CASE REPORT
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Double Primary Cancers of Earlobe Merkel Cell Carcinoma and Lung Adenocarcinoma

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Merkel cell carcinoma (MCC) is an aggressive neuroendocrine carcinoma with a high rate of metastasis. MCC is rarely suspected during clinical examination, thus requiring biopsy to establish a pathologic diagnosis. In addition, MCC sometimes occurs in double primary cancers. Although there have been reviews on double primary cancers, only a few cases involving MCC have been described. Herein, we report a case of a 54-year-old female patient who presented to our clinic with a diagnosis of earlobe MCC following an excisional biopsy performed by another clinic. Further evaluation, including chest imaging, revealed a mass in the lung. The patient underwent a wide excision of the right earlobe, and video-assisted thoracic surgery on the lung. Pathology confirmed MCC in the right earlobe and adenocarcinoma in the lung. The patient underwent postoperative adjuvant chemotherapy followed by radiotherapy. Up to this point, 3 years after the surgery, there has been no evidence of recurrence.

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Keywords: Merkel cell carcinoma; Neuroendocrine tumor; Earlobe; Lung; Case report.

Introduction

Merkel cell carcinoma (MCC) is a rare neuroendocrine carcinoma that occurs in 0.35 per 100,000 men and in 0.15 per 100,000 women [1]. It is an aggressive tumor with a high rate of metastasis, and the 5-year overall survival ranges from 50.6% for patients with local disease to 13.5% for patients with distant metastases. It was first described by Toker in 1972 as a trabecular carcinoma originating from Merkel cells located between the epidermis and dermis [2]. Most MCCs present as rapidly growing red or violaceous firm nodules on the sun-exposed skin of fair-skinned Caucasians older than 60 years. Approximately 44.5% of MCCs occur in the head and neck area [3]. In the field of ENT, 43% of MCC cases involve the ear, 39% involve mucosal sites, and 18% involve the remaining areas [4]. Although there have been reviews on double primary cancers, only a few cases have been described. In this cese report, we describe a patient with MCC in an earlobe who underwent further cancer evaluations to reveal a second primary cancer in the lung.

Case Report

A 54-year-old female patient presented with a 1-month history of a 0.3×0.5-cm round tumor on the right earlobe. Excisional biopsy was performed in the local orthopedic surgery clinic, and the histologic examination revealed a malignancy, suggestive of a neuroendocrine carcinoma such as MCC. With this pathologic result, the patient visited our otorhinolaryngology clinic for further evaluation and management. The skin lesion recovered and exhibited a reddish color change (Fig. 1). We performed a cancer evaluation, including temporal bone computed tomography (CT), chest CT, neck magnetic resonance imaging, and positron emission tomography CT. The temporal bone CT showed no definite lesion of right ear (Fig. 2A), while revealed a 7×5-mm enhancing lymph node in the

right parotid gland (Fig. 2B). And the chest CT revealed a mass in the left upper lung (LUL), suggestive of lung cancer such as adenocarcinoma (Fig. 2C). With the impression of MCC in the right earlobe and the adenocarcinoma in the LUL, a meeting was held among the otorhinolaryngology, oncology, radiology, radiotherapy, and cardiothoracic surgery departments. After the meeting, surgery was performed by the otolaryngology and cardiothoracic surgery departments. We performed wide excision of the right earlobe tumor with 1-cm resection margin and partial parotidectomy with selective neck dissection of levels II and III (Fig. 3). The cardiothoracic surgery involved video-assisted thoracic surgery of the LUL with lymph node dissection. Pathology confirmed remnant MCC in the right earlobe with clear resection margin, and a metastatic intraparotid lymph node (Fig. 4A-C). On the other hand, the pathology of the lung lesion revealed adenocarcinoma (Fig. 4D). After the operation, the patient first went through 4 cycles of adjuvant chemotherapy for the lung adenocarcinoma followed by adjuvant radiotherapy (55–60 Gy/6 weeks) on the right ear tumor bed. Up to this point, 3 years after the surgery, the patient is currently being regularly followed up with no ev-

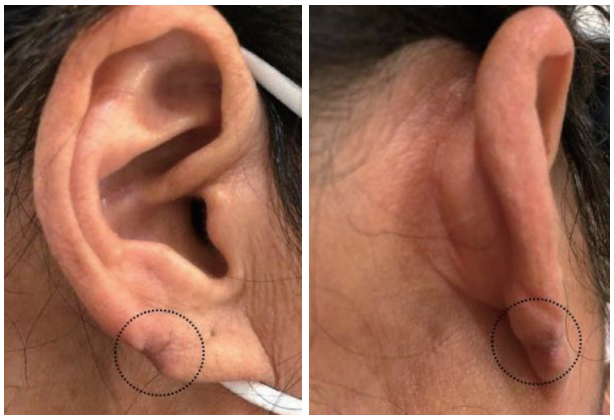

Fig. 1. Clinical image of patient's right ear. The skin lesion recovered with reddish color change after initial excisional biopsy (dotted circle).

