Photodynamic therapy for pulmonary mucoepidermoid carcinoma

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ABSTRACT

Pulmonary mucoepidermoid carcinoma (PMEC) are rare, accounting for 0.1–0.2% of all malignant lung tumors. Furthermore, endobronchial lesions are rare and are more commonly found in the segmental or lobar bronchi. We present, to the best of our knowledge, the first case of successful treatment with photodynamic therapy (PDT) for PMEC. A 77-year-old male presented with cough and hemosputum for 4 months. Chest computed tomography showed a mass in the right intermediate bronchus. Endobronchial biopsy revealed a diagnosis of PMEC. An optimal surgical technique to preserve respiratory function was desirable as most of the tumor emerged from the bronchial glands in the central airways and was of low-grade type. Hence, PDT was performed. Repeat bronchoscopies were performed 5 years after the PDT and showed no evidence of tumor recurrence. PDT is more likely to be effective for low-grade PMECs that are visible on bronchoscopy.

1. Introduction

Pulmonary mucoepidermoid carcinoma (PMEC) are mucus-secreting squamous epithelial intermediate tumors characterized by a combination of cell types and are defined as either low- or high-grade [1,2]. Usually, the treatment of central-type PMEC entails sleeve lobectomy or bronchoplasty. In this article, we report a new modality, bronchoscopic photodynamic therapy (PDT), for the treatment of PMEC. To the best of our knowledge, this is the first report of the use of PDT for PMEC.

2. Case report

The patient was a 77-year-old male who was referred to our hospital for PDT after recurrence of PMEC. The patient, who had a heavy smoking history, had initially presented with continuous cough and blood in the sputum for 4 months. Chest radiograph and computed tomography (CT) revealed a polypoid mass in the right intermediate bronchus without atelectasis. Bronchoscopy revealed a protuberant 2.0-cm tumor in the intermediate bronchus (Fig. 1A). The tumor cells were alveolar, sheet-like, densely proliferated, and had round, relatively aligned nuclei. Mucus-producing cells proliferated while forming ducts of various sizes. The patient was diagnosed with low-grade mucoepidermoid carcinoma (MEC). 18F-fluorodeoxyglucose positron emission tomography/computed tomography (F-FDG PET/CT) was performed, which revealed no intense FDG uptake in the polypoid mass or the mediastinal lymph nodes. Bronchoscopy revealed a protuberant 2.0-cm tumor in the intermediate bronchus (Fig. 1A). The tumor cells were alveolar, sheet-like, densely proliferated, and had round, relatively aligned nuclei. Mucus-producing cells proliferated while forming ducts of various sizes. The patient was diagnosed with low-grade mucoepidermoid carcinoma (MEC).

18F-fluorodeoxyglucose positron emission tomography/computed tomography. (18F-FDG PET/CT) was performed, which revealed no intense FDG uptake in the polypoid mass or the mediastinal lymph nodes. Bronchoscopy demonstrated a polypoid tumor arising from the right intermediate bronchus. The tumor was resected using a high-frequency electrosurgical snare and bronchoscopic neodymium yttrium aluminum garnet (Nd-YAG) laser surgery in another hospital (Fig. 1B). Recurrence of the tumor was observed on a CT scan of the chest 6 months after surgery, and the patient was referred to our hospital for PDT (Fig. 1C).

We re-assessed the patient at our hospital using white-light and autofluorescence bronchoscopy. The tumor was present in the same place (1.0 cm in diameter) in the intermediate bronchus (Fig. 1D). We performed re-biopsy. The tumor consisted of both mucus-producing cells and non-mucus-producing cells. The non-mucus-producing cells were positive for 34 beta E12 and showed nuclear staining of p63; therefore, the...
diagnosis was recurrence of MEC (Fig. 2). The clinical stage was deemed IA1 (T1aN0M0) after histopathological examination. We decided to perform PDT in this case because the complete response rate of centrally located lung cancers ≤1.0 cm in diameter has been reported to be 94% (66/70) with N-aspartyl chlorin e6 (NPe6)-PDT [3].

2.1. Photosensitizer and laser unit

NP6 (talaporfin sodium, Laserphyrin, Meiji Seika, Tokyo, Japan), which is a second-generation water-soluble photosensitizer with a molecular weight of 799.69 g/mol and a chlorine annulus, was used. It has wavelengths of 407 nm and 664 nm at the greatest absorbing peaks. We used 664-nm diode continuous-wave lasers (SAFE-3000, Matsushita Electric Industrial Corporation, Osaka, Japan) to excite Laserphyrin.

