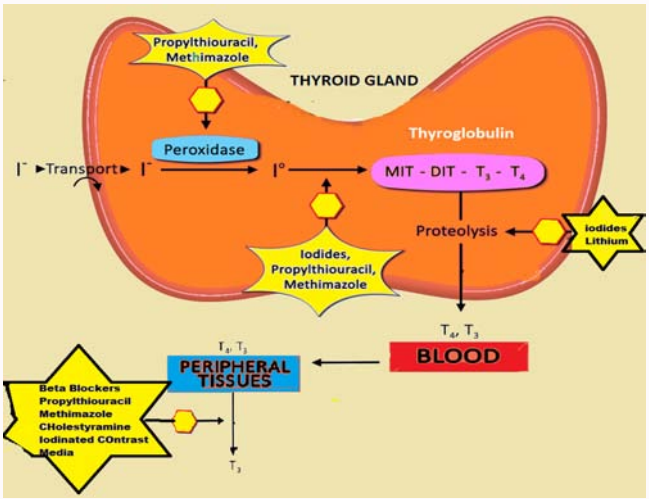

Figure 1: This diagram depicts the formation of thyroid hormone, as well as the mechanism and site of action of anti-thyroid.
I^-: Iodide Ion; I°: Elemental Iodine

Metabolism of Thyroid Hormone- Iodine is essential in production of the thyroid hormones Thyroxine (T4) and Triiodothyronine (T3). Iodide ion is actively taken up by follicular cells, where it is converted to elemental iodine by thyroidal peroxidase. Activation of Thyroxine (T4), to the active form, Triiodothyronine (T3), by 5′-Deiodinase type 2 (D2) is the key mechanism in TH regulation. The thyroid secretes iodine-containing hormones in 2 forms- Thyroxine (T4) and Triiodothyronine (T3). Tyrosine residues in thyroglobulin are iodinated to form Monoiodotyrosine (MIT) or Di-Iodotyrosine (DIT) in a process known as iodine organification. Proteolysis of thyroglobulin liberates T4 and T3, which are then released from the thyroid gland. T4 and T3 are transported in the blood bound to thyroxine-binding globulin, a protein synthesized in the liver. (Pharma Katzung Chapter 38 - Thyroid & Antithyroiddrugs).

Table 2: Investigations on readmission.

	Reference range	Day 1	Day 10	Day 24	Day 31
Total bilirubin	5.0-3.0 (umol/L)	143.1	32.4	19.8	13.9
Direct bilirubin	2.0-7.0 (umol/L)	113	-	-	-
Indirect bilirubin	(umol/L)	29.9	-	-	-
Alkaline phosphatase	32-103(U/L)	868	396	287	180
Alanine transaminase	10-55 (U/L)	189	61	47	38
Aspartate transaminase	10-45 (u/L)	183	58	62	51
Prothrombin time	9.5-11.5 sec	9.7	-	-	-
GGT	5-50 (u/L)	1000	553	277	166
T4	10.00-20.00 pmol/L)	6.24	22.03	35.26	58.7
TSH	0.400-4.99 (mIU/L)	4.99	0.04	0.011	<0.010
CRP	<3.0 (mg/L)	12	-	-	-
Procal	0.00-0.50 (ug/L)	0.14	-	-	-

hoarse voice and took 4 mg twice daily instead of thrice a day, on a good day. Cholestyramine was subsequently increased to 8 mg thrice daily and lithium was eventually added as FT4 was markedly raised (FT4 of 58.7), (Table 2). Prednisolone was given a day prior to radioactive iodine therapy. Cholestyramine and lithium were subsequently reduced and discontinued.

