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Spontaneous regression of FDG/PET positive lung adenocarcinoma in an elderly man

The authors declare do financial disclosure

Abstract

Spontaneous cancer regression, either partial or complete, is a rare phenomenon, particularly in patients with lung cancer. The present paper is the case report of an elderly lung cancer patient aged 80 who exhibited spontaneous regression of the primary lesion, without receiving any treatment. Spontaneous regression commenced two years after obtaining pathological specimens by transbronchial biopsy from the pulmonary lesion. It is interesting that the tumor lesion had a strong uptake (standardized uptake value max: 26.3) in ^{18}fluorodeoxyglucose positron-emission tomography before biopsy and that the regression occurred after a long interval after the biopsy, and that the regression developed in an elderly man. It is unknown why spontaneous regression was observed in this case and what kind of mechanism was involved in the phenomenon. Even in the elderly, as observed in our case, spontaneous regression can occur. The patient should be closely followed up to monitor the clinical course of such an unusual phenomenon.

Key words: spontaneous regression, FDG/PET, lung adenocarcinoma

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Introduction

In a variety of malignant diseases, among others in lung cancer, spontaneous regression has been reported [1, 2]. The conditions most commonly exhibiting this rare phenomenon include malignant melanoma, neuroblastoma and renal cell carcinoma [1, 2]. "The partial or complete disappearance of a malignant tumor in the absence of treatment or in the presence of therapy considered inadequate to exert a significant influence on the disease" is the standard definition of spontaneous regression [1]. As there is no consensus due to its rare occurrence, the distinct pathogenetic mechanism underlying spontaneous regression in malignant tumors remains unclear. We report herein a case of an elderly man with primary lung adenocarcinoma that showed ^{18}fluorodeoxyglucose (FDG) uptake on positron-emission tomography (PET), but its size was found to have reduced spontaneously in CT scan taken 27 months after the diagnosis of lung cancer.

Case report

An 80-year-old man with hypertension was referred to our hospital due to a mass incidentally noted on chest radiograph. The patient also had elevated serum level of carcinoembryonic antigen (CEA). The man was a heavy smoker, with past history of pulmonary tuberculosis at the age of 45. There was no recurrence of the disease after receiving the optimum duration of treatment of

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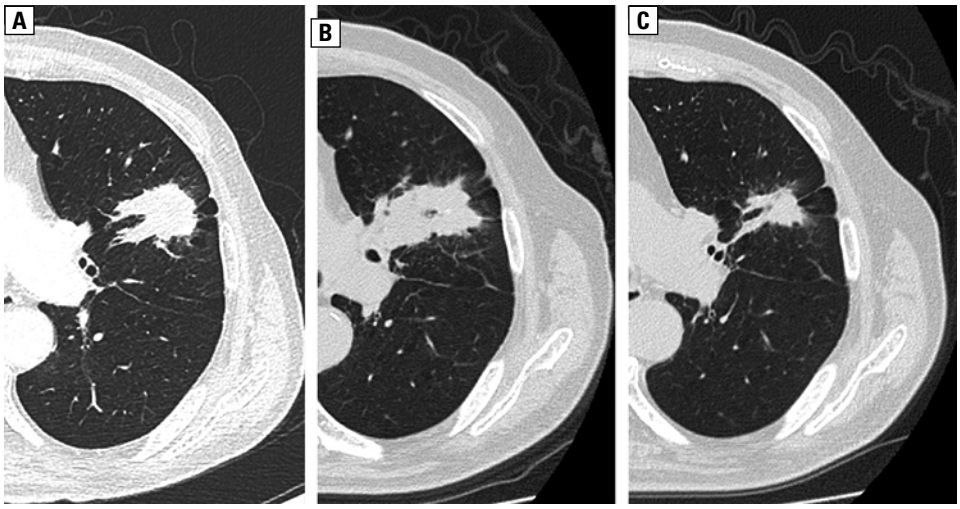

Figure 1. Chest CT scan at the time of the diagnosis of lung adenocarcinoma (A), chest CT scan taken 19 months after the diagnosis of lung adenocarcinoma (B), and spontaneous regression of the mass was identified on a chest CT scan 27 months after the diagnosis of lung adenocarcinoma (C)