2.2. Treatment protocol

First, we administered Laserphyrin (40 mg/m²) intravenously. Four hours after administration of Laserphyrin, we administered local anesthesia with 4% xylocaine, inserted a fiber similar to bronchofiberscopy and performed PDT (Fig. 3A). We irradiated the tumor with a bronchoscope using a 664-nm laser and a directional quartz fiber (with straight-type power density, 150 mW/cm²; energy level, 100 J/cm²). The straight tip of the quartz fiber was maintained at a distance of 1–2 cm from the lesion and the surface was irradiated.

Repeat bronchoscopies were performed at 1, 3, and 6 months, and 1, 2, 3, 4, and 5 years after the PDT, and showed no evidence of tumor recurrence (Fig. 3B).

3. Discussion

PMEC constitutes only 0.1–0.2% of primary lung cancers and is a rare tumor. PMEC is morphologic and is classified based on histology into low- and high-grade groups, according to the 2015 World Health Organization classification [4]. PMEC was first described as a subtype of bronchial adenoma in 1952 by Smetana [5]. MECs consist of a varied mixture of cells and goblet cells secreting viscous liquid with a column and secrete mucus. Furthermore, they are characterized by a combination of intermediate cell types with myxopoiesis, a gland, and squamous epithelial cells. Qiu et al. examined the survival rates of 585 PMEC patients. The 5-year cancer-specific survival (CSS) rate of stage I-II PMEC patients was 91.4%. The 5-year CSS rate for patients with stage III-IV PMEC was 32.1%. The survival curves showed that older age, larger tumor size, lower differentiation, and higher Tumor-Node-Metastasis stage were associated with significantly worse prognosis [6].

Surgical resection is the standard therapy for patients with PMEC, and in recent years, this surgery has often been performed by video-assisted thoracoscopic surgery [7]. In addition, resection based on bronchoplasty or sleeve lobectomy for preservation of pulmonary function is also performed. The 3-, 5-, and 10-year survival rates are 94%, 88% and 88%, respectively, and low-grade MECs generally have a good prognosis. However, high-grade MECs have a much poorer prognosis, and the rate of recurrence after surgery is 25% [8]. Non-surgical treatments for non-small cell lung cancer include chemotherapy and...
Fig. 2. A, B: Histopathological findings of the tumor. The tumor is composed of squamous, mucous, and intermediate cells, with no clear findings of mitosis or necrosis. C, D: Immunostaining showed that the non-mucus-producing cells were positive for 34βE12 and showed nuclear staining of p63.

Fig. 3. A: Photodynamic diagnosis with the SAFE-3000 before photodynamic therapy. B: No evidence of tumor recurrence 5 years after photodynamic therapy.
molecular-targeted drugs. However, while the combination of carboplatin and paclitaxel has been reported to be effective, there is no evidence of efficacy or guidelines for chemotherapy for PMEC [9]. Interestingly, a few cases of PMEC with minor EGFR mutations (e.g., L861Q) have been identified in Asian populations [10]. However, the mutational status of these driver genes in PMEC is not well-understood.

Three cases of endoscopic MEC removal have been reported, but follow-up was not possible in two cases, and one patient with recurrence after 2.5 years overlooked the symptoms [11]. The recently introduced bronchoscopic Nd-YAG laser surgery facilitates complete removal of the tumor with control of bleeding. Furthermore, Li et al. reported that Nd-YAG laser surgery was effective for treatment of low-grade MECs because there was no postoperative pneumonitis and hilar lymph nodes were not affected [12].

In our case, there was no tumor recurrence at 5 years after PDT, but the tumor recurred 6 months after Nd-YAG laser surgery. We also think that treatment of low-grade MECs is difficult using only Nd-YAG laser surgery. Therefore, we believe that PDT is more likely to be effective for low-grade PMECs in the bronchoscopic visible field.

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Author contributions

MK and KM conceived the idea, analyzed the data, and drafted the manuscript. RI, YY, and TK contributed to the research design and reviewed the manuscript. TO and KI participated in data analysis. NI designed the research framework and coordinated the study. All authors read and approved the final manuscript. All authors have confirmed that the manuscript is not under consideration for review at any other Journal.

Declaration of competing interest

The authors declare no conflicts of interest in this work.

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