Case Report

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Decelerated tumor growth due to hypothyroidism with prolongation of survival in a patient with lung adenocarcinoma: a case report

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Abstract

Lung adenocarcinoma is a form of non-small-cell lung cancer with high mortality in the advanced stages, and is one of the most common histological subtypes of lung cancer in most countries. Prognosis of lung adenocarcinoma is generally poor, with a median survival of 4–13 months. We report a case of unusually prolonged survival of a patient with advanced lung adenocarcinoma complicated by hypothyroidism. A 71-year-old man with stage IV lung adenocarcinoma presented with hypothyroidism. Surprisingly, without any anti-tumor and anti-hypothyroidism therapy, he survived this lung cancer for longer than 2.5 years before his last follow-up visit. Patients with advanced lung adenocarcinoma rarely survive for longer than 2 years, even after therapy. We hypothesize that hypothyroidism is the cause for this discrepancy. Thyroid hormones can promote growth of carcinoma. Therefore, hypothyroidism appears to be beneficial to anti-cancer therapy. We believe that hypothyroidism, as an adverse event commonly occurring in anti-tumor therapy (e.g., an immune checkpoint inhibitor), might not be able to be completely eliminated.

Keywords

Lung adenocarcinoma, hypothyroidism, thyroid hormone, adverse event, immune checkpoint inhibitor therapy, thyromegaly

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Introduction

Lung adenocarcinoma is a malignant adenoepithelial tumor and is the most common histological subtype of lung tumors in most countries, accounting for almost half of all lung cancers.[1] Hypothyroidism has been reported to prolong survival of patients with certain types of cancers.[2] We report a patient with advanced lung adenocarcinoma complicated by hypothyroidism. He was treated by supportive therapy with moxifloxacin hydrochloride and cefmetazole, and managed to survive for a period exceeding 2.5 years leading up to his most recent follow-up visit. To the best of our knowledge, this case is unique and our findings might improve our understanding of adverse events commonly associated with anti-tumor therapy.

Case report

A 71-year-old man with a history of 300 packs per year smoking habit presented with shortness of breath, bloody sputum, and dyspnea for 4 months. He was diagnosed with advanced lung cancer radiologically during his first hospitalization and pathologically at his second hospitalization. A computed tomography (CT) scan showed thyromegaly and thyroid function tests indicated hypothyroidism.

Laboratory studies showed a low hemoglobin level of 85.50 g/L. Arterial blood gas analysis showed a pH of 7.41, PO_2 of 58.28 mm Hg (80–100 mm Hg), actual bicarbonate level of 25 mmol/L, and oxygen saturation of 90%. CT imaging showed thyromegaly (Figure 1a) and bilateral pulmonary multiple nodules on 29 December 2015 (Figure 1b). The following

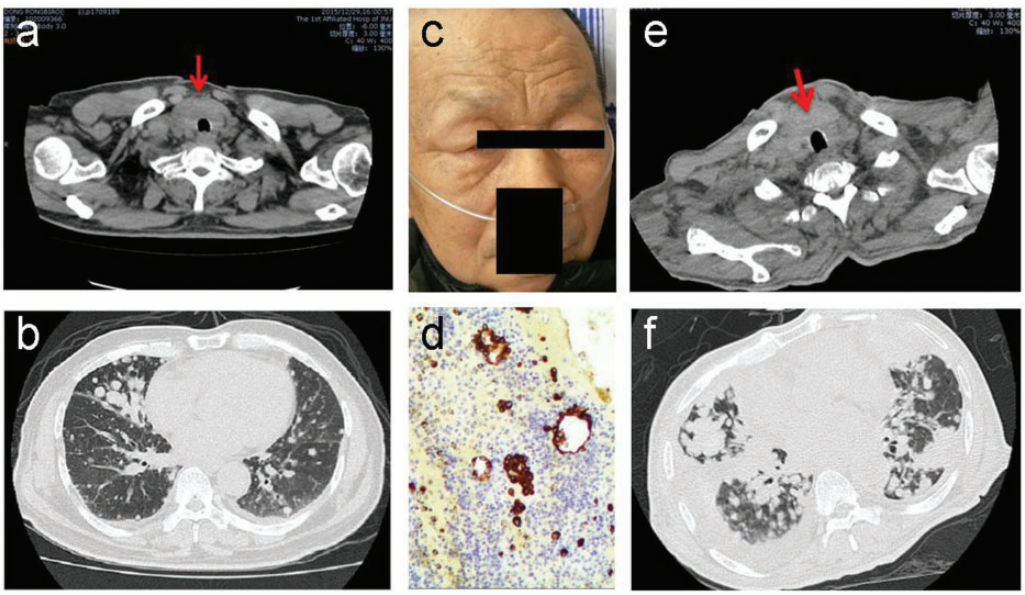

Figure 1. A 71-year-old male patient had not undergone any anti-tumor or anti-hypothyroidism treatment. A chest computed tomography scan showed thyromegaly in 2015 (a) and 2018 (e), and bilateral pulmonary multiple nodules in 2015 (b) and 2018 (f). A physical examination shows a myxedematous face (c). A paraffin section of pleural effusion cells shows scattered adenocarcinoma cells (d). The red arrows indicate thyromegaly.

