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Case Report

Resolution of atelectasis during radiochemotherapy of lung cancer with serious implications for further treatment. A case report

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ABSTRACT

Local failure is a major cause for low overall survival rates in advanced non small cell lung cancer (NSCLC). Among others, radioresistant tumor clones as well as geographical miss can explain these high local failure rates. One reason for geographical miss is a change of tumor related atelectasis in the course of radiotherapy. We present the case of a patient with UICC Stage IIIb NSCLC who presented with a large tumor related atelectasis. During definitive radiochemotherapy, the atelectasis resolved, which resulted in a massive tumor shift out of the planning target volume within 2 days. Without close monitoring by cone beam CTs and prompt replanning, this would have led to a geographical miss and relevant underdosage of the tumor. Furthermore, changes in anatomy and pulmonary function during treatment had implications for organs at risk and opened windows for dose escalation.

We suggest at least biweekly CBCTs in patients with poststenotic atelectasis to ensure the rapid detection of geographical changes of the target and subsequent intervention if necessary.
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Introduction

In non-small cell lung cancer (NSCLC), local failure after definitive radiochemotherapy is frequent and has significant implications on overall survival [1]. In contemporary series, local failures were seen in 30–40% [2]. While this high incidence clearly reflects the biological aggressiveness of the disease, geographical misses also contribute to local failure. Besides respiratory motion, the majority of geographic uncertainty is caused by anatomical changes such as tumor regression and baseline shifts [3]. Schmidt et al conclude that anatomical changes during chemoradiation of advanced NSCLC have a greater impact on the radiation dose applied to the tumor than respiratory motion [4]. Another source of geometric changes that might result in inferior treatment outcome is the development or resolution of atelectasis [4,5].

Herein, we present a case of a patient with UICC stage IIIb NSCLC treated with definitive chemoradiation, with a resolving atelectasis during radiotherapy and subsequent implications for target volume coverage, pulmonary function and doses to organs at risk.

Case

In December 2016, a 58-year-old patient with a history of heavy smoking (40 pack years) presented with dyspnea, productive cough and yellow sputum. Clinically, pneumonia of the upper left lobe was diagnosed and confirmed by chest X-ray. Despite antibiotic treatment, the pneumonia persisted clinically and on X-ray, prompting further investigation by cross sectional imaging. CT showed a mass obstructing the lingula segment as well as enlarged mediastinal lymph nodes (Figs. 1a and 1b). On bronchoscopy, an exophytic tumor that completely obstructed the lingula segment was seen. The lingula could not be recanalized by bronchoscopy. Histologically a squamous cell carcinoma of the lung was diagnosed. Subsequently, whole body FDG-PET-CT scan displayed no further metastases. Taken together with the histological findings of a mediastinoscopy, staging examinations resulted in NSCLC UICC Stage IIIb (cT3 pN2 cM0). The pulmonary function tests (PFT) of the patient showed signs of a restrictive lung disease with a forced expiratory volume in one second (FEV1) of 1.6 litre and also a limited diffusion capacity (DLCOc 69%). The multidisciplinary tumor board recommended a definitive radiochemotherapy approach.

A total dose of 64 Gy in 2 Gy fractions was prescribed concomitantly with two cycles of chemotherapy (Cisplatin 80 mg/sqm on d1 and Vinorelbin 20 mg/sqm on d1 and d8). Treatment planning with intensity modulated radiotherapy was based on a 4D CT scan and showed a large tumor related atelectasis in the anterior part of

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the left upper lobe that had evolved in the meantime. The tumor showed no significant respiratory movement. Due to the limited pulmonary function, an involved field strategy was used for treatment planning with only very limited elective volumes included in the target volume. For the latter 45 Gy were prescribed. A margin of 10 mm was added to the GTV to account for daily geographical uncertainties and microscopic disease.