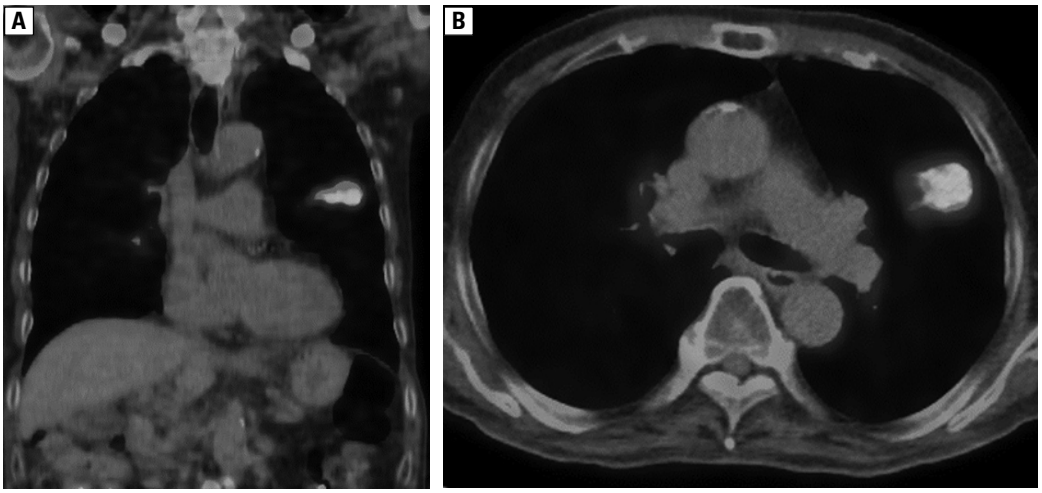

Figure 2. Positron emission tomography/computed tomography (PET/CT) showed 18F-fluorodeoxy glucose (FDG) uptake in the mass (standardized uptake value max: 26.3)

isoniazid, rifampicin, and ethambutol. At the first presentation, there was no remarkable finding in his physical examination but he had cognitive impairment. A chest CT scan revealed a mass lesion in the left upper lobe of the lung (Fig. 1 A). Positron emission tomography/computed tomography (PET/CT) showed 18F-fluorodeoxy glucose (FDG) uptake in the mass (standardized uptake value max: 26.3) (Fig. 2). The laboratory examination revealed a white blood cell count of 5,700/μl, a C-reactive protein level of 1.94 mg/dl, and elevated carcinoembryonic antigen (CEA) level of 22.1 ng/ml. Serum level of beta-D-glucan was within normal range. Serum *Aspergillus* antigen and *Candida* antigen were both negative. On the basis of the biopsy examination using the specimen obtained from the lesion by fiberoptic bronchoscopy, the mass lesion was thereafter diagnosed as pulmonary adenocarcinoma (Fig. 3A) without epidermal growth factor receptor (EGFR)-activating mutation or echinoderm microtubule-associated protein-like 4 (EML4)-anaplastic lymphoma kinase (ALK). The immunocytochemical expression of thyroid transcription factor-1 (TTF-1) (Fig. 3B), surfactant apoprotein A (SP-A), cytokeratin 7, and CEA all showed positive reaction. Neither inflammation nor direct neoplastic infiltration was found in bronchoscopy. There was no secretion suggesting inflammation. Tracheobronchial lavage fluid was negative for acid-fast stain, bacterial, fungal, and acid-fast culture, and PCR-negative for *Mycobacterium tuberculosis*, *M. avium*, and

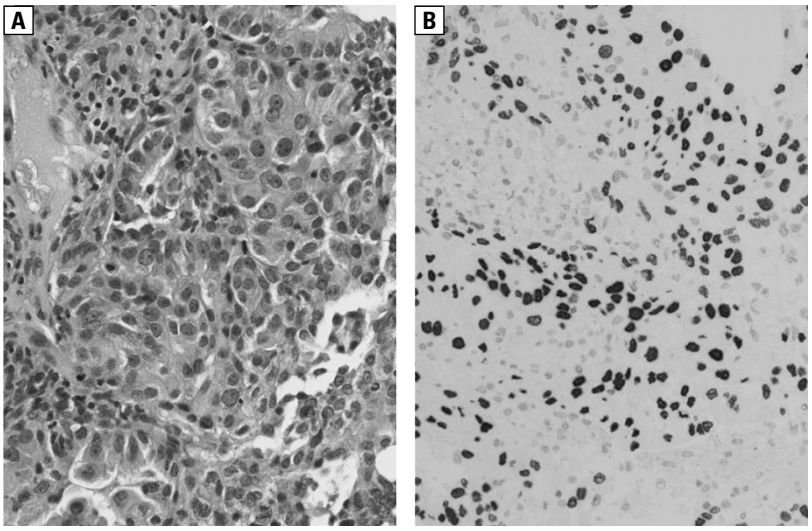

Figure 3. Biopsy specimen obtained from the lesion by fiberoptic bronchoscopy revealed that the mass lesion was diagnosed as pulmonary adenocarcinoma (**A**). The immunocytochemical expression of thyroid transcription factor-1 (TTF-1)(**B**)

