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Review Article

Subclinical Hyperthyroidism: A Review of the Clinical Literature

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ABSTRACT

Subclinical hyperthyroidism (SCHyper) is a biochemical diagnosis characterized by a decreased serum thyroid-stimulating hormone (TSH) and normal serum thyroxine (T4) and triiodothyronine (T3) concentrations. Because SCHyper can be resolved, it is recommended to repeat serum TSH, T3, and T4 concentrations in 3 to 6 months before confirming a diagnosis of SCHyper to consider treatment. Proposed grading systems distinguish between mild (TSH, 0.1-0.4 mIU/L) and severe SCHyper (TSH, <0.1 mIU/L) and are used alongside patients' age and the presence of risk factors and symptoms to guide treatment. Appropriate evaluation includes an investigation of the underlying cause and assessment of an individual's risk factors to determine the necessity and type of treatment that may be recommended. SCHyper may be associated with increased risks of cardiovascular-related adverse outcomes, bone loss, and in some studies, cognitive decline. Treatment may include observation without therapy, initiation of antithyroid medications, or pursuit of radioiodine therapy or thyroid surgery. Considerations for treatment include the SCHyper etiology, anticipated long-term natural history of the condition, potential benefits of correcting the thyroid dysfunction, and risks and benefits of each treatment option. The purpose of this overview is to provide a guide for clinicians in evaluating and managing SCHyper in the routine clinical practice.

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Clinical Vignette

A 66-year-old woman with a history of prediabetes and osteoporosis presented with intermittent palpitations and a 5-lb unintentional weight loss over the past month. She was not taking any medications or supplements. Her family history consists of Graves' disease in her mother. On exam, she had normal vital signs and a palpable and diffusely enlarged thyroid gland. Her laboratory results revealed a serum thyroid-stimulating hormone (TSH) level of 0.01 mIU/L (reference range, 0.3-4.7 mIU/L), free thyroxine of 1.2 ng/dL (reference range, 0.8-1.7 ng/dL), and free triiodothyronine of 333 pg/dL (reference range, 222-383 pg/dL). In this article, we review the evidence and recommendations regarding the evaluation and treatment of this patient's clinical presentation.

Definition and Diagnosis

Subclinical hyperthyroidism (SCHyper) is a biochemical diagnosis characterized by normal serum thyroxine (T4) and triiodothyronine (T3) levels in a setting of decreased serum TSH concentrations regardless of the presence or absence of symptoms. In contrast, overt hyperthyroidism is characterized by an elevated serum T3 and/or T4 with decreased TSH levels. A proposed grading system distinguishes mild from severe SCHyper, according to the degree of TSH reduction (mild SCHyper, TSH 0.1-0.4 mIU/L; severe SCHyper, TSH <0.1 mIU/L).[1]

Epidemiology

The prevalence of SCHyper is dependent on age, ethnicity, sex, and iodine intake.[2-4] In a United States' population survey, 1.3% of individuals aged ≥12 years were found to have hyperthyroidism

Abbreviations: ATA, American Thyroid Association; AACE, American Association of Clinical Endocrinologists; BMD, bone mineral density; CI, confidence interval; COVID-19, coronavirus disease-2019; ETA, European Thyroid Association; HR, hazard ratio; hCG, human chorionic gonadotropin; IRR, age-adjusted incidence rate; MMI, methimazole; RAI, radioiodine; SCHyper, subclinical hyperthyroidism; TSH, thyroid-stimulating hormone; T4, thyroxine; T3, triiodothyronine; TMNG, toxic multinodular goiter; TRAb, thyrotropin receptor antibody; TBII, TSH-binding inhibitory immunoglobulin.