Discussion

It is known that the prevalence of thyroid disorders increases with age [1]. Hyperthyroidism in the elderly is a common but serious clinical disorder. Peak incidence of hyperthyroidism is in the 2nd and 3rd decades with 10% to 15% of the hyperthyroid patients older than 60 years [2]. Graves' disease is the most common cause of hyperthyroidism in all age groups, accounting for fifty to seventy percent of cases and the remaining 30% to 40% are due to toxic multi nodular goiter [3]. Recognition and diagnosis of thyroid diseases among the elderly is challenging because symptoms are subtle and non-specific, and therefore, clinicians need to have a high index of suspicion and a low threshold to investigate for thyroid abnormalities [4].

With ageing, the thyroid gland undergoes moderate atrophy and develops non specific histopathologic changes such as fibrosis increasing numbers of colloid nodules, and some lymphocytic infiltration. Thyroidal iodine uptake decreases with age, leading to decreased production of T4 by about 30% between young adulthood and advanced age [4,5]. Age-related histological changes make physical examination of thyroid less helpful in the diagnosis of thyroid disorders. Thyroid glands may not be palpable in most of the elderly patients with thyroid disorders. Since history and physical examination are both non-specific for thyroid disorders, a high index of suspicion is important for early diagnosis and management of thyroid disorders in order to avoid major complications that may result from this otherwise easily treatable problem [6].

The clinical features of hyperthyroidism are due to over stimulation of the sympathetic system and the direct effects of thyroxin on end organs [7]. Younger patients tend to exhibit symptoms of sympathetic over-activation, such as anxiety, hyperactivity, and tremor In older patients they may be apathetic, rather than hyperactivity [8,9]. Graves ophthalmopathy is due to sympathetic overactivity, possibly mediated by increased alpha-adrenergic receptors in some tissues are less common in elderly [4,9,10]. Older patients have more cardiovascular symptoms, including dyspnea, increased cardiac output, atrial fibrillation with unexplained weight loss [8]. Weight loss is due primarily to increased metabolic rate and increased gut motility, associated with increased defecation and malabsorption older patients may also present with persistent constipation [11]. Thyroid hormone stimulates bone resorption, resulting in increased porosity of cortical bone and reduced volume of trabecular bone, aggravating postmenopausal osteoporosis in elderly [2,12]. Hyperthyroid patients tend to have low serum total and High-Density Lipoprotein (HDL) cholesterol concentrations and a low total cholesterol/HDL cholesterol ratio [13]. Older patients with Graves' hyperthyroidism are less likely to have goiter. Tachycardia of 100 beats per minute is absent in 40% of older hyperthyroid patients, due primarily to coexistent conduction system disease [11]. Urinary frequency and nocturia are common, although the mechanism is uncertain. The elderly may experience behavioral and personality changes, such as psychosis, agitation, and depression.

Some of the signs and symptoms of hyperthyroidism commonly seen among the elderly and are often mistaken as age related changes, such are fatigue, weakness, agitation, confusion, dementia, myopathy or may be mistaken for underlying malignancy such as anorexia and weight loss [14].

In a cross-sectional study of 3,049 consecutive patients with hyperthyroidism presenting to a single secondary/tertiary care clinic, majority of patients were older than 61 years had two or more symptoms. The subjects reporting five or more symptoms were found among those older than 61 years. Increasing age was associated with reduced adjusted odds ratio for the presence of most classical symptoms except for weight loss and shortness of breath, independent of disease severity [15].

The cardiovascular system retains its sensitivity to thyroid hormone among the elderly. Hyperthyroidism exerts its effects on the sympathetic system, with over activity characterized by increase in resting heart rate, stroke volume, ionotropic effects with increased myocardial contractility, ejection fraction and an improvement in diastolic relaxation, which is similar to a state of increased adrenergic activity [16]. In the early stage, it causes high cardiac output and left ventricular hypertrophy. In the later stage, it causes biventricular dilatation and congestive heart failure. Atrial fibrillation and pulmonary arterial hypertension also add to the increased morbidity of untreated hyperthyroidism [17]. Patients with hyperthyroidism may manifest findings of congestive heart failure in the absence of prior cardiac injury [18]. They present with typical symptoms of heart failure like dyspnea on exertion, fatigue, and fluid retention with peripheral edema, pleural effusion, hepatic congestion, and pulmonary arterial hypertension [16,19].

