Chapter 13
Hypothyroid Myopathy and Thelogen Effluvium

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Objectives

Describing common and uncommon manifestations of hypothyroidism and rapid changes in thyroid function.

Case

A 20-year-old woman received 8 mCi I-131 for Graves' disease. She had received methimazole for the 2 months preceding the treatment and was euthyroid at the time of her treatment. However she had developed a rash while on methimazole and this prompted the I-131 treatment. Four weeks after I-131 treatment she presented for a scheduled follow-up appointment. She felt well and her TFTs demonstrated euthyroidism, albeit with a suppressed TSH (Table 13.1). One month later, she presented with severe muscle pains, rated at 8/10. Pains were most prominent in the left calf, which appeared slightly larger in diameter than the right, and in the right thigh, which appeared normal. Her laboratory tests (see Table 13.1) showed markedly elevated TSH, undetectable FT4 and extremely low T3 and Vitamin D. Her CPK was markedly elevated and her creatinine was in the normal range. Thyroxine, 100 mcg orally daily was prescribed. In addition, she was treated with lyothyronine 25 mcg twice a day orally for 10 days, with the purpose or restoring euthyroidism rapidly. High dose Vitamin D supplementation was also administered. Her symptoms improved rapidly and resolved completely in 1 week. Two months later blood

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Table 13.1 Thyroid function test and CPK course. Levothyroxine replacement treatment was started on day 60

Days after I-131	TSH (mcU/L), 0.4–5.0	FT4 (ng/mL), 0.9–1.8	T3 (ng/dL), 60–181	CK (IU/L), 40–150
0	0.01	1.2	192	
28	<0.01	1.2	145	
60	170.88	<0.4	13	
61				4,878
64	119.30	0.7	49	3,405
94	0.15			
175	0.04	1.7		83

tests showed normal thyroid function and her CPK was in the normal range. She felt very well. One month later, she presented with complaint of severe hair loss. She described clumps of hair falling with each shower and was worried that she "would go bald." On exam there were no patches of baldness or male pattern alopecia. The hair was slightly thinner all over. Her thyroid function tests remained normal. She was reassured that this was a transient phenomenon. Three more months later, the hair loss had stopped and 6 months later she reported a complete restoration of her previous hair quality.

Review of How the Diagnosis Was Made

This patient presented with severe muscle aches and objective findings of muscle swelling. Her muscle enzymes demonstrated severe hypothyroid myopathy, in association with rapid onset post-I-131 hypothyroidism. Her subsequent course was characterized by hair loss. The exam of her scalp revealed only mild hair thinning and no focal areas of alopecia, leading to a diagnosis of telogen effluvium.

Lessons Learned

Statistically, the symptoms of hypothyroidism are correlated to the severity of the hormonal deficiency [1]. However there is significant variability [2]. Some patients may report prominent fatigue with modest TSH elevations, while others may be surprisingly free of symptoms, even when profoundly hypothyroid. Unrecognized individual factors may play a role in this variability. The rate of thyroid hormone loss may also be important, with patients in whom hypothyroidism develops rapidly being more symptomatic. Patients with thyroid cancer and surgical hypothyroidism whose thyroxine replacement dose is suddenly held in preparation of radioiodine scanning become typically very symptomatic in a short period of time. Of course

these patients are also profoundly hypothyroid, more so than the average patient with Hashimoto's thyroiditis, whose milder hypothyroidism develops over a long period of time.

Mild muscle and joint aches are common in hypothyroidism. In a study from Canaris [1] muscle aches were among the most specific symptoms in identifying patients with hypothyroidism. Moderately to markedly elevated creatine phosphokinase (CPK) levels are observed in up to 60 % of patients with overt hypothyroidism [3]. These manifestations have been loosely referred to as "hypothyroid myopathy." The etiology of hypothyroid myopathy remains unclear. A few pathology studies have shown selective loss of type-II fibers, increased nuclear counts and diffuse glycogen inclusions [4]. The range of clinical manifestations is wide, ranging from patients being completely asymptomatic with minimal CPK elevation, some others with significant but nonprogressive myalgias and a small minority developing severe myopathy, rhabdomyolisis, compartment syndrome, and renal failure [5]. The concurrent use of statins may be a risk factor for the development of hypothyroid myopathy. This is demonstrated in several case reports of patients who developed the condition after many years of statin treatment when the hypothyroidism occurred [6]. Thus so far one can draw the following clinical suggestions:

1. Hypothyroidism should always be considered in the evaluation of a myopathy, whether in the setting of clinically silent CPK elevation, or in the presence of symptomatic muscle damage.
2. Patients who develop hypothyroidism while taking statins should be monitored carefully for evidence of muscle damage. Special caution should be used in thyroid cancer patients in whom rapid and profound hypothyroidism is purposely precipitated for radioiodine scanning and treatment.
3. Patients who develop significant muscle aches with severe hypothyroidism should be carefully monitored for the development of compartment syndrome and renal failure. Euthyroidism should be restored as quickly as possible. Lyothyronine in addition to thyroxine may prove beneficial although caution should be used in the elderly or cardiac patient.