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(SCHyper, 0.7%; overt hyperthyroidism, 0.5%).[3] In the TEARS Scottish study, SCHyper was described at a prevalence of 0.63% and an incidence of 29 per 100 000 individuals.[4] Furthermore, this longitudinal study reported that 6.1% of individuals with SCHyper progressed to overt hyperthyroidism in the first year; of the remainder, only 0.5% to 0.7% developed overt hyperthyroidism over 7 years.[4] In addition, the majority (63%) remained persistently SCHyper without treatment, while 36% spontaneously returned to normal serum thyroid function, especially those with TSH concentrations between 0.1 and 0.4 mIU/L, over the 7-year follow-up.[4] In general, there is a higher prevalence of SCHyper among women, older individuals, and those living in iodine-deficient regions.[2-5] Blacks and smokers have been noted to have lower biochemical TSH values, which may not represent true SCHyper biologically, but instead reflect a leftward shift in the TSH setpoint in these groups.[3,6]

Etiologies of SCHyper

The causes of SCHyper can be distinguished between endogenous versus exogenous etiologies of hyperthyroidism and transient versus persistent sources of the thyroid dysfunction. The exogenous causes of SCHyper may be intentional, for example as part of the treatment of some differentiated thyroid cancers, although may also be surreptitious, if thyroid hormone is used by some in an attempt for weight loss. Thyroid hormone replacement, such as levothyroxine, liothyronine, or desiccated thyroid extract, in patients treated for hypothyroidism may also overestimate physiologic needs and may result in SCHyper.[7,8] The endogenous causes of SCHyper include thyroiditis, toxic thyroid nodules, toxic multinodular goiter (TMNG), and Graves' disease. Graves' disease may be more prevalent in younger patients, while TMNG is more common in older patients.[9,10]

Despite being transient, SCHyper may last up to 3 to 6 months, depending on the etiology.[11] SCHyper can be transient as a result of the treatment of overt hyperthyroidism with radioiodine (RAI) therapy or antithyroid medications during the transition to euthyroidism. It may also be transient due to the various forms of thyroiditis (ie, subacute thyroiditis, painless thyroiditis, postpartum thyroiditis, lithium-induced thyroiditis, immune-related thyroiditis related to the use of immune checkpoint inhibitors, and amiodarone-induced thyroiditis).[12-15] Other medications known to cause thyroiditis include interferon-α, interleukin-2, and tyrosine kinase inhibitors.[11]

It is significant to note, however, that SCHyper does not warrant treatment in some cases. Differentiating true SCHyper from other causes of low TSH concentration will help guide the next steps in its workup and whether treatment is indicated. During pregnancy, human chorionic gonadotropin (hCG) levels are particularly elevated in early gestation and in those with hyperemesis gravidarum. Owing to the structural homology between hCG and TSH, hCG in pregnant women can stimulate TSH receptors to increase thyroid hormone production, resulting in a decreased TSH level that may be confused as SCHyper.[16] The majority of women with hyperemesis gravidarum will have spontaneous remission of these abnormal thyroid function tests when vomiting ceases in pregnancy.[17]

Additionally, iodine is frequently found in high amounts in some vitamins and supplements and commonly as a component of radiologic contrast media. Acute or chronic iodine exposure, especially in those with pre-existing thyroid disease or other risk factors, can induce SCHyper.[18] A Brazilian study reported a positive association between SCHyper and panic disorders, although a negative association between SCHyper and anxiety disorders, suggesting a link between psychiatric disorders and thyroid dysfunction.[19] Critically ill patients may also present with low to normal serum TSH levels as a part of non-thyroidal illness, depending on the phase of the illness.[20] Other causes of decreased TSH levels that are not necessarily indicative of the endogenous causes of SCHyper include hypothalamic and pituitary dysfunction, TSH-β gene mutations, spurious thyroid function tests caused by the interference of heterophile antibodies and paraproteins, and the use of medications that include biotin, metformin, dopamine agonists, glucocorticoids, dopamine, and somatostatin analogues.[11,21,22,23,24,25]

