

Spontaneous Regression of Large Cell Carcinoma of the Lung, a Case Report

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Abstract

Spontaneous regression of malignancies are a rare biological phenomenon, especially in lung cancer. Here, we present a case of an 80-year old man, with a cT2aN3M1b non-small cell lung cancer of the left upper lobe, whose tumor regressed spontaneously without any treatment. The cause of the spontaneous tumor remission remains unknown in this case. We describe this rare case and review the literature pertaining to spontaneous regression of lung cancer.

Introduction

Spontaneous regression of malignancies are a rare biological phenomenon, especially in lung cancer. It is defined as a complete or partial disappearance of the tumor in the absence of treatment or in the presence of therapy that is considered inadequate to exert a significant influence on malignant disease [1-3]. For several types of cancer spontaneous regression of cancer has been reported [4]. There are 76 cases of spontaneous regression of thoracic malignancies described between 1951 and 2008 [5]. Most of these cases concerned metastatic disease of malignancies that originated outside the thoracic cavity such as renal cell carcinoma (60%), hepatocellular carcinoma, endometrial stromal sarcoma, pleomorphic liposarcoma, esophageal cancer and leiomyosarcoma [5]. Only a few case reports described spontaneous regression of primary thoracic malignancies [5-16]. Here, we report on a case of spontaneous regression of pathologically proven non-small-cell lung cancer (NSCLC).

Case Report

An 80-year-old male was referred to the chest physician in March 2014 with complaints of progressive dyspnea and anemia. He had lost 5 kgs of weight in the last months and also experienced pain in his right hip that radiated to his lower leg accompanied by muscle weakness. The patient had a smoking history of 65 pack years and a WHO performance score of 1. A CT-scan of the thorax/abdomen showed mediastinal and hilar lymphadenopathy, abdominal lymphadenopathy, a tumor in the left upper lobe and multiple pulmonary nodules in both lungs (Figure 1).

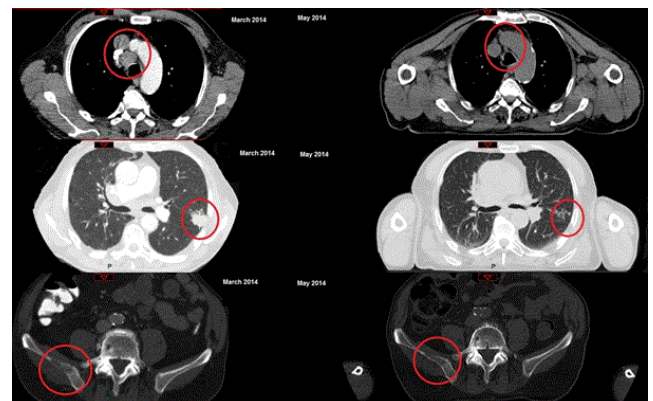


Figure 1: Left: diagnostic CT-scan March 2014; Right: Radiotherapy planning CT-scan May 2014; Top: mediastinal lymph node metastasis; Middle: primary lung tumor left upper lobe; Bottom: bone metastasis pelvis.

Furthermore, enlarged adrenal glands were seen on the CT-scan, and a small liver lesion in segment 4, suspect for metastasis. In the right ilium and 6th left costa, osteoblastic lesions suspect for bone metastases were visible (Figure 1). An MRI-scan of the lumbar-spine showed an abnormal signal in multiple corpora, suspect for metastases. Both fine needle aspirate of a pleural pulmonary nodule as well as a CT-guided biopsy of a lesion in the right ilium, were inconclusive. Endo-bronchial- ultra-sound (EBUS) fine needle aspiration of Naruke stations 4R and 7 showed atypical epitheloid cell groups highly suspicious of malignancy, compatible with a non-small cell lung carcinoma (Figure 2). There was not enough material however for immunocytochemical or molecular analysis. It was concluded that this patient had stage IV (cT2aN3M1b) NSCLC.

