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Exceptionally elevated creatine kinase levels in a laryngectomized patient: hypothyroid myopathy

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Abstract
We present a laryngectomized patient with unspecific complaints of fatigue whose laboratory findings were out of proportion with the clinical presentation. The enormously high blood levels of creatine kinase (CPK) (8000 IU/l, normal range 30–190 IU/l) and thyroid-stimulating hormone (100 mU/l, normal range 0.5–4.5 mU/l) led to diagnosis and treatment of and recovery from hypothyroid myopathy. Hypothyroidism reduces the ability of the muscle to maintain its adequate energetic economy, via several suggested mechanisms. This may lead to injury (myopathy) that allows enzymes such as CPK to leak out of cells and causes elevation of their serum levels. To our knowledge, this is the first reported case of a patient previously treated for head and neck cancer who developed hypothyroid myopathy, presenting with exceptionally elevated CPK levels. This is noteworthy, since hypothyroidism may be easily avoided by a comprehensive follow-up of patients treated for head and neck cancer.

Key words: Laryngectomy; Fatigue; Creatine

Introduction

Hypothyroidism is a well documented sequela of radiation therapy to the head and neck. Previous or subsequent head and neck surgical procedures such as laryngectomy and/or thyroidectomy may increase its incidence. Moreover, in some cases, hypothyroidism may manifest only after a period of time.[1–5] Blood analysis of individuals with hypothyroidism may reveal not only elevated levels of thyroid-stimulating hormone (TSH) but moderate elevation of creatine kinase (CPK) and lactate dehydrogenase (LDH). This enzyme elevation is caused by muscle injury associated with lack of thyroid hormone, that is, hypothyroid myopathy.[6,7]

This report is the first presentation of a patient previously treated for head and neck cancer who developed hypothyroid myopathy, an easily avoided complication that is not often mentioned in the otolaryngologic literature.

Case report

Four months after he had a total laryngectomy because of glottic carcinoma, a 34-year-old male had his tracheostomy narrowed by keloid tissue and was hospitalized with a mild airway obstruction. After dilatation of the stoma and introduction of a laryngectomy tube resolved the problem, the patient complained of being depressed and fatigued, which he attributed to his domestic affairs. He recounted that three years earlier the diagnosis of glottic cancer had been made, but he had failed to receive the full therapeutic radiation course (he received less than 2000 cGy of the 6600-cGy course). The patient was also unsuccessful in receiving his recent post-operative follow-up.

On admission, the patient's physical examination did not reveal any additional overt findings. The blood count was normal, as were the blood levels of sodium, potassium, glucose and urea and the patient's chest X-ray. A low total calcium level of 7.2 mg/dl (normal range 8.2–9.2 mg/dl) was explained by hypoalbuminaemia of 1.9 g/dl (corrected calcium value 8.8 mg/dl). The LDH was high (1200 IU/l, normal range 105–320 IU/l) and the CPK level was extremely elevated (8000 IU/l, normal range 30–190 IU/l). Further investigation revealed severe hypothyroidism, with the serum TSH level being outstandingly high (100 mU/l, normal range 0.5–4.5 mU/l). Oral thyroid replacement was initiated. Ten weeks of treatment led to resolution of fatigue, and all the blood tests returned to normal levels.

Discussion

The clinical manifestations of hypothyroid myopathy are obscure complaints such as fatigue and myalgia, coupled with hypothyroidism and elevated blood levels of enzymes abundant in muscle tissue (CPK and LDH).[6–9]

This report presents a laryngectomized patient with unspecific complaints whose laboratory findings were out of proportion with the clinical presentation. The enormously high CPK and TSH blood levels led to diagnosis and treatment.

Thyroid hormone regulates muscle activity as well as its energetic maintenance by several suggested mechanisms:

(1) At the deoxyribonucleic acid level, the hormone causes a genomic modulation that leads to an increased

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activity of the Ca^{2+}-adenosine triphosphatase in the sarcoplasmic reticulum of the myocyte, therefore increasing the myocyte energy turnover during contraction and rest.[10,11]

(2) A genomic modulation by the thyroid hormone that controls the expression levels of enzymes related to energy metabolism in the muscle (adenosine monophosphate-activated protein kinase and acetyl-CoA carboxylase).[12]

(3) Thyroid hormone may influence the control of ion channels associated with intracellular Ca^{2+} content responsible for muscle contraction strength at a non-genomic (protein regulation) level.[11,13,14]

(4) Lower levels of regulatory proteins of the mitochondria respiratory chain are found in muscle cells of individuals with hypothyroidism.[15]

- **This paper describes a patient who, following laryngectomy and radiotherapy, presented with fatigue and an exceedingly high serum creatine level; hypothyroid myopathy was subsequently diagnosed**
- **An endocrine cause should be considered in such cases, rather than dismissing the patient's symptoms**

Therefore, hypothyroidism reduces the ability of the muscle to maintain its adequate energetic economy, leading to injury (myopathy) or even destruction (rhabdomyolysis).[16] When muscle cells are injured or diseased, enzymes leak out of the cells and enter the bloodstream, elevating their serum levels. Creatine kinase is a most abundant enzyme in the muscle, where it plays a major role in energy production since it catalyses the reversible conversion of adenosine diphosphate and phosphocreatine into adenosine triphosphate and creatine.[17] Most patients have a blood CPK range of a few hundred to a few thousand IU/l. However, reports have been published of two patients with extremely high levels of CPK, one with a prolonged hypothyroid condition and the other with hypothyroid myopathy. Nevertheless, neither patient had been treated for head and neck cancer.[18,19]

Thyroid replacement usually resolves the myopathy in a few months.[9] The physical and laboratory abnormalities of the patient presented in this case report resolved after 10 weeks of treatment.

This case report of a patient who developed hypothyroid myopathy after previous treatment for a head and neck cancer is the first to be presented. It should emphasize the need for a comprehensive follow-up of patients treated for head and neck cancer, in order to avoid unnecessary complications.

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