Since the identification of severe acute respiratory syndrome coronavirus 2 in 2019, which sparked the coronavirus disease-2019 (COVID-19) pandemic, there has been a growing research assessing the effects of the infection on serum thyroid function. One retrospective study reported a high prevalence of SCHyper in COVID-19 patients associated with high circulating levels of interleukin-6, due to a proposed mechanism of destructive thyroiditis.[26] This is consistent with another study that noted 10 of 191 COVID-19 patients developed SCHyper due to thyroiditis.[27] Several series have described lower than normal TSH values among those with COVID-19, and those with severe infections have particularly decreased TSH values.[26-29] These patterns may be due to possible direct viral effects on TSH-secreting cells in the pituitary gland, disruption in the pituitary-thyroid feedback loops from COVID-19 and its therapies, or non-thyroidal illness.[26-29]

Diagnostic Evaluation of SCHyper

Recommendations for the diagnostic evaluation of SCHyper vary among major medical societies. For example, the U.S. Preventive Services Task Force recommends refraining from serum thyroid function screening in nonpregnant, asymptomatic patients, whereas the American Association of Clinical Endocrinologists (AACE) advocates for an aggressive case-finding approach to identify individuals who are most likely to have thyroid dysfunction and will likely benefit from its treatment.[30,31] Furthermore, the American Thyroid Association (ATA) and European Thyroid Association (ETA) recommend monitoring younger subjects <65 years old at regular 6- to 12-month intervals and correction of SCHyper only if the TSH is persistently <0.1 mIU/L.[11,32] The ETA further recommends a treatment consideration in this specific group when the serum thyrotropin receptor antibody (TRAb) titer is persistently detectable, and/or thyroid RAI uptake is increased.[32]

The clinical presentation of SCHyper can vary from the absence of symptoms to mild symptoms of hyperthyroidism, such as arrythmias, heat intolerance, insomnia, increased appetite, diarrhea, weight loss, hair loss, diaphoresis, abnormal menses, and hand tremors. The initial serologic workup following the finding of SCHyper consists of repeating the thyroid function tests. These should include the measurement of serum TSH and free and/or total T4 and T3 concentrations. If the biochemical abnormalities are confirmed, the titers of serum thyroid antibodies, such as TRAb, TSH-binding inhibitory immunoglobulin (TBII), thyroid-stimulating immunoglobulin, and thyroglobulin antibody, may be obtained if an autoimmune thyroid etiology is suspected. Serum thyroid-stimulating immunoglobulin, TBII, and TRAb are highly sensitive and specific, cost efficient, and readily available; test positivity would suggest a diagnosis of Graves' disease as the cause of the SCHyper.[11,33] An elevated serum thyroglobulin level would support a diagnosis of thyroiditis, whereas a low thyroglobulin level would suggest an exogenous thyroid hormone use, which can be intentional or unintentional.[14] Other lab tests that help in the diagnosis of thyroiditis include elevations in erythrocyte sedimentation rate, C-reactive protein, white blood cell count, and thyroid peroxidase antibody. Moreover, a decreased hemoglobin level may be detected as part of the complete blood count.[11] Because iodine is

predominantly renally excreted, an elevated spot urine iodine concentration can be helpful in ruling in recent iodine exposure as a cause of the SCHyper.[34]

Moreover, imaging can be pursued to help differentiate between etiologies and guide the treatment of SCHyper if indicated. A thyroid ultrasound with Doppler flow can be used to detect hypervascularity that is suggestive of Graves' disease. Thyroid scintigraphy with ^{123}I or ^{99M}Tc can be obtained to assess thyroid gland activity. Low scintigraphic uptake would suggest thyroiditis or exogenous thyroid hormone use, while focally increased uptake is consistent with toxic thyroid nodule(s), and diffuse increased uptake is diagnostic of Graves' disease.