Untreated high output state and hyperthyroidism, can lead to heart failure and high morbidity especially in the elderly. A study done by Mitchel et al. [20] showed hyperthyroid patients had 60% risk of mortality compared to euthyroid patients with heart failure. Treatment decisions must be individualized, taking into account comorbidities, projected lifespan and side effects of therapy.

Therapeutic options in controlling hyperthyroidism include medical management or thyroid ablative therapy in the form of surgery or radioiodine therapy, as summarized in Figure 1. Radioiodine is preferred over surgery in the elderly with hyperthyroidism due to increased risk of perioperative morbidity and mortality associated with surgery [21]. Radioiodine therapy is considered a safe primary treatment in the elderly with hyperthyroidism [2]. The cell necrosis induced by radioiodine occurs gradually hence its effect may not be achieved immediately [22]. Initial complications include, local reaction such as swelling and tenderness of the thyroid gland which is mild and not noticeable by patient, exacerbation of hyperthyroidism, mild bone marrow suppression which is clinically insignificant, low thyroid hormone levels after one year seen in more than half of patients [23-25]. New onset of atrial fibrillation with spontaneous reversion to sinus rhythm may occur in up to 50%, within a few months after restoration of normal thyroid function [26]. There is no increase in cancer risk (leukemia and thyroid) associated with radioactive iodine treatment in a very reassuring data accumulated for over 60 years, although data suggested a small increase in the risk of upper gastrointestinal cancer in elderly men, but this has not been confirmed by other studies [27,28].

Anti thyroid medications commonly used are carbimazole, methimazole, and propylthiouracil (Figure 1). They are used as short-term preparation for definitive or curative treatment with radioiodine

or surgery, or inducing remission in cases of thyrotoxicosis due to Graves' disease and for control of clinical and biochemical thyroid hormone excess [29].

Methimazole can be given once a day dosing and is considered first line treatment due to safety and convenience. They are good option for frail elderly with limited life expectancy and for those patients who cannot follow radiation safety protocols [30]. Side effects like fever, rash, and arthralgia occurred among 1% to 5% of the patients. A granulocytosis is more commonly seen with propylthiouracil, and is seen within 3 months of starting treatment [31]. Other serious side effects can occur, notably anti-neutrophil cytoplasmic antibody-associated-vasculitis (typically associated with prescription of propylthiouracil), and modest alteration in liver function is a common liver manifestation of thyroid disease [29]. However, cholestatic jaundice and fulminant hepatic necrosis are rare complications [31]. Even though hepatic dysfunctions are rare, these are absolute contraindications to further use of thionamides [29].

Surgery is indicated for suspicious or malignant thyroid nodule, or in case of goiter causing obstruction to neighboring structures particularly, trachea and esophagus [31]. Surgery should only be considered in the circumstance when rapid control of hyperthyroidism is required and antithyroid medications cannot be used. Factors that may militate against the choice of surgery include comorbidities such as cardiopulmonary disease, end-stage cancer, or other debilitating disorders, or lack of access to a high-volume thyroid surgeon [29].

In elderly, the long term morbidity and mortality benefit with early control of hyperthyroidism outweighs the concern of late complications of radioiodine therapy [2]. A major concern of radioiodine therapy is the precipitation of thyroid crisis during ablation.

After radio ablation, anti-thyroid drugs are usually restarted on days 3 to 7 for patients at risks of complications such as worsening angina pectoris, congestive heart failure, or disturbances of rhythm such as atrial fibrillation or even ventricular tachycardia for patients with cardiac disease. Thyroid storm and even death have also been reported [32-34]. Other complications like worsening of hyperthyroidism due to radiation thyroiditis, worsening ophthalmopathy have also been reported [36,37]. This can be alleviated by prior treatment with anti-thyroid medications. Beta-adrenergic blockade should be considered even in asymptomatic patients who are at increased risk for complications due to worsening of hyperthyroidism (i.e., elderly patients and patients with cardiac comorbidities [29].

