Acute and Progressive Tracheal Stenosis after Proton Beam Therapy with Concurrent Chemotherapy for Non–Small Cell Lung Cancer

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Case Presentation

A 53-year-old never-smoking woman with abnormal findings on the chest radiograph was referred to our hospital. Computed tomography of the chest revealed a mass in the left lower lobe, and 2-[^{18}F]-fluoro-2-deoxy-D-glucose positron emission tomography showed a metabolically active mass in the left lower lobe and uptake in the mediastinal lymph nodes (1R, 2R, 4R, and 11L according to the International Association for the Study of Lung Cancer map). The patient was diagnosed with stage IIIB (cT2aN3M0 according to the TNM classification, seventh edition) adenocarcinoma of the lung. In this case, on account of the extensive locoregional involvement, treatment planning for definitive conventional photon radiotherapy indicated excessive doses to the organs at risk, including the normal lung and spinal cord. Therefore, the patient was administered proton beam therapy (PBT) with 4-week cycles of concurrent cisplatin (80 mg/m^2 on day 1) and vinorelbine (20 mg/m^2 on days 1 and 8). PBT was administered five times per week at a planned total dose of 60 Gy-equivalents in 30 fractions consisting of elective nodal irradiation of up to 40 Gy-equivalents, followed by boost therapy to the primary tumor and metastatic lymph nodes. The color wash dose distribution of PBT is shown in Figure 1.

Radiological evaluation after PBT with concurrent chemotherapy revealed 21% tumor shrinkage; however, 3 months after completion of treatment the patient presented with progressively worsening cough and dyspnea. Computed tomography and bronchoscopic examination revealed severe tracheal stenosis

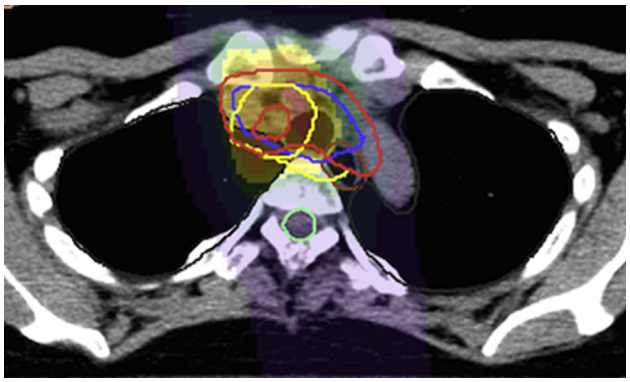

Figure 1. Dose distribution of proton beam therapy to the metastatic mediastinal lymph nodes and trachea. Each color wash isodose in orange, yellow, green, and purple represents 100%, 90%, 50%, and 20% of the total prescribed dose, respectively.

(Figs. 2*A*, *C*, and *E*), and the results of biopsy of specimens from the stenosed area were negative for tumor cells. Then, a meticulous review of the dose distribution in the PBT planning was performed retrospectively;