After restoration of euthyroidism, the patient reported concerning hair loss. Hair changes are common in hypothyroidism. In the era of sensitive TSH testing and frequent screening, most patients with hypothyroidism are diagnosed with early and mild forms. The classical finding of coarse, brittle, and sparse hair, which is typically seen only in profound and prolonged hypothyroidism, is nowadays rarely observed. Alopecia areata can be observed with increased frequency in patients with Hashimoto's thyroiditis [7]. The association is independent of thyroid function status and reflects the common autoimmune background of the two conditions. Alopecia areata is characterized by patchy hair loss developing over a period of weeks or months. The condition is self-limited and remitting in a majority of cases, but it may result in partial or total permanent scalp hair loss (alopecia totalis) [8]. In our patient, the absence of patchy hair loss made alopecia areata unlikely. The history of sudden hair loss, without focal or regional baldness, in coincidence with recent rapid changes suggests the diagnosis of telogen effluvium. Human adult hair

cycle is asynchronous, in that at any given moment there is a fraction of hair in the anagen, catagen, or telogen phase, respectively. As a consequence a small constant number of hairs is shed every day, as they end the telogen phase. In telogen effluvium, hair becomes synchronized and the majority of hair rapidly enters the telogen phase at the same time and is subsequently shed. This phenomenon is observed after pregnancy. During pregnancy hair is held in prolonged anagen as a consequence of the hormonal changes associated with pregnancy. This larger-than-normal proportion of hair in anagen then progresses to telogen synchronously after delivery. When the telogen phase is completed, some 3–4 months later, this hair is shed simultaneously, resulting in the distressing observation of large clumps of hair in the shower. However the intact follicles start producing new hair right away and over the next few months the hair is restored to its original thickness and quality. A similar phenomenon occurs after acute illnesses, except that the pathophysiology is sudden and synchronous exit from anagen [9]. This variety of telogen effluvium is particularly common after rapid changes in thyroid hormone levels. It is seen both after correction of hyperthyroidism or hypothyroidism, and after patients become suddenly hypothyroid, for example in preparation of whole body scanning. It is quite common to receive the distressed phone call from a patient who has noticed "clumps and clumps of hair coming off my scalp every day." In spite of the frequency of this observation, the literature on this topic is surprisingly limited. A few months after stable normal levels of thyroid hormone are achieved, hair regrowth and restoration of previous hair quality are observed. Since there is no known treatment or prevention for this self-limited condition, patients need only be counseled on its reversible nature. Rare forms of chronic telogen effluvium occur, but can be only diagnosed when failure of remission is observed. Understanding of this phenomenon by the endocrinologist will spare unnecessary dermatological consultations.

Questions

1. A 68 y/o woman is referred for evaluation of hyperlipidemia. Her only medical problem is hypertension, controlled with hydrochlothiazide and a beta-blocker. Her total cholesterol is elevated at 312 mg/dL, her HDL is normal at 46 mg/dL, and her triglycerides are slightly elevated at 202 mg/dL. Her TSH is markedly elevated at 79 mU/L. As a next step, you:

   (a) Start levothyroxine, adjust the dose at 6 weeks intervals until her TSH is normalized, and then recheck her lipid profile
   (b) Start levothyroxine and a statin; recheck her TSH at 6 weeks intervals until her TSH is normalized.
   (c) Measure her FT4, then start a statin only if her FT4 is in the normal range, and start levothyroxine.
   (d) Measure thyroid-peroxydase antibody.

2. In hypothyroidism, multiple symptoms and signs can be present. In general:
   (a) Symptoms and manifestations are directly correlated to the thyroid hormone level.
   (b) Symptoms and manifestations occur in a ordinated fashion, with cardiovascular symptoms appearing with minimal thyroid dysfunction, metabolic symptoms with moderate thyroid dysfunction, and muscular-skeletal symptoms only present with profound thyroid dysfunction.
   (c) Symptoms and manifestations are highly variable from patient to patient and are not correlated to the thyroid hormone level.
   (d) Male-pattern baldness occurs in most females with hypothyroidism.
3. Which of the following is not a typical manifestation of hypothyroidism:
   (a) Myalgias
   (b) Arthralgias
   (c) Hair thinning
   (d) Bradycardia

Answers

1. (a) Marked hypothyroidism is a possible cause of hyperlipidemia. The hyperlipidemia associated with hypothyroidism is reversible with restoration of euthyroidism. Therefore, in patients with hypothyroidism, treatment of hyperlipidemia should be instituted only if the hypercholesterolemia persists after euthyroidism is restored. Starting a statin in a hypothyroid patient increases the risk of myopathy.
2. (c) Classical symptoms of hypothyroidism are for the most part nonspecific and are present with surprising variability in different patients.
3. (c) Hair thinning is not typically seen in hypothyroidism. The classical description includes “sparse coarse hair.”

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