Abstract

Multiple primary lung cancers (MPLC) are named synchronous if determined simultaneously with the index tumor, and metachronous if the second tumor is diagnosed with an accepted time after the first tumor. It is important for both the rate of survival and treatment alternatives to differentiate synchronous MPLCs from the metastases of the primary lung tumors, and also from the multiple pulmonary metastases of the extra pulmonary tumors. In this study, clinical characteristics, diagnosis and treatment processes of three synchronous MPLC cases diagnosed in our department were assessed.

Keywords: Lung cancer, neoplasm metastases, synchronous multiple primary neoplasms

INTRODUCTION

Multiple primary lung cancers (MPLC) are divided into two categories, namely synchronous and metachronous. If tumors are determined simultaneously, they are called synchronous, but if the second tumor is determined after a certain time from the detection of the initial lesion, it is called metachronous. In recent years, in parallel with the usage of multislice computed tomography (CT) and positron emission tomography with 18F-fluorodeoxyglucose (FDG-PET), the incidence of synchronous MPLCs has increased. It is highly important to distinguish synchronous MPLCs from both lung metastases of primary tumors and multiple lung metastases of non-lung tumors.

In this study, clinical features, diagnosis, and treatment periods of three synchronous MPLC cases diagnosed in our clinic were examined.

CASE PRESENTATIONS

Case 1
A 68-year-old male patient presented with the complaint of shortness of breath, fatigue, and weight loss. His physical examination findings were normal. His chest x-ray revealed bilateral hilar fullness and properly limited opacity in the right middle zone. A mass surrounding the intermediate bronchial wall in the right lobe, a 4 cm lobulated lesion at the apical segment of the right lower lobe, a 2.5 cm lobulated lesion in the right middle lobe, a soft tissue appearance, and mediastinal hilar lymph nodes were detected on thorax CT (Figure 1a, b). The patient’s bronchoscopy revealed tumor lesions in the right intermediate bronchial wall and at the entry of the left upper lobe bronchus. Histopathological examination of the biopsy taken from the intermediate bronchus revealed the presence of small-cell carcinoma, and the diagnosis of squamous cell carcinoma was also established with the examination of the biopsy taken from the lesion in the left upper lobe (Figure 2).

On the cranial magnetic resonance imaging (MRI) performed for the purpose of staging, a 2×2 cm mass consistent with metastasis was observed in the left frontal lobe. Common liver, muscle, and bone metastases were detected on FDG-PET. The maximum standardized uptake value (SUVmax) was 7.65 for the mass in the left frontal lobe.
the mass around the right intermediate bronchus and 6.81 for the mass in the left lung (Figure 1b). The patient for whom radiotherapy for brain metastasis and zoledronic acid treatment for bone metastasis were initiated was followed up with palliative support treatment because of poor performance scores.

Case 2
A 56-year-old male patient who presented with the complaints of shortness of breath, headache, nausea, and vomiting was examined. His chest x-ray revealed irregular-margined opacities in the left upper zone. Thus, contrast-enhanced thoracic CT was performed and a 7×5 cm, 5 cm irregular-margined lobulated mass in the apicoposterior segment of the left upper lung lobe and a solid, linear and nodular lesion which did not show certain mass formation were observed (Figure 3a). Cranial MRI revealed metastatic lesions of approximately 3 cm in diameter in the left temporal and right frontal lobes (Figure 3b). The patient, who was consulted with brain surgery, underwent urgent metastasectomy and postoperative cranial radiotherapy was administered. After the operation, the general condition of the patient improved and bronchoscopy revealed a mucosal irregularity at the entry of the upper right lobe and a tumoral lesion obstructing the apicoposterior segment of the left upper lobe completely. From the mucous biopsy samples, poorly differentiated squamous cell carcinoma and large cell neuroendocrine carcinoma were diagnosed. Besides, the biopsy sample taken from the patient during the operation performed for metastatic brain tumor was found to be consistent with large cell neuroendocrine carcinoma. Chemotherapy was initiated and the patient was followed up.

Case 3
The thoracic CT of the 74-year-old male patient, who presented with the complaint of shortness of breath, revealed a lobulated mass lesion, the largest axial dimension of which was measured to be about 25×45 mm, in the right hilar region, an approximately 25×40 mm sized mass lesion associated with the pleura in the upper lobe of the right lung, and a mass lesion in the bilateral adrenals (Figure 4a, b). Because the result of the transthoracic biopsy performed for the peripheral mass in the upper lobe of the right lung was consistent with adenocarcinoma, the patient was referred to our clinic. In the bronchoscopy performed at our clinic, a mucosal irregularity, which was 1 cm away from the carina in the anterior wall of the right main bronchus, extending to the upper lobe bronchus and blocking the anterior segment entry, was observed. Moreover, mucosal irregularity, which obstructed the lumen at the rate of 40-50%, was seen in the middle lobe entry. Mucosa biopsy was taken separately from the middle and upper lobes and bronchoalveolar lavage was taken from the upper lobe. In the pathological examination, mucosa samples taken from the upper right and middle lobes were consistent with small-cell lung carcinoma. On FDG-PET, the SUV$_{max}$ of the irregular-margined, 23×36 mm sized mass lesion in the right lung anterior segment was 16 and of the right hilar conglomerate lymph node was 16.1. In addition, increased metabolic activity involvement was observed in the right lower paratracheal and bilateral adrenal glands (Figure 4c, d). On cranial MR, no metastasis was detected. The patient whose general condition was poor and hypoxemic was followed up with supportive treatment after prophylactic brain radiotherapy.

DISCUSSION
The incidence of synchronous MPLC is between 0.2% and 20% and an increase is observed in the frequency of these tumors with the
In synchronous MPLIC cases, survival is quite variable. It was revealed that the 5-year survival rate ranged from 0% to 79% in cases in which both tumors were classified as stage 1 (1, 10-12). Van Rens et al. (13) reported that the 5-year survival rates of synchronous MPLIC patients were worse than those of patients with one primary cancer in similar stages (19% vs. 41%, respectively). In the same study, the most advanced stage among the synchronous MPLIC patients was the best predictor for survival. Because survival rate is lower in synchronous MPLIC patients than in patients with similar stages, it is recommended that scanning tests, including remote organ metastasis examination and mediastinoscopy, be performed with additional care (4).

The differentiation of synchronous MPLIC and lung metastasis is significant. It has been revealed that the long-term survival rate in synchronous MPLIC patients who have undergone resection is higher than that in stage 3B and stage 4 patients. Therefore, surgical resection, especially aggressive surgical approaches, is thought to be an important treatment option for long-term survival in these patients (14). Because all of the patients in our study had metastatic cancer, it was not possible to consider the surgical treatment option. Chemotherapy was administered to two of the patients and one patient received palliative support treatment. The patients are still being followed up in our clinic.

CONCLUSION
For the patients who are followed up because of the diagnosis of lung cancer and who have more than one lesion, the possibility of synchronous MPLIC should be considered and histopathological sampling should be performed for each lesion separately. Although the survival rates in these patients are worse than those in patients with primary lung cancer at the same stage, aggressive surgery options should be considered for suitable patients.

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REFERENCES