Resumption of methimazole reduced the magnitude of shrinkage of goiter obtained by radioiodine, and has been shown to result in less post therapy rebound hyperthyroidism [37,29]. Thyroid function monitor is recommended at monthly basis. The antithyroid medication can be stopped once TSH rises above normal. Replacement with thyroxine then commences, and doses titrated accordingly [2].

Madam T developed significant hyperbilirubinemia, with obstructive hepatitis picture within five weeks of starting carbimazole, despite improvement of the serum thyroxin level. Work up for painless obstructive jaundice turned out negative and the cause of obstructive jaundice was thought to be due to Carbimazole. Her serum ALP, AST and AST continued to rise for one more week after stopping the offending drug, which eventually took 2 months to normalize.

Hyperthyroidism *per se* can affect liver function tests, although rarely reported. It causes a reversible and mild elevation in the liver enzymes [38]. In addition, cholestatic jaundice can occur due to severe hyperthyroidism [39]. Madam T didn't receive any other medications that could account for cholestasis. The viral infection she had was unlikely to be the cause as it happened several weeks ago. The pathophysiology of liver dysfunction secondary to hyperthyroidism is not well established. Autoimmune hepatitis may be associated with Graves' disease; however autoimmune hepatitis is more commonly seen in younger patients [40]. Liver specific antibodies such as ANA wasn't done in this patient to rule out autoimmune cause as she did not have any other features suggestive of autoimmune disorders.

The other possible causes of obstructive jaundice in Madam T's case include congestive cause or ischemic hepatitis. Congestive hepatomegaly is often associated with moderately elevated transaminases; two to three times the upper limit and an increase in both the direct and indirect bilirubin [41]. However, congestive hepatomegaly with jaundice is a rare finding and the total bilirubin level is rarely greater than 50 μmol/L. Madam T presented with heart failure and NTEMI, congested hepatitis is however, unlikely since her AST level with about three times upper limit of normal, with normal ALT level and her serum bilirubin level is much higher than expected in congestive hepatomegaly.

Cardiac failure also known to cause altered liver functions. The underlying mechanisms are ischemic hepatitis or venous congestion in severe right heart failure [42]. The hallmark of ischemic hepatitis are severe jaundice, with a bilirubin level as high as 250 μmol/L, elevation of AST to more than ten times the upper reference range limit, which is not the case for this patient. Echocardiography didn't reveal evidence of right heart failure [41].

All antithyroid drugs (methimazole, carbimazole, and propylthiouracil) can affect the liver on rare occasions and the nature of hepatic injury is drug specific. Carbimazole and methimazole, were associated with cholestatic jaundice (mainly hyperbilirubinemia) without evidence of hepatic necrosis on liver biopsy [43]. Hyrostatic medications like carbimazole or propylthiouracil) can be interchanged without increasing risk of further liver damage. Carbimazole causes intracanalicular cholestasis while propylthiouracil causes hepatocellular injury [44]. The mean time of onset of hepatotoxic changes after starting treatment is 36 days [45]. Most patients recover on drug discontinuation. Its hepatotoxic effect is dose-independent and may occur despite previous uneventful exposure to the drug. It is seen in less than 1% of patients, with predisposition for younger women (age <30 years) [44,46].

The proposed mechanism of carbimazole-induced cholestasis is not fully understood, but it is thought to be a hypersensitivity reaction, occurring with patients receiving normal doses of the drug [29,47]. Carbimazole induced a blastogenic response of patients' lymphocytes in vitro suggestive of involvement of an immune-mediated reaction. The sensitized lymphocytes may produce a cholestatic factor on stimulation with antigen [29]. Occasional reports of severe and fatal cases of methimazole induced fulminant liver failure [48,49]. Fortunately, Madam T showed a rapid improvement of cholestatic jaundice after cessation of carbimazole.