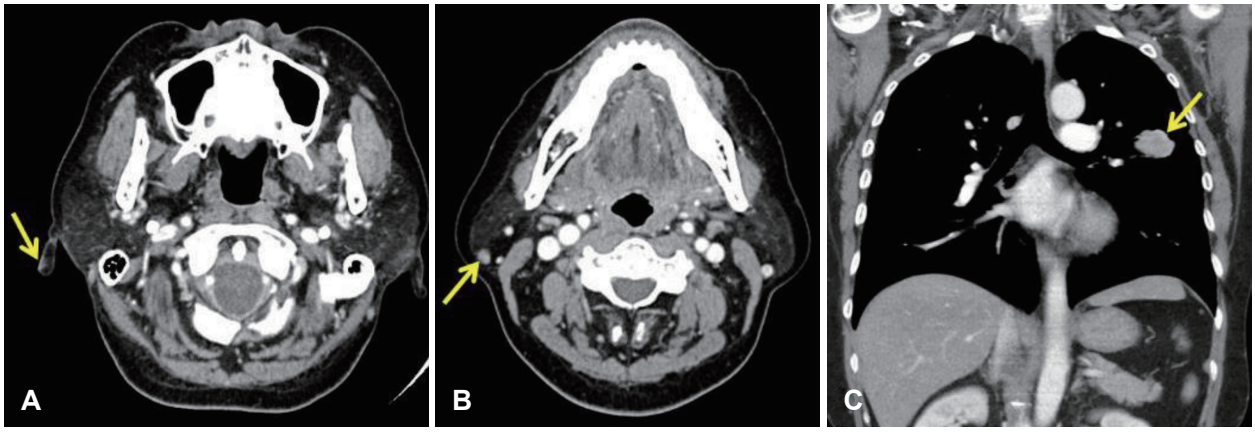

Fig. 2. Computed tomography examination for cancer evaluation. A: Temporal bone computed tomography showed no definite lesion of right ear after initial excisional biopsy (arrow). B: Temporal bone computed tomography revealed 7×5-mm enhancing lymph node in the right parotid gland (arrow), suggestive of metastatic lymph node. C: Chest computed tomography revealed about 3.5 cm-sized mass with irregular shape, spiculated margin, and homogenous contrast enhancement in the left upper lung (arrow), suggestive of lung cancer such as adenocarcinoma.

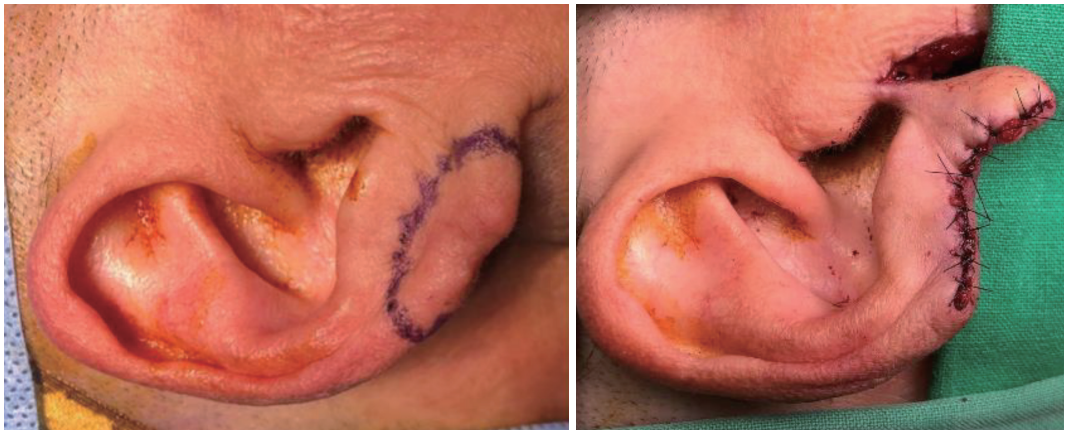

Fig. 3. Intraoperative image of patient's right ear. Wide excision of the right earlobe tumor with 1-cm resection margin and partial parotidectomy with selective neck dissection of levels II and III.

