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CASE REPORT

Spontaneous regression of non-small cell lung cancer that progressed after multiple chemotherapies: A case report

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Abstract

Spontaneous regression (SR) of cancer is defined as a complete or partial, temporary or permanent disappearance of all or at least some relevant parameters of malignant disease with inadequate or no treatment. SR of cancer is an extremely rare phenomenon. We report a case of a 67-year-old man who experienced SR of non-small-cell lung cancer (NSCLC), which progressed after fifth-line chemotherapy and regressed after chemotherapy ceased. Surprisingly, the primary tumor size continued to decrease for more than 13 months and his general condition markedly improved after discontinuation of the chemotherapy. To our knowledge, this is the first report of SR in a patient with NSCLC that was not responsive to a fifth round of chemotherapy.

Introduction

In general, cancer progresses rapidly after the failure of previous chemotherapy. However, it is true that spontaneous regression (SR) of cancer occurs very rarely. The definition of SR of cancer is a complete or partial, temporary or permanent disappearance of malignant disease with inadequate or no treatment.[1] The incidence of SR is about one in 60 000 to 100 000 patients with cancer.[1–3] There are several case reports describing SR of various cancers, including renal cell carcinoma, leukemia/lymphoma, malignant melanoma, and neuroblastoma. The incidence of SR of advanced non-small-cell lung cancer (NSCLC) is relatively low; about 20 cases were reported from 1950 to 2004.[1–3] Interestingly, the majority of SR of NSCLC cases involved squamous cell carcinoma, and most reports showed SR of advanced NSCLC with no treatment.[4,5] We report a case of SR of advanced squamous cell lung cancer that progressed after a fifth round of chemotherapy, regressed after interrupting the chemotherapy, and maintained SR for over 13 months.

Case report

A 67-year-old male patient with a right middle lobe (RML) mass was referred to the pulmonary department (Fig 1a). Chest computed tomography (CT) showed multiple small nodules in both lower lung fields (Fig 1b) and a right adrenal gland mass, suggesting metastasis (Fig 1c). Bronchoscopic biopsy showed squamous cell carcinoma expressing p63 (Fig 1d–f). A positron emission tomography (PET)-CT scan also showed lung to lung and adrenal gland metastases, but the standardized uptake value (SUV) of the RML mass was about 2.2 (Fig 2a). The patient was finally diagnosed as stage IV (T4N0M1b) lung squamous cell carcinoma and began first line platinum-based combination chemotherapy using gemcitabine. The tumor size decreased after chemotherapy (Fig 2b) and progression-free survival (PFS) was 23 months. Second-line treatment commenced with gefitinib and PFS was seven months. The lung lesion progressed again and the patient underwent third-line chemotherapy with weekly docetexel. After nine cycles of docetaxel monotherapy, the

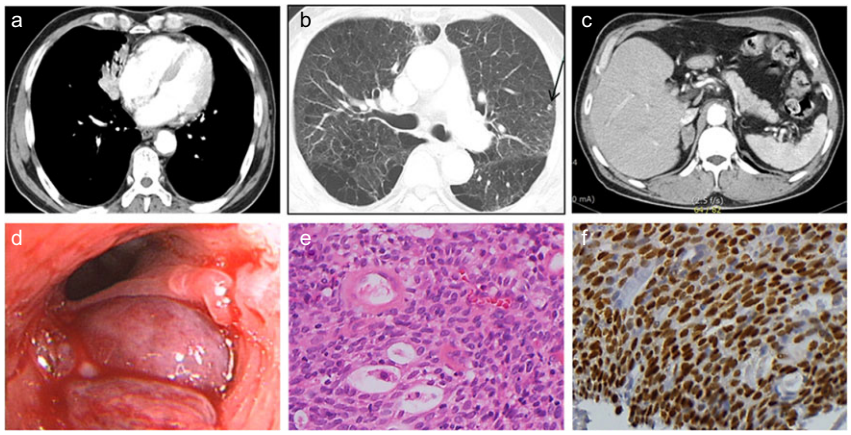

Figure 1 (**a**) Initial chest computed tomography revealed a right middle lobe (RML) mass. (**b**) Multiple non-calcified nodules in the superior and basal segment of both lower lobes, suggesting metastasis (arrow). (**c**) Bulging contoured mass of right adrenal gland. (**d**) Bronchoscopy showed endobronchial mass on RML. (**e**) Bronchoscopic biopsy specimen showing non-small-cell lung cancer, specifically squamous cell carcinoma (hematoxylin-eosin, original magnification ×400). (**f**) Immunohistochemistry revealed that the bronchoscopic biopsy specimen expressed p63 (original magnification ×400).

tumor progressed and he was treated with weekly vinorelbine as fourth-line chemotherapy. For five months, the status of the NSCLC was stable (Fig 2e). After five months the tumor progressed once more and we considered close observation and supportive care, but the patient was willing to undergo treatment with chemotherapy if possible. We decided to retreat him with platinum-based gemcitabine combination therapy because this combination effectively controlled the tumor for 23 months during the first-line chemotherapy. Unfortunately, the chemotherapy was ineffective and a follow-up chest CT after two cycles of chemotherapy showed disease progression (Fig 2c). He finally decided to discontinue treatment and was followed-up regularly in our outpatient department.