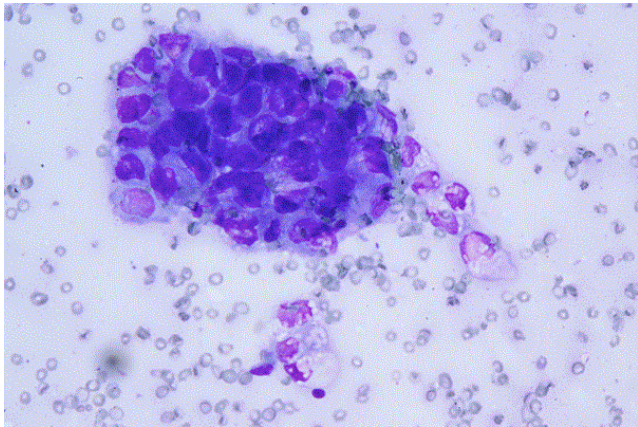


Figure 2: Tumor positive cytological findings from fine needle aspiration of Naruke station 4R and 7.

Following the multidisciplinary tumor board discussion, a palliative plan was established consisting of irradiation of the bone metastasis in the pelvis to relieve the pain, thoracic irradiation for prevention of a vena cava superior syndrome, and chemotherapy. However, at the first visit of the radiotherapy department the patient reported an improvement in shortness of breath and condition. Besides this, he had gained 3 kg of weight. The pain in his right leg and right pelvis however was still present. A new CT-scan, planned to prepare for the irradiation and performed 2 months after the diagnostic CT, showed a spontaneous regression of the enlarged mediastinal lymph nodes (Figure 1). The vena cava was no longer compressed and the pulmonary lung nodules completely disappeared. Also the primary tumor had decreased in size. The femoral head showed a pathological fracture. Due to the spontaneous regression of the pulmonary lesions the pathology report was reassessed which confirmed the initial diagnosis of a NSCLC. Finally it was decided to irradiate the right femoral head and ilium, with a single fraction of 8 Gray. A Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)-CT-scan showed further regression with residual scarring in the left upper lobe without any FDG uptake. The mediastinal lymph nodes demonstrated low FDG uptake (SUV max 3.1). The irradiated location of the fracture in right femoral head showed an increase of sclerotic tissue and FDG uptake. In costa 6 sparse uptake was seen. A follow up CT-scan, 4 months later, showed further regression of the lesion in left upper lobe and mediastinal lymph nodes. The pulmonary nodules had totally disappeared. The patient was in good condition and there were no pulmonary complaints or weight loss.

Discussion

Spontaneous regression (SR) of cancer is a rare phenomenon. The Everson and Cole review report 176 SR cases between 1900 and 1964 [17]. Challis and Stam updated that review to 489 cases in the period from 1900 to 1987 [4]. These case reports do not represent the true incidence of SR. Cole [18] estimated the incidence of SR to occur in 1 of 60.000 to 100.000 cancer individuals. However, most SR cases described, apparently occur in a few types of cancer: malignant melanoma, low-grade non-Hodgkin's lymphoma, renal cell cancer, chronic lymphocytic leukemia and neuroblastoma in children [4,17]. SR seems even more uncommon in NSCLC [4,5,17]. To our knowledge

only 15 cases of SR of NSCLC have been described in the literature [5-16]. The mechanisms for spontaneous regression are entirely hypothetical and the pathophysiology remains unclear. Associated mechanisms are immune response, tumor inhibition by growth factors and/or cytokines, apoptosis, differentiations, hormones, angiogenesis inhibition, telomerase inhibition and psychoneuroimmunological response [11]. In our case, the patient did not receive any treatment at the time of SR. Later on, radiotherapy was given for the bone metastasis, which might have further induced regression due to an abscopal effect [19] (A reaction produced following irradiation but occurring outside the zone of actual radiation absorption). A number of preclinical and clinical studies are ongoing to study the pro-immunogenic effects of local radiotherapy [20,21].

A limitation of this case report is that the diagnosis was based on a fine needle aspiration of mediastinal lymph nodes. There was no biopsy and not sufficient material for additional immunohistochemical or molecular analysis. We did not provide evidence of malignancy of the primary tumor in the left upper lung, nor the bone metastasis. However there was no doubt about the pathology diagnosis of NSCLC in the lymph nodes. The cause of the spontaneous tumor remission remains unknown in this case. Further studies are imperative to explain the underlying mechanism of SR.

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