M. intracellulare. The family of the patient did not want intensive therapy because of his age and impaired cognitive function, so he was followed up thereafter. Chest CT taken 19 months after the diagnosis of lung adenocarcinoma revealed progression of a mass lesion (Fig. 1B). But, spontaneous regression of the mass was identified on a chest radiograph and CT scan 27 months after the diagnosis (Fig. 1C). Now he is well and followed up for 31 months and further shrinkage of the lesion has been confirmed in chest radiograph.

Discussion

In line with a generally accepted definition, spontaneous regression of malignant disease is a complete or partial, temporary or permanent disappearance of all or at least certain relevant parameters of a soundly diagnosed malignant disease, without any medical treatment or with treatment that is considered inadequate to produce the resulting regression [1]. The present case may be classified as a partial spontaneous regression according to this definition. Everson *et al*. [1] reviewed only 176 cases of spontaneous regression between 1900 and 1964, with an estimated incidence of 1/60,000–100,000 cancer patients. Challis and Stam reported that 741 cases of spontaneous regression of malignant diseases were described in the literature between 1900 and 1987 [2]. Although spontaneous regression has been reported in various malignant diseases [2]. Despite its incidence in a variety of malignant disorders, spontaneous regression in lung cancer is considered to be a particularly rare event [1–10]. There have been some reports on spontaneous regression of FDG/PET positive tumors [10–13]. All of them concerned patients with hematological malignancies [11–13] except for one patient with lung cancer [10]. In this lung cancer patient, squamous cell carcinoma was confirmed pathologically by surgical resection performed several months after PET/CT scan [10].

Regarding the regression seen on the imaging in the described patient, the important point is how we prove that it was not caused by the remission of inflammation. We consider the following six facts as the grounds that inflammation is not involved in spontaneous regression in this patient, 1) there were no clinical symptoms suggesting involvement of inflammation throughout the clinical course, 2) there were no serological and bacteriological data suggesting involvement of inflammation throughout the clinical course, 3) there was no findings suggestive of inflammation in bronchoscopical examination, 4) there was no inflammatory cell infiltration in the biopsy specimen from the lesion, 5) There was no need for antibiotic administration to shrink the tumor, and 6) there was a shrinkage in the part of the tumor where FDG/PETCT scan was positive. We previously reported two patients aged 74 and 65, both of them had lung adenocarcinoma, exhibiting spontaneous regression [3, 4]. In the first case, spontaneous regression of the scalp metastatic lesion developed after 1 month following biopsy of the scalp mass and the regression of the primary lung lesion also developed 1 month after a transbronchial biopsy [3]. In the second case, spontaneous regression occurred not only

in metastatic lesion of the cervical lymph nodes, but also in the primary lung lesion 1 month after obtaining the pathological specimens [4]. It is noteworthy that, in these two patients, spontaneous regression developed shortly after a direct invasive approach to the tumor lesions, which is highly suggestive of an association between the onset of the regression and a change in the intratumoral immunological mechanism between the host and the tumor. The likely explanation is that there may be a stimulus associated with the direct invasive approach to the lesions, which initiates the spontaneous regression. In the present case, spontaneous regression developed 27 months after a direct invasive approach to the primary lesion, which was apparently different from the two previous patients we encountered. Therefore, it is suggested that a mechanism different from "a stimulus associated with the direct invasive approach to the lesion" is involved, but what mechanism, it is beyond our knowledge at present.

Regarding spontaneous regression, it is suggested that some immune mechanism is involved [14]. Immune checkpoint inhibitors have become available in clinical practice, there is particular interest in tumor regression due to the involvement of immune mechanisms. The precise mechanism of spontaneous regression remains unclear and future studies are required to elucidate this process. Although very rare, there have been six case reports which showed spontaneous regression in lung cancer patients over the age of 70 [3, 5–9]. The eldest one was a 84-year-old female NSCLC patient [7]. A later report may reveal the causes and broaden the knowledge regarding this uncommon phenomenon. Even in the elderly, as observed in the previous case reports and ours, spontaneous regression can occur. The patient should be closely followed up to monitor the clinical course of such an unusual case.

Conflict of interest

The authors declare no conflict of interest.

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