Combined modality treatment was well tolerated apart from CTCAE grade three leukopenia after the first cycle of chemotherapy prompting no further intervention. During the fourth week of treatment at a dose of 32 Gy, cone beam CT (CBCT) showed that the atelectasis of the left upper lobe had almost completely resolved within one day, resulting in a massive tumor shift with insufficient coverage by the planning target volume. While the tumor was initially located at the level of the aortopulmonary window, it had moved caudally towards the ventricle after resolution of the atelectasis (Fig. 1c–e). The tumor had almost completely moved out of the planning target volume, which would have resulted in a target miss at subsequent treatments. Therefore, next day, a repeat 4D CT for plan adaptation was carried out, furthermore PFT were repeated. Due to the re-ventilation of the previously atelectatic lung tissue, total lung capacity had increased by 15% and the FEV1 had increased by approximately 10% to 1.87 litre compared to the initial pulmonary function test. The change in anatomy had significant implications on cardiac dose with a mean heart dose that increased from 14.7 Gy with the initial anatomy to 18.5 Gy after the tumor shift. In the absence of cardiac comorbidities this increase was not dose limiting. At the same time, the impact of the new anatomy on lung DVH parameters was marginal (Fig. 2c). Since the pulmonary function had improved and had previously been considered dose limiting, a higher dose than initially planned was discussed, which was declined by the patient. Hence,