Lithium has been used in the treatment of several thyroid diseases, because of its ability to inhibit thyroxine secretion and it prolongs the retention of radioiodine in the thyroid gland, which increases the effectiveness of radioiodine therapy [50]. The cure rate was slightly higher in patients given lithium (900 mg/day) for 12 days starting at

5 days before radioiodine (91 *vs.* 85%; p=0.03), but this result was not duplicated in a randomized trial of radioiodine alone versus radioiodine plus lithium (900 mg/day). Lithium is not recommended for use as first-line therapy, because of unfavorable side effect profile and potential drug interactions [50]. Madam T received Lithium as the second line option when her FT4 remained elevated after 2 weeks of cholestyramine, and she was not fully compliant with cholestyramine.

Lithium toxicity occurs when serum lithium is high. Lithium toxicity presents with symptoms of mild confusion to delirium, tremors, hyperreflexia, nystagmus and ataxia [51]. Gastrointestinal symptoms are seen immediately within 1 h of intoxication. Renal toxicity is common for patients on long term treatment, which may cause acute kidney injury, minimal change disease, acute tubular necrosis, chronic tubulointerstitial nephropathy, nephrogenic diabetes insipidus, (Lithium is the most common cause of drug-induced NDI), sodium-losing nephritis and nephrotic syndrome [51-54]. The risk of AKI increases if there is concurrent use of Thiazide, ACEI and dehydration. The safe and effective use of lithium requires regular monitoring of renal function. Sinus node dysfunction is a common conduction defect associated with Lithium, followed by QT prolongation and U waves on ECG [55,56].

For Madam T, Lithium was used with extreme caution. She had risk factors to develop kidney injury and Lithium toxicity due to her concomitant use of furosemide and Losartan. She was also dehydrated because she is on fluid restriction and she has a habit of minimizing her fluid intake because she does not like to trouble her caregivers for toileting needs. She was therefore advised to stop both furosemide and losartan, with a short admission to carefully monitor her renal function, fluid status, cardiac function and thyroid function. Under close supervision, she did not develop any problems with Lithium.

Cholestyramine used in combination with thionamide can lead to a more rapid decline in thyroid hormone levels than with standard therapy alone [57,58]. Cholestyramine is an effective treatment option in Graves' hyperthyroidism and iodine contrast-induced hyperthyroidism that was refractory to conventional treatment. Cholestyramine works by enhancing the enterohepatic excretion of thyroxine [59,60]. Lin et al. [60] stated that "complete normalization of free thyroid hormones and notable symptom improvement have occurred within one week of instituting cholestyramine". The optimal dosage is 4 g at 2 to 4 times daily for four weeks.

Prior to radioiodine Rx, Madam T was given prednisolone. Prednisone increased the effectiveness of the therapy with radioiodine [55]. Steroids works by inhibiting the conversion of Thyroxine (T4) to Triiodothyronine (T3) in the periphery [11]. Prednisolone also blocks the release of thyroxine from the thyroid gland [61]. Radioiodine (RAI) therapy may cause progression of mild Graves' opthalmopathy, which is preventable by oral prednisone [35]. TSH receptor antibodies seem to be responsible for the pathological changes of the eyes. A cohort study conducted at a University Centre found that lower dose prednisone about (0.2 mg/kg bw) is effective in reducing graves ophthalmopathy may present in early stages with complaints of dry eyes, eyelid swelling or puffiness, lid retraction, and subsequently developed to proptosis and squint [62-64].

Conclusion

Thyroid dysfunction is prevalent in older individuals and is associated with significant morbidity if left untreated. Clinical features of thyroid disorders in the elderly are subtle, making diagnosis difficult; hence high index of suspicion is warranted. Effective medical and surgical options are widely available, with good results.