Because SCHyper can spontaneously resolve, it is recommended to repeat serum TSH, T3, and T4 concentrations in 3 to 6 months before confirming a diagnosis of SCHyper and considering treatment.[11] Patients at a high risk of SCHyper-related complications may have thyroid function tests performed earlier (eg, 2-6 weeks).[11] In case of abnormal thyroid function tests resulting from the use of biotin-streptavidin immunoassays, ATA recommends abstaining from biotin for at least 2 days before repeating the blood tests.[11]

Adverse Effects Of SCHyper

Cardiovascular Effects

Thyroid hormone is significant in the regulation of cardiac function, and SCHyper may adversely affect cardiac morphology and function.[35] SCHyper is associated with increased heart rate, atrial arrhythmias, and especially atrial fibrillation, atrial and ventricular premature beats, elevated nocturnal arterial blood pressure, increased QT interval dispersion, and heart rate variability.[35-41] One population-based cohort study of 586 460 individuals (mean age, 50.2 ± 16.9 [standard deviation {SD}] years; 39% men) with SCHyper showed increasing incidence rates of atrial fibrillation with decreasing TSH levels (1.16 % if TSH 0.1-0.2 mIU/L vs 1.41% if TSH <0.1 mIU/L).[37] Cardiac structural changes associated with SCHyper include an increased left ventricular mass due to an increase of septal and posterior wall thickness, potentially causing diastolic dysfunction.[35,36] Tadic et al has described the echocardiographic changes that can occur in some individuals with SCHyper as having a notably impaired right atrial and right ventricular function in both systole and diastole as well as a hyperkinetic cardiovascular state that leads to hemodynamic overload.[42]

Several studies have shown that SCHyper is associated with increased all-cause mortality, major adverse cardiovascular events mostly due to heart failure, and adverse prognoses in those with pre-existing heart failure as well as increased coronary heart disease mortality and events.[38,43,44,45] In a systematic review of 52 674 individuals (median age, 59 years; 58.5% women) with a median follow-up of 8.8 years and a total follow-up of 501 922 person-years, the overall age- and sex-adjusted hazard ratios (HRs) for those with SCHyper compared with euthyroid patients was 1.24 for total mortality (95% confidence interval [CI], 1.06-1.46), 1.29 for coronary heart disease mortality (95% CI, 1.02-1.62), 1.21 for coronary heart disease events (95% CI, 0.99-1.46), and 1.68 for incident atrial fibrillation (95% CI, 1.16-2.43).[38] In a retrospective Danish cohort study of 563 700 individuals (mean age, 48.6 ± 18.2 [SD] years; 39% men), all-cause mortality was increased among those with SCHyper (age-adjusted incidence rate, 15.3 per 1000 person-years; incidence rate ratio [IRR], 1.23; 95% CI, 1.16-1.30) compared with euthyroid patients.[43] In this analysis, SCHyper subjects also had an elevated risk of major adverse cardiovascular events (IRR, 1.09; 95% CI, 1.02-1.16) and heart failure (IRR, 1.20; 95% CI, 1.10-1.31).[43] On the other hand, another prospective study found no association between SCHyper and other cardiovascular disorders or mortality.[39] A study of community-dwelling adults aged ≥65 years in the U.S. (n =3233) similarly reported no increased risk of all-cause death among those with SCHyper (HR, 1.08; 95% CI, 0.72-1.62) after adjusted analyses.[39] Risks for coronary heart disease mortality, heart failure, and atrial fibrillation may be dependent on the severity of SCHyper and are higher in those with serum TSH levels <0.10 mIU/L than in those with lower degrees of SCHyper.[38,46]

The association between SCHyper and stroke is less well understood. One meta-analysis showed no evidence supporting an increased risk of stroke in those with SCHyper.[43,47] Other studies have reported that patients with SCHyper were at an increased risk of functional disability, worsened prognosis, and unsuccessful reperfusion after ischemic stroke compared with euthyroid individuals.[48,49]

Bone Loss

Thyroid hormone also plays major roles in the regulation of bone metabolism. Excess thyroid hormone leads to increased osteoclastic activity and net bone loss. Overt hyperthyroidism is a well-established cause of secondary osteoporosis and increases the risk of fractures.[50]