findings were consistent with a diagnosis of severe hypothyroidism: free triiodothyronine level, 1.71 pmol/L (3.09–7.42 pmol/L); free thyroxine level, 0.86 pmol/L (7.64–16.03 pmol/L); and thyroid-stimulating hormone level, 62.21 mIU/L (0.49–4.91 mIU/L), with a myxedematous face (Figure 1c). An exfoliative cytological pleural effusion test showed adenocarcinoma. Immunohistochemical staining was positive for cytokeratin 7, and negative for thyroid transcription factor-1, napsin A, P40, prostate-specific antigen, and P504S in the following year (Figure 1d). A follow-up chest CT scan showed thyromegaly (Figure 1e) and increased nodules in both lungs on 8 January 2018 (Figure 1f and Supplemental video).

The patient's blood pressure was 140/76 mm Hg, heart rate was 76 beats/minute, respiratory rate was 24 breaths/minute, and oxygen saturation was 85%–90%. He presented with shortness of breath and orthopnea. There was evidence of symmetric edema in both eyelids and the lower extremities. Percussion of the lungs revealed a dull sound. Auscultation indicated weak breathing sounds and moist rale in both lungs. There was a hard, non-sliding, swollen lymph node without tenderness on both sternocleidomastoids.

Our patient with lung cancer (stage IV) had never previously received any anti-tumor therapy or anti-hypothyroidism therapy, such as systemic chemotherapy, radiotherapy, and local treatment, for the tumor. He only accepted supportive therapy, such as moxifloxacin hydrochloride and cefmetazole, during his three periods of hospitalization. His symptoms of shortness of breath, bloody sputum, and dyspnea improved and he was discharged. He had survived the lung cancer for 30 months leading up to the most recent follow-up visit.

All procedures were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This report was conducted with approval from the Clinical Trial Ethics Committee of the First Affiliated Hospital of Jinan University (reference number: 2019-156). Written informed consent was obtained from the patient.

Discussion

Lung cancer is one of the most malignant tumors, with the fastest growth and mortality rate, and it is regarded as the greatest threat to the health and life of the population.[1] Approximately 40% of patients with lung cancer suffer from adenocarcinoma, which is one of three main subtypes of non-small cell lung cancer. There are no obvious symptoms or characteristic signs of adenocarcinoma during the early stage, resulting in the majority of the patients being unaware of their condition until the late stages, when the survival time diminishes without timely anti-tumor therapy. Although the molecular biology of adenocarcinoma is well understood, the survival rate of patients at advanced stages remains low, with an average survival time of only approximately 4 to 13 months.[3,4]

Hypothyroidism is a common pathological condition where the thyroid gland does not produce a sufficient amount of thyroid hormones. This may affect normal physiological processes, such as growth, maturation, and metabolism. In a similar manner, tumor cells are kept under control by thyroid hormones. The levels of thyroid hormone are likely to be involved in regulating proliferation, invasion, and metastasis of tumors, ultimately affecting the prognosis of patients with cancer.[5]

Thyroid hormones can promote cell division and inhibit cell apoptosis,[2] and the physiological concentration of thyroid hormones can promote angiogenesis.[6] Thyroid hormones might be mediated by phosphatidylinositol-3-kinase and the mitogen activated protein kinase pathway, and

involve stimulation of angiogenesis via the $\alpha v\beta 3$ pathway.[7] Additionally, an increase in thyroid hormones or a decrease in thyroid-stimulating hormone can promote progression of cancer, and regulate proliferation and differentiation of cancer cells in various types of cancers, such as prostate cancer, breast cancer, glioblastoma, and liver cancer.[8–11]

Hypothyroidism is an adverse event following immune checkpoint inhibitor therapy.[12] In patients who receive an immune checkpoint inhibitor and develop hypothyroidism, the median overall survival is significantly longer than that in those without hypothyroidism.[13] Similar adverse events have been found in the treatment of colorectal cancer, breast cancer, and renal clear cell carcinoma.[14,15] Similarly, we believe that a decrease in thyroid levels can prolong the survival time of patients with lung adenocarcinoma.

Hypothyroidism was likely to be a complication of lung cancer in our case, but could not have been an adverse reaction of anti-cancer treatment because the patient did not receive any anti-cancer treatment. Based on our patient's prolonged survival, hypothyroidism appears to be involved in inhibition of proliferation, invasiveness, and metastasis of cancer. However, lung cancer progressed in our patient. This finding indicates that hypothyroidism might only slow development of cancer, but fails to stop it completely, as indicated by chest CT scans in 2015 and 2018. Therefore, prospective clinical cancer research, especially using methods for inducing hypothyroidism, should be performed to confirm the relation between cancer and hypothyroidism. Furthermore, hypothyroidism, which is an adverse event that commonly occurs in anti-tumor therapy, such as immune checkpoint inhibitor therapy, might not be able to be completely eliminated.

Authorship

Xing-Dong Cai contributed to the diagnosis and acquisition of data. Jia Hou, Shan-Shan Xiong, and Zhao-Qi Huang contributed to drafting the manuscript and literature review.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Supplemental Material

Supplemental material for this article is available online.

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