Hepatic toxicity is a rare but serious side effect of anti-thyroid medications. Doctors managing patients on anti-thyroid medications should be aware of such potentially fatal complications. Regular monitor of liver function and Full blood count is recommended. Cases where the elderly develop serious drug related complications, radioactive iodine may be a safer option, with thyroxine replacement to follow.

References

1. Kennedy JW, Caro JF. Tha ABC of managing hyperthyroisdim in the older patient. Geriatrics. 1996;51(5):22-32
2. Ajish TP, Jayakumar RV. Geriatric thyroidology: An update. Indian J Endocrinol Metab. 2012;16(4):542-7.
3. Klein I, Danzi S. Thyroid disease and the heart. Circulation. 2007;116(15):1725-35.
4. Gesing A. The thyroid gland and the process of aging. Thyroid Res. 2015;8(Suppl 1):A8.
5. Irvine RE. Thyroid disease in old age. In: Brock Lehurst JC, editor. Text book of pediatric medicine and gerontology. New York: Churchill Livingstone; 1973. p. 435-58.
6. Gambert SR. A typical presentation of thyroid disease in the elderly. Geriatrics. 1985;40(2):63-5,68-9.
7. Polikar R, Burger AG, Scherrer U, Nicod P. The thyroid and the heart, originally published 1 May 1993, Circulation. 1993;87:1435–41.
8. Frost L, Vestergaard P, Mosekilde L. Hyperthyroidism and risk of atrial fibrillation or flutter, a population-based study. Arch Intern Med. 2004;164(15):1675-8.
9. Trivalle C, Doucet J, Chassagne P, Landrin I, Kadri N, Menard JF, et al. Differences in the signs and symptoms of hyperthyroidism in olderand younger patients. J Am Geriatr Soc. 1996;44(1):50–3.
10. Bilezikian JP, Loeb JN, The influence of hyperthyroidism and hypothyroidism on alpha- and beta-adrenergic receptor systems and adrenergic responsiveness. Endocr Rev. 1983;4(4):378-88.
11. Bonnema SJ, Bennedbaek FN, Gram J, Veje A, Marving J, Hegedus L. Resumption of methimazole after 131I therapy of hyperthyroid diseases: Effect on thyroid function and volume evaluated by a randomized clinical trial. Eur J Endocrinol. 2003;149(6):485-92.
12. Ross DS. Hyperthyroidism, thyroid hormone therapy, and bone. Thyroid. 1994;4(3):319-26.
13. O'Brien T, Katz K, Hodge D, Nguyen TT, Kottke BA, Hay ID. The effect of the treatment of hypothyroidism and hyperthyroidism on plasma lipids and apolipoproteins AI, AII and E. Clin Endocrinol (Oxf). 1997;46(1):17-20.
14. Kindler DL, Lippa J, Rootman J. The initial clinical characteristics of Graves' orbitopathy vary with age and sex. Arch Ophthalmol. 1993;111(2):197–200.
15. Boelaert K, Torlinska B, Holder RL, Franklyn JA. Older subjects with hyperthyroidism present with a paucity of symptoms and signs: a large cross-sectional study. J Clin Endocrinol Metab. 2010;95(6):2715-26.
16. Vargas-Uricoechea H, Bonelo-Perdomo A. Sierra-Torres CH. Effects of thyroid hormones on the heart. Clin Investig Arterioscler. 2014;26(6):296-309.
17. Osuna PM, Udovcic M, Sharma MD. Hyperthyroidism and the heart. Methodist Debakey Cardiovasc J. 2017;13(2):60–63.

18. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med. 2001;344(7):501-9.

19. Biondi B. Review Mechanisms in endocrinology: Heart failure and thyroid dysfunction. Eur J Endocrinol. 2012;167(5):609-18.

20. Mitchell JE, Hellkamp AS, Mark DB, Anderson J, Johnson DW, Lee KL, et al. Thyroid function in heart failure and impact on mortality. JACC Heart Fail. 2013;1(1):48-55.