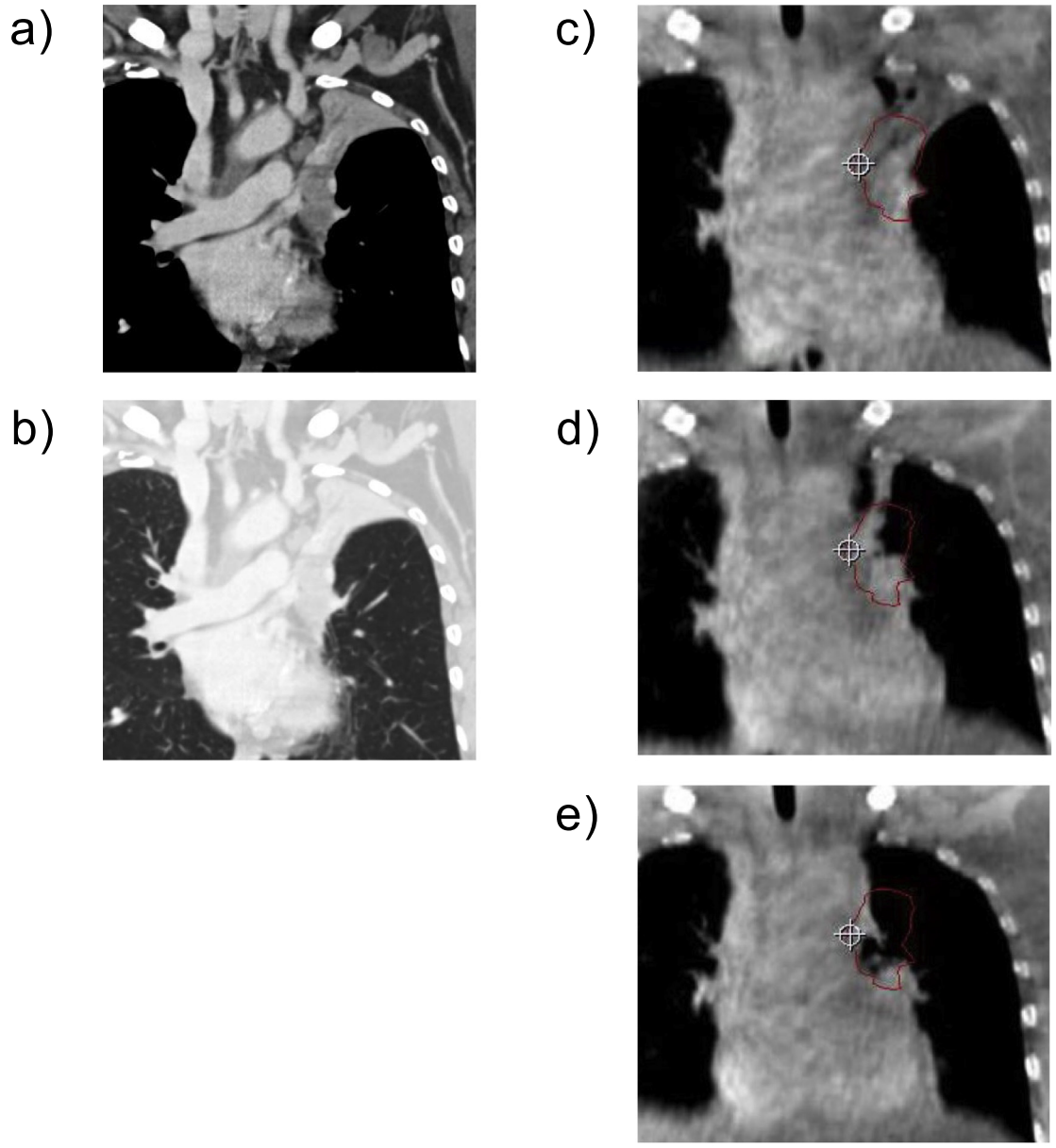

Fig. 1. Contrast enhanced CT images before radiochemotherapy with mediastinal (a) and lung windows (b) and cone beam CTs acquired at 30 Gy (c), 32 Gy (d) and 34 Gy (e). The red contour represents the site of the GTV at the planning CT. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