However, data on the association between SCHyper and its effects on bone health remain inconsistent. In a recent meta-analysis of 13 prospective cohort studies with 70 298 individuals (median age, 64 years; 61.3% women), SCHyper was found to be associated with an increased risk of hip (HR = 1.36; 95% CI, 1.13-1.64) and any fracture defined as any non-vertebral or vertebral fracture (HR = 1.28; 95% CI, 1.06-1.53), particularly in those with serum TSH levels <0.10 mIU/L and those with endogenous etiologies of SCHyper, such as Graves' disease, TMNG, and toxic thyroid nodules.[51] Similarly, another study found a significant bone loss in the lumbar spine and hips of postmenopausal women who had SCHyper on suppressive thyroid hormone therapy.[52] Other prospective studies have found no associations between SCHyper and its effects on bone turnover among older men and on bone mineral density (BMD) measurements among healthy middle-aged adults.[53,54] In one large prospective study with 3338 men aged 70-89 years, there was no association of hip fracture and SCHyper ($P = .254$).[53]

Other data demonstrate that the treatment of SCHyper can have positive effects on the bone and may prevent the continued loss of bone mass up to 2% per year.[41,55] Faber et al similarly examined the effects of RAI therapy on BMD in 16 postmenopausal women with SCHyper from multinodular goiter. The authors noted an increased spinal BMD of 1.9% and 1.5% at 1- and 2-year follow-up, respectively, and an increased hip BMD of 2.3% and 1.7% at 1- and 2-year follow-up, respectively.[55] Mudde et al studied 16 postmenopausal women with endogenous SCHyper from multinodular goiter and noted that in those treated with methimazole (MMI, n = 8), mean BMD was increased and continued bone loss at the distal forearm was halted compared with untreated controls.[56] In this study, despite BMD gains, bone turnover serum markers did not significantly change.[56]

Dementia and Cognitive Decline

Evidence supporting the association between SCHyper and cognitive decline is equivocal. A meta-analysis suggested that there may be an elevated risk of dementia and Alzheimer disease associated with SCHyper; however, the thyroid dysfunction is not associated with faster neurocognitive decline as assessed by Mini-Mental State Examination results [57]. Other studies suggest associations between SCHyper and cognitive impairment, overall

Table 1
Recommendations for the Management of Subclinical Hyperthyroidism (adapted from 2016 ATA[11] and 2011 AACE guidelines[14])

	TSH 0.1-0.4 mIU/L[a] (Mild SCHyper)	TSH <0.1 mIU/L (Severe SCHyper)
Aged <65 y[b]		
Asymptomatic	Monitor	Consider treating
Asymptomatic with risk factors[c]	Consider treating	Consider treating
Symptomatic	Consider treating	Treat
Aged ≥65 y		
Asymptomatic	Consider treating	Treat
Asymptomatic with risk factors[c]	Consider treating	Treat
Symptomatic	Consider treating	Treat

Abbreviations: ATA = American Thyroid Association; AACE = American Association of Clinical Endocrinologists; SCHyper = subclinical hyperthyroidism.
[a] 0.4 mIU/L is the lower limit of most reference ranges
[b] Please see special considerations for pregnant women in the text.
[c] Risk factors= cardiac disease, osteoporosis, and menopausal women not on estrogens or bisphosphonates.

dementia, vascular dementia, and Alzheimer disease in men.[58,59] Among older adults, those with serum TSH levels <0.10 mIU/L were at a higher risk of developing dementia and increased cognitive decline than those with more mildly decreased serum TSH levels.[60] However, another prospective study of men and women aged 70-82 years (n = 5154) found no associations between SCHyper and cognitive impairment or decline.[61]

Other Adverse Effects

There is growing research on the association of other clinical outcomes and SCHyper. From limited literature, SCHyper is correlated with metabolism and increases the risk of hyperglycemia and decreased serum total cholesterol, LDL-cholesterol, and HDL-cholesterol levels.[62,63] In addition, SCHyper can impair the quality of life as a result of an increased adrenergic state due to heat intolerance, sweating, palpitations, hand tremors, and anxiety; such symptoms may warrant treatment and symptom alleviation with cardioselective beta blockers.[64]