21. Diez JJ. Hyperthyroidism in patients older than 55 years: An analysis of the etiology and management. Gerontology. 2003;49:316–23.

22. Azevedo T, Martins T, Neto J, Oliveira S, Rovira E, Rodrigues F. Radioiodine treatment of hyperthyroidism in the elderly. Endocrine Abstracts. 2013.

23. Edsmyr F, Einhorn J. Complications in radioiodine treatment of hyperthyroidism. Acta Radiologica: Therapy, Physics, Biology. 1966;4(1):49-54.

24. Bitan HD, Leibner A, Amitai O, Cohen TD, Hirsch D, Benbassat C, et al. Bone-marrow suppression in elderly patients following empiric radioiodine therapy: Real-life data. Thyroid Radiol Nucl Med. 2019;29(5).

25. Radioiodine treatment for thyrotoxicosis. A guide for patients and their carers. The Christie: NHS Foundation Trust.

26. Nakazawa HK, Sakurai K, Hamada N, Momotani N, Ito K. Management of atrial fibrillation in the post-thyrotoxic state. Am J Med. 1982;72(6):903–06 .

27. Metso S, Jaatinen P, Huhtala H, Luukkaala T, Oksala H, Salmi J. Long-term follow-up of radioiodine treatment for hyperthyroidism. Clin Endocrinol. 2004;61:641-8.

28. Ron E, Doody MM, Becker DV, Brill AB, Curtis RE, Goldman MB, et al. Cancer mortality following treatment for adult hyperthyroidism. JAMA. 1988;280(4):347–55.

29. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. Thyroid. 2016;26(10):1343-421.

30. Makin V. Management of hyperthyroidism in the older adult, it's important to consider this often-missed diagnosis. 2015.

31. Martin FI, Deam DR. Hyperthyroidism in elderly hospitalised patients: Clinical features and treatment outcomes. Med J Aust. 1996;164(4):200–3.

32. Creutzig H, Kallfelz I, Haindl J, Thiede G, Hundeshagen H. Thyroid storm and iodine-131 treatment. The Lancet. 1976;308(7977):145.

33. Lamberg BA, Hernberg CA, Wahlberg P, Hakkila R. Treatment of toxic nodular goiter with radioactive iodine. Acta Med Scand. 1959;165:245.

34. McDermott MT, Kidd GS, Dodson Jr LE, Hofeldt FD. Radioiodine-induced thyroid storm. Case report and literature review. Amer J Med. 1983;75(2):353-9.

35. Bartalena L, Baldeschi L, Dickinson AJ, Eckstein A, Kendall-Taylor P, Marcocci C, et al. Consensus statement of the European Group on Graves' Orbitopathy (EUGOGO) on management of Graves' orbitopathy. Eur J Endocrinol. 2008;158(3):273-85.

36. Sridama V, DeGroot LJ. Treatment of Graves' disease and the course of ophthalmopathy. Amer J Med. 1989;87(1):70-73.

37. Shafer RB, Nuttall FQ. Acute changes in thyroid function in patients treated with radioactive iodine. Lancet. 1975;2(7936):635-7.

38. Fong TL, Mc Hutchinson JG, Reynolds TB. Hyperthyroidism and hepatic dysfunction. J Clin Gastroenterol. 1992;14(3):240–4.

39. Yao JD, Gross JB, Ludwig J, Purnell DC. Cholestatic jaundice in hyperthyroidism. Am J Med. 1989;86(5):619–20.

40. Solomon B, Glinoer D, Lagasse R, Wartofsky L. Current trends in the management of Graves' disease. J Clin Endocrinol Metab. 1990;70(6):1518-24.

41. Tajiri J, Noguchi S. Antithyroid drug-induced agranulocytosis: Special reference to normal white blood cell count agranulocytosis. Thyroid. 2004;14(6):459–62.