Four months after the cessation of chemotherapy, the patient's chest X-ray unexpectedly showed that the main mass had decreased in size. Chest CT also revealed that the mass size had decreased from 7.1 × 5.0 cm to 6.5 × 5.0 cm (Fig 2e). After seven and 10 months of follow-up, chest CT revealed that the mass had continued to significantly decrease in size. Three months later, a PET-CT scan showed no gross interval change in the size of the RML mass (Fig 2d).

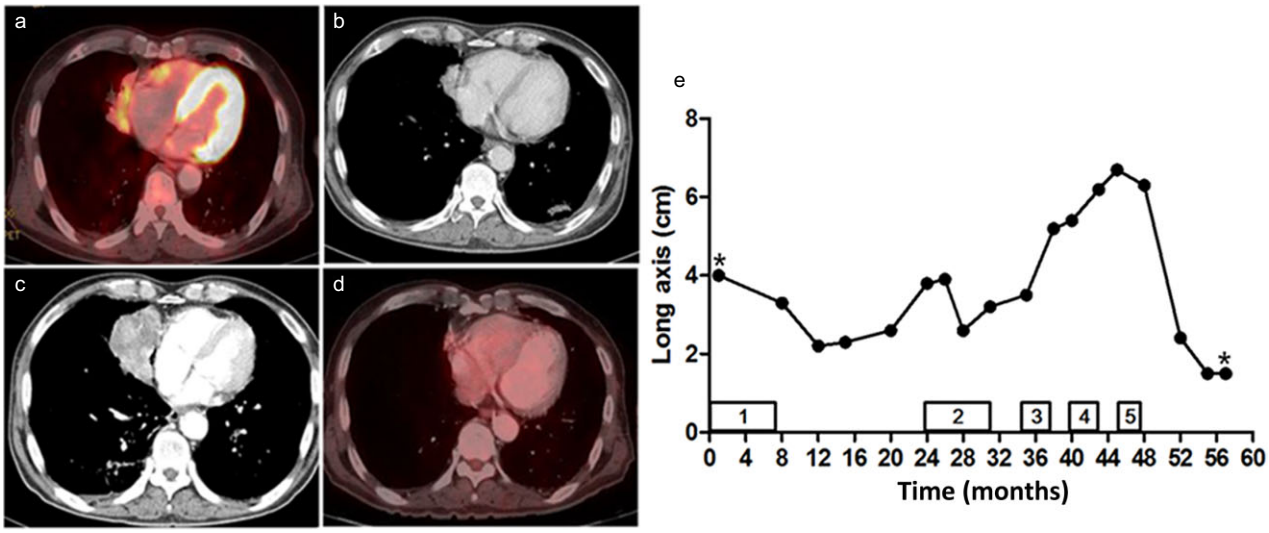

Figure 2 (**a**) Initial positron emission tomography-computed tomography (PET-CT). (**b**) Follow-up chest CT after first line chemotherapy. (**c**) Follow-up chest CT after fifth line chemotherapy. (**d**) PET-CT performed 13 months after discontinuing chemotherapy. (**e**) The course of the long diameter of the tumor during treatment and observation. Asterisks denote the dates of PET-CT. The number of boxes indicates the order of chemotherapy regimens; 1. combination of cisplatin and gemcitabine; 2. gefitinib; 3. docetaxel; 4. vinorelbine; and 5. combination of carboplatin and gemcitabine.

Discussion

Spontaneous regression of cancer is an exceedingly uncommon phenomenon, even rarer in lung cancer. Almost all case reports describe SR of an untreated lung cancer.[3,6] However, we herein report the SR of intractable NSCLC treated with five chemotherapy protocols. To our knowledge, this is first case report to describe SR of NSCLC that was treated with multiple chemotherapies and regressed after interrupting the chemotherapy regimen.

With respect to the mechanisms of SR of cancer, several theories have been proposed to induce SR.[2,4,5] Immunologic modulation is often thought to play an important role in SR through mediating T-cell activation and release of cytokines, such as interleukin-2.[7] There are three case reports of SR of small cell lung cancer patients with paraneoplastic antineuronal antibodies.[8]

Hormonal mechanisms related to pregnancy and oophorectomy have been suggested to act as mediators of SR in breast and ovarian cancers.[9,10] Apoptosis, induction of differentiation, and angiogenesis inhibition have also been implied to be involved in SR of cancer.[1] Discovery of the mechanism of SR and characterization of SR patients will have a significant impact on the concept of cancer.

Our patient had relatively longer PFS than the median PFS of NSCLC patients.[11] The Ki-67 index of specimen was less than 5% and the SUV of the mass was not significantly increased at the initial or last follow-up. Some reports demonstrate that SUV has a strong correlation with lung cancer proliferation and the prognosis of NSCLC.[12,13] We speculate that slow proliferation and low glucose metabolism contributed to the long PFS and SR phenomenon of this case.

The patient advised that he often took several kinds of herbs during chemotherapy and also after treatment. However, in our experience, few patients' condition improved with the use of herb medications.

Discontinuation of chemotherapy because of tumor progression usually leads to very rapid tumor advancement. In this case, however, the tumor continued to decrease for more than 13 months after the cessation of chemotherapy. This case report implies that even intractable NSCLC can spontaneously regress.

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Disclosure

No authors report any conflict of interest.

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