SCHyper in Pregnancy

In pregnancy, SCHyper is relatively uncommon and typically does not warrant treatment, in contrast to overt hyperthyroidism. Studies suggest that SCHyper occurs in 1.7% of singleton pregnancies and may be more common in African American and/or parous patients.[65] SCHyper does not appear to be associated with increased risks of maternal, obstetric, or neonatal morbidities, when compared to euthyroid pregnant women, and instead may even have decreased risks of gestational hypertension.[65,66] Several recommendations suggest that SCHyper in pregnancy does not necessarily require treatment and may be monitored.[65-67] However, SCHyper during 4 to 8 weeks of pregnancy has also been reported to be associated with a decreased incidence of abortion, although is a risk factor for preeclampsia and placental abruption.[68]

It should be noted that serum TSH concentrations may vary across different ethnicities; thus, mildly abnormal values may be observed during pregnancy and may not suggest a clinically significant SCHyper.[69-71] Future research is needed in this arena to better understand the clinical effects of SCHyper in pregnant women and the fetus as well as in women during preconception.

Indications for the Treatment of SCHyper

Guidelines from ATA and AACE suggest that individuals with SCHyper should be treated when serum TSH is <0.1 mIU/L in those aged ≥65 years with cardiac risk factors, heart disease, or osteoporosis; postmenopausal women who are not on estrogens or bisphosphonates; and in individuals with hyperthyroid symptoms (Table 1).[11,14] Treatment should also be initiated in individuals aged <65 years, with or without hyperthyroid symptoms, whose serum TSH levels remain persistently <0.1 mU/L (Table 1).[11,14]

In 2015, ETA published similar guidelines regarding the treatment of SCHyper.[32] The guidelines recommend treatment in those aged >65 years with serum TSH levels <0.1 mIU/L and a strong consideration for treatment in those aged >65 years with serum TSH levels between 0.1 and 0.39 mIU/L, especially in those with pre-existing cardiovascular disease or comorbidities, such as peripheral arterial disease, stroke, diabetes, or renal failure.[32] The guidelines recommend that the decision to treat should be individualized for those aged <65 years, especially if the individual has persistent or overt symptoms of hyperthyroidism, and in patients with serum TSH <0.1 mIU/L and cardiovascular-related comorbidities.[32] These recommendations state that treatment in younger asymptomatic patients is not warranted. Such individuals can be monitored with serial serum thyroid function tests due to the low risk of transition into overt hyperthyroidism and likely spontaneous remission of the SCHyper. Supporting reasons for the early treatment of SCHyper in appropriate candidates include avoiding the progression to overt hyperthyroidism and increased total mortality, cardiovascular mortality, atrial fibrillation, and fracture risks in untreated individuals.[11,32,72,73]

Treatment of SCHyper

Options for the treatment of SCHyper follow the same principles as overt hyperthyroidism and include thionamides (ie, MMI or propylthiouracil),^{131}I-radioactive therapy, and thyroid surgery. Adrenergic symptoms can be treated with cardioselective beta blockers, such as propranolol, atenolol, or metoprolol, and titrated to achieve the goal heart rate of <90 beats/min.[11] One should closely monitor blood pressure in individuals managed with beta blockers due to the side effect of hypotension. The type of beta blocker, especially in those with polypharmacy or history of noncompliance, should be an additional consideration (ie, atenolol can be dosed once a day, whereas propranolol is dosed every 4-6 h).

MMI is a reasonable treatment option in appropriate individuals, especially in young patients in whom remission is likely and those with mild disease. One study suggests that MMI of up to over 8 years of use was as safe and effective as RAI therapy in treating TMNG.[74] In older adults, both RAI therapy and low-dose MMI can be used safely and effectively in the treatment of SCHyper.[75] Another study assessing long-term thionamide use has suggested that the remission of Graves' hyperthyroidism occurs mostly after 4-11 years of treatment and those with a disappearance of serum TBII titers within 5 years or without TBII fluctuation or enlargement of goiter may suggest a better prognosis.[76] This is consistent with the findings from a systematic review and

meta-analysis that favored longer treatment with antithyroid medications, which showed a remission rate of 16% for each year of continued treatment (95% CI, 10%-27%).[77] Another prospective randomized controlled trial with 302 patients with Graves' hyperthyroidism found that the administration of low-dose MMI for 60-120 months safely and effectively treats Graves' hyperthyroidism, with much higher rates than those attained by the conventional duration of 18-24 months.[78]