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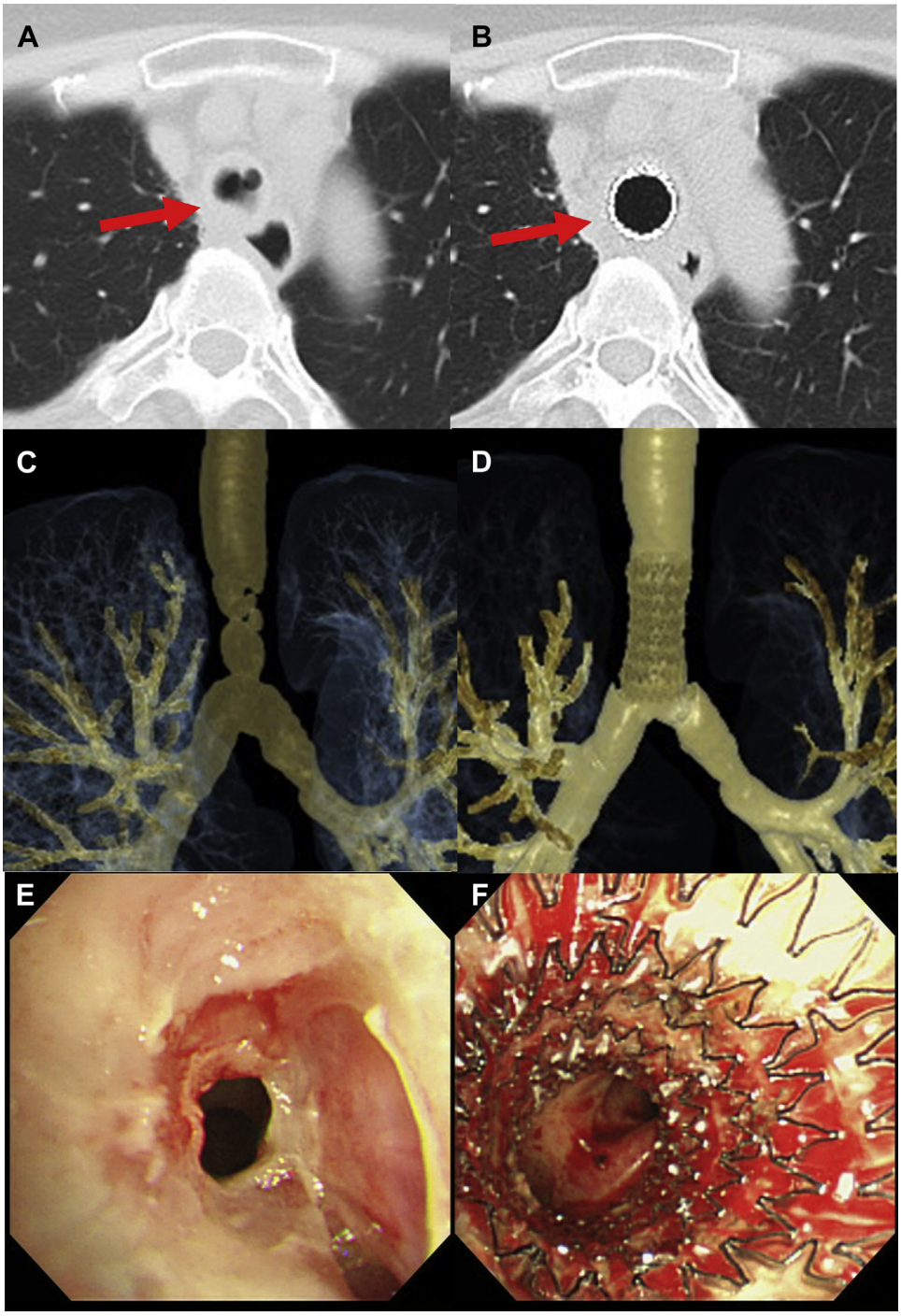

Figure 2. (*A*) Chest computed tomography (CT) image showing the tracheal stenosis before stenting (*arrow*), (*B*) chest CT image showing improvement of the tracheal stenosis after stenting (arrow), (*C*) three-dimensional CT coronal reconstruction image before stenting, (*D*) three-dimensional CT coronal reconstruction image after stenting, (*E*) bronchoscopic view of the trachea showing the stenosis, and (*F*) bronchoscopic view of the trachea after stenting.

however, evaluation of the dose to the trachea using the two-calculation method, a pencil beam, and the Monte Carlo algorithm did not reveal any hot spots (i.e., any areas irradiated with an unexpectedly high dose) in the organ. Stent placement was performed to alleviate the severe tracheal stenosis. A fully covered hybrid stent (Aero Stent, Merit Medical Endotek, South Jordan, Utah) was placed after balloon dilatation of the stenotic trachea under intravenous deep sedation (Figs. 2*B*, *D*, and *F*). Placement of the stent resulted in a dramatic improvement of the respiratory symptoms with no local relapse near the trachea.

Comments

Chemoradiotherapy is the standard treatment for patients with inoperable locally advanced non–small cell lung cancer. PBT, through its characteristic Bragg peak, has the potential to decrease unintended doses to the surrounding normal organs and provides a better dose distribution than photon radiotherapy.[1] Actually, our patient reported here was not a suitable candidate for photon radiotherapy. Compared with during photon radiotherapy, the doses to deeply located structures including the spinal cord, esophagus, lung, and heart are reduced in PBT. In contrast, the surface doses tend to be higher in PBT than in x-ray therapy because of the absence of buildup. Sejpal et al. reported increased skin reactions in patients with non–small lung cancer who received PBT.[2] They postulated that the increased surface dose to the skin may have contributed to the high incidence of dermatitis. The trachea is an air passage lumen, and its internal wall is lined by respiratory mucosa. Excessive doses to the trachea or bronchi sometimes cause necrosis of the trachea or bronchi; however, stenosis has been considered a late effect of radiation. In the current case, progressive stenosis occurred as early as 3 months after treatment. We reviewed the dose distribution of PBT; however, no hot spots or unintended high-dose areas were identified around the trachea or bronchi. The exact reason for the tracheal stenosis remains unclear, although we speculate that irradiation of the entire trachea might have resulted in an unexpectedly increased local effect on the respiratory mucosa, causing prolonged inflammation and subsequent stenosis of the organ. This is an issue of concern not only in PBT, but also in photon radiotherapy. In addition, occurrence of unexpected interaction between the PBT and chemotherapeutic agents causing increased local effects cannot be excluded. We succeeded in rescue stent placement for the tracheal stenosis after PBT; thus, stent placement should be considered an option for severe tracheal stenosis after PBT or photon radiotherapy with concurrent chemotherapy.

Acknowledgments

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