42. Alvarez AM, Mukherjee D. Liver abnormalities in cardiac diseases and heart failure. Int J Angiol. 2011;20(3):135-42.

43. Mikhail NE. Methimazole induced cholestatic jaundice. South Med J. 2004;97(2):178–82.

44. Rathi MS, Ward EG. Carbimazole-induced acute cholestatic hepatitis in patient with Graves' disease. Endocrine Abstracts. 2009;19:P348.

45. Woeber KA. Review: Methimazole-induced hepatotoxicity. EndocrPract. 2002;8(3):222-4.

46. Ozenne G, Manchon ND, Doucet J, Hémet J, Schrub JC, Bercoff E. Carbimazole-induced acute cholestatic hepatitis. J Clin Gastroenterol. 1989;11(1):95-7.

47. Blom H, Stolk J, Schreuder HB, von Blomberg-van der Flier M. A case of carbimazole-induced intrahepatic cholestasis. An immune-mediated reaction? Arch Intern Med. 1985;145(8):1513-5.

48. Backer B, Shapiro B, Fig LM, Woodbury D, Sisson JC, Beierwaltes WM. Unusual complications of antithyroid drug therapy: Four cases reports and review of literature. Thyroidology. 1989;1(1):17–26.

49. Bethesda (MD). LiverTox: Clinical and research information on drug-induced liver injury. National Institute of Diabetes and Digestive and Kidney Diseases. 2012.

50. Bal CS, Kumar A, Pandey RM. A randomized controlled trial to evaluate the adjuvant effect of lithium on radioiodine treatment of hyperthyroidism. Thyroid. 2002;12(5):399-405.

51. Davis J, Desmond M, Berk M. Lithium and nephrotoxicity: A literature review of approaches to clinical management and risk stratification. BMC Nephrol. 2018;19(1):305.

52. Mohandas E, Rajmohan V. Lithium use in special populations. Indian J Psychiatry. 2007;49(3):211-8.

53. Jefferson JW. A clinician's guide to monitoring kidney function in lithium-treated patients. J Clin Psychiatry. 2010;71(9):1153-7.

54. Tandon P, Wong N, Zaltzman JS. Lithium-induced minimal change disease and acute kidney injury. N Am J Med Sci. 2015;7(7):328–31.

55. Oszukowska L, Kucharska MK, Makarewicz J, Lewiński A. The influence of thiamazole, lithium carbonate, or prednisone administration on the efficacy of radioiodine treatment (131I) in hyperthyroid patients. Endokrynol Pol. 2010;61(1):56-61.

56. Canan F, Kaya A, Bulur S, Albayrak ES, Ordu S, Ataoglu A. Lithium intoxication related multiple temporary ECG changes: A case report. Cases J. 2008;1(1):156.

57. Tsai WC, Pei D, Wang TF, Wu DA, Li JC, Wei CL, et al. The effect of combination therapy with propylthiouracil and cholestyramine in the treatment of Graves' hyperthyroidism. Clin Endocrinol (Oxf). 2005;62(5):521–4.

58. Alswat KA. Role of cholestyramine in refractory hyperthyroidism: A case report and literature review. Am J Case Rep. 2015;16:486–90.

59. Lin D, Suwantarat N, Bornemann M. Cholestyramine for thyrotoxicosis? J FamPract. 2013;62(4):E1–2.

60. Franklyn JA, Boelaert K. Thyrotoxicosis. Lancet. 2012;379(9821):1155-66.

61. Lithium: Drug information, Lexicomp.

62. Lai A, Sassi L, Compri E, Marino F, Sivelli P, Piantanida E, et al. lower

dose prednisone prevents radioiodine-associated exacerbation of initially mild or absent graces orbitopathy: A restrospective cohort study. J Clin Endocrinol Metab. 2010;95(3):1333-7.

63. Thyroid eye disease: A brief overview, 1 Jun 2016| Sing Health Medical News, Medical News.

64. Lerma EV. Renal toxicity of lithium. Uptodate.