If treatment is not initiated, trending serum thyroid function tests can be performed every 3 months, especially in those in whom there is a high chance of spontaneous resolution of the biochemical abnormality.[11]

For lactating mothers with SCHyper managed with a thionamide, the medication should be administered just after breastfeeding, which provides a 3- to 4-h interval prior to subsequent lactation.[79,80] Pregnancy should be deferred for 6 months in those who have received ^{131}I treatment due to the risk of fetal/neonatal hypothyroidism.[79] The use of ^{131}I is contraindicated during lactation; if ^{123}I is needed for diagnostic studies, breast milk should be pumped and discarded for 3 to 4 days before breastfeeding resumes.[79]

Serum thyroid function tests should be obtained 2 to 6 weeks after the initiation of an antithyroid medication, to ensure that the dose may be adjusted accordingly.[11] Serum TSH should be cautiously interpreted as it may remain suppressed for several months after thionamide therapy initiation. Once the patient is biochemically euthyroid, MMI dosing can be reduced by 30% to 50%; repeat thyroid function tests and antithyroid medication doses can be adjusted every 4 to 6 weeks; the long-term use of thionamide can be monitored with serum thyroid function tests in 2- to 3-month intervals.[11] Patients on antithyroid medications should be counseled on the rare side effects of agranulocytosis, hepatotoxicity, vasculitis, and skin rashes. ATA guidelines for hyperthyroidism do not recommend monitoring white blood cell and liver function tests in those on antithyroid medications.[11]

As another treatment option, those with SCHyper due to TMNG or toxic thyroid nodule(s) can consider treatment with RAI therapy or thyroid surgery, with the latter preferred if there are compressive symptoms or concerns for malignancy.[11,32] Those receiving RAI therapy or thyroid surgery should be forewarned as regards the risk of hypothyroidism and the need for long-term thyroid replacement.

The goal of treatment in individuals with SCHyper is the normalization of serum thyroid function to achieve a euthyroid state with the goal of reducing cardiac, bone, and other complications of SCHyper.[11] No randomized controlled trials have been found to suggest the decreasing rates of atrial fibrillation or decreased mortality with treatment. However, there is evidence of reversible cardiac effects with correction of the SCHyper, which may theoretically decrease future adverse cardiovascular events.[40,81] Other studies demonstrate an improved BMD in postmenopausal women and an improved quality of life following treatment with either beta blockers or antithyroid medications in those with SCHyper.[35,36,55,56] It is significant to counsel patients on the potential benefits versus the areas in which the supporting evidence is less clear when considering the treatment of SCHyper.

Recommendations for Our Patient

The patient described in the vignette above has a decreased serum TSH concentration and normative free thyroxine and free triiodothyronine levels. Clinically, she has mild symptoms of hyperthyroidism. The patient is not taking any medications or nonprescription supplements that may cause laboratory interference. A repeat set of serum thyroid function tests should be repeated in 3 to 6 months to confirm the persistence of SCHyper. If the repeated blood tests are similar, the appropriate further workup should be pursued, which may include serum thyroid antibodies, thyroid ultrasound, and thyroid scintigraphy. If an endogenous etiology for the SCHyper is confirmed from this evaluation, the patient's older age (≥65 years), presence of hyperthyroid symptoms, and osteoporosis would support treatment. A discussion to guide the choice of whether a thionamide should be initiated or ^{131}I radioactive therapy or thyroid surgery pursued should take into account the etiology of the SCHyper, anticipated long-term natural history of the condition, potential benefits of correcting the thyroid dysfunction, and the risks and benefits of each treatment option.

Disclosure

The authors have no multiplicity of interest to disclose.

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