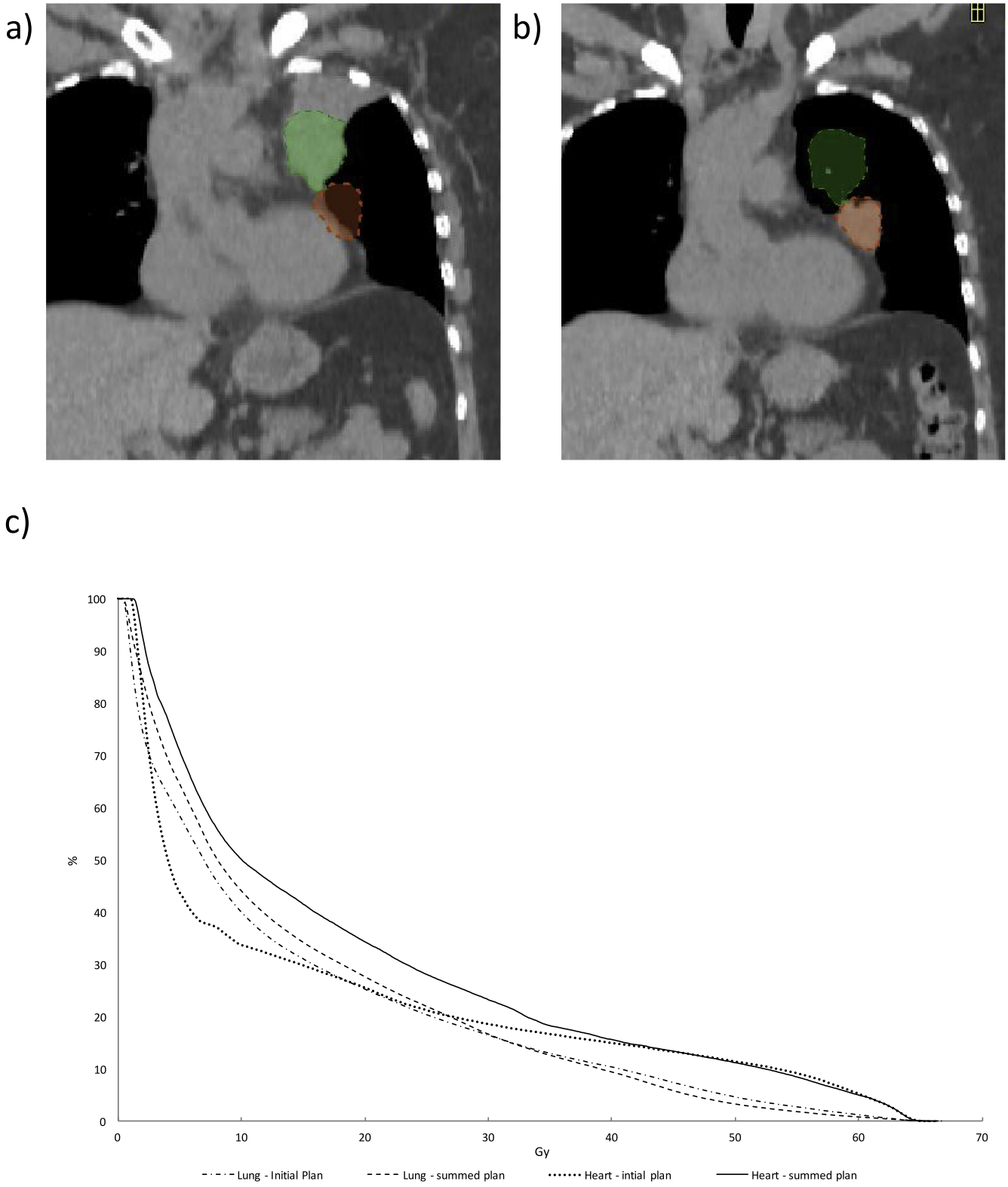

Fig. 2. Relevant shift of tumor location from initial planning CT (a) to repeated imaging at a dose of 34 Gy (b). The atelectasis is no longer visible. The primary tumor site at planning CT is depicted in green, the tumor site at 34 Gy in red. The new anatomy resulted in a relevant increase in cardiac dose without affecting lung dose-volume histogram parameters (c). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

treatment was terminated after a total dose of 64 Gy and one cycle of chemotherapy. The second cycle of chemotherapy was omitted due to previously described leukopenia. No further toxicity higher than CTCAE grade II was observed.

Conclusion

With an incidence of 10–40%, atelectasis is a common phenomenon associated with advanced lung cancer [3,6–9]. For

treatment planning as well as the realization of radiotherapy, several challenges are linked with atelectasis. Even on contrast enhanced planning CT scans, delineation of gross tumor volume can be demanding. Hence, a PET-CT scan might be helpful for the planning process, even more as this has been shown to reduce the differences in the inter-observer GTV delineation [10–13]. Furthermore, and as in this case, the resolution of the preexisting atelectasis had serious implications for further treatment: First, plan adaptation can rapidly be needed to ensure sufficient target coverage. Second, the new anatomy can require a re-appraisal of the doses applied to organs at risk and third, the improvement in pulmonary function opens a window for higher doses to the target volume [3,7,14]. Finally, mass and density changes caused by reinflation of atelectatic lung tissue can cause unpredictable dosimetrical changes [14]. This might result in serious toxic side effects since in the treatment of advanced NSCLC, the dose constraints to organs at risk often are the main dose limiting factor [4,5].

A recent study by Moller et al. showed that in the evaluation of daily CBCTs of 163 patients treated for lung cancer, 9% experienced a relevant tumor shift, and 12% would have benefitted of replanning [7]. The most common reason for replanning was a change in tumor-related atelectasis [7]. Recently, a similar case report on a patient with stage I NSCLC and associated segmental atelectasis, treated with SBRT, has been published by Mao et al. After the delivery of a single daily dose of 5 Gy, a segmental atelectasis had resolved and led to a tumor shift by 15 mm resulting in the need of plan adaptation to ensure tumor coverage in the subsequent 4 fractions [15]. In our opinion, these reports together with ours emphasize that the development and resolution of atelectasis during treatment might be an underestimated problem. Since the resolution can happen within very few days, we suggest CBCTs at least twice weekly to ensure timely detection of relevant changes [9].

To summarize, as shown in this case, anatomical changes of the target volume due to changes of atelectatic lung tissue is a phenomenon which can have detrimental consequences for the patients by missing the target and administering doses exceeding the limiting constraints to the organs at risk. Especially in patients with tumor related atelectasis, particular attention should be paid to detect relevant anatomical changes of the target volume as early as possible.

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Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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