CLINICAL VIGNETTE

Severe Hypothyroidism Developing After Breast Cancer Treatment

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Introduction

Hypothyroidism is relatively common in the US.[1] While the most common cause of hypothyroidism is autoimmune thyroiditis, other causes can be iatrogenic, including secondary to radiation therapy.[2] Hypothyroidism following radiation for head and neck cancers is a well-documented adverse effect.[1] While hypothyroidism is less commonly associated with breast cancer radiation, published studies report this outcome.[3] This patient presented with hypothyroidism less than one year after completing breast cancer treatment.

Case

A 57-year-old female with history of right sided breast cancer presented to establish care. She was diagnosed with breast cancer in January of 2021, underwent lumpectomy and chemotherapy and completed XRT in September of 2021. She presented with multiple complaints, including shortness of breath, neuropathy, anemia, and significant fatigue. She was not followed by a primary care physician and been evaluated for these symptoms which developed after completing breast cancer treatment. Her initial evaluation noted a TSH of 195 mcIU/mL (0.4-4.5 mcIU/mL) and free T4 0.7 ng/dL. CK was also significantly elevated at 552 U/L. Sodium was normal at 141 mmol/L. Her severely elevated TSH and symptoms raised concern for risk of myxedema coma and she was sent to the ED for further evaluation. ED vital signs and exam were within normal limits. Cortisol level was found to be normal. Endocrinology was consulted and she was started on oral levothyroxine. TPO antibodies returned negative, suggesting that her hypothyroidism was due to her radiation treatment as she had no prior thyroid surgery and was not taking any medications that could contribute to thyroid dysfunction. She also had no personal or family history of autoimmune disease. She was discharged from the ED to follow up with Endocrine to adjust her thyroxine dose. Unfortunately, she did not return for further follow up.

Discussion

Hypothyroidism affects 0.3% of the US population. Control of thyroid function starts with the hypothalamus. The hypothalamus secretes thyrotropin releasing hormone, which promotes TSH release from the pituitary gland, leading to T4 and T3 production.[1] Symptoms of hypothyroidism are very non-specific, which can contribute to potential delays in diagnosis if it is not considered in the initial differential. Symptoms include fatigue, lethargy, constipation, and dry skin.[1] An elevated TSH with a low T4 is consistent with hypothyroidism (normal TSH range is 0.4 to 4-4.5 mcIU/mL)[1]. Treatment consists of thyroid hormone replacement with levothyroxine. This typically starts at a dose of 1.5-1.8 mcg/kg in patients under age 60 and titrated to a normal TSH level every 6-8 weeks.[1]

Autoimmune thyroiditis is the most common cause and is associated with positive TPO antibodies.[1,2] Radiation for head and neck cancer can iatrogenically lead to hypothyroidism. While breast cancer radiation is not typically included as a treatment that can cause hypothyroidism, prior studies have reported this association.[3] One Korean study, reported the 8-year incidence of hypothyroidism of 9.3% in patients with breast cancer treated with radiation.[4] It has also been suggested that radiation treatment for breast cancer is targeted to the supraclavicular area or regional lymph nodes, is associated with a higher risk for hypothyroidism.[3,4] An Egyptian study reported the incidence of clinical and subclinical hypothyroidism in breast cancer patients receiving supraclavicular lymph node radiation. During 18 month follow up, 20.8% of patients developed hypothyroidism. They reported a baseline TSH greater than 1.42 mcIU/mL more highly correlated with the development of post radiation hypothyroidism.[5] A Danish study also reported women with a history of breast cancer were more likely to develop hypothyroidism than matched controls and found that patients who received both chemotherapy and radiation were at a higher risk of developing hypothyroidism.[6] Despite multiple studies, it is not completely clear which factors increase risk of developing hypothyroidism after radiation treatment for breast cancer, nor the mechanism for developing hypothyroidism. Multiple factors have been proposed, including alterations to the hypothalamic-pituitary-thyroid axis and direct damage to the thyroid cells and vessels from radiation.[3] Radiation to the supraclavicular lymph nodes likely confers higher risk, as a portion of the thyroid is typically included in the irradiated area.[5]

Myxedema coma is a dangerous clinical condition with a 25-60% mortality rate.[1] Myxedema coma is more common in older patients. Typically, electrolyte derangements including hyponatremia are present as well as altered mental status.[1,7] Low cortisol is present if a patient has concurrent adrenal insufficiency.[1] Myxedema coma requires inpatient management, typically with initial dose of IV levothyroxine and stress dose steroids until adrenal insufficiency is ruled out.[7] In this case,

while initial concern was raised for development of myxedema coma, the patient did not require IV treatment and remained hemodynamically stable.

This patient illustrates the importance of considering hypothyroidism in patients presenting with fatigue, particularly those with a history of breast cancer. Given the severe elevation this patient's TSH, she likely had symptoms for months. Left untreated, she was at risk for myxedema coma. One study investigating the risk of hypothyroidism after breast cancer treatment reported, thyroid function tests are not routinely obtained after breast cancer treatment, and the true incidence is not known. Hypothyroidism should remain on the differential when evaluating breast cancer survivors. Hypothyroidism can be easily treated with dramatic improvement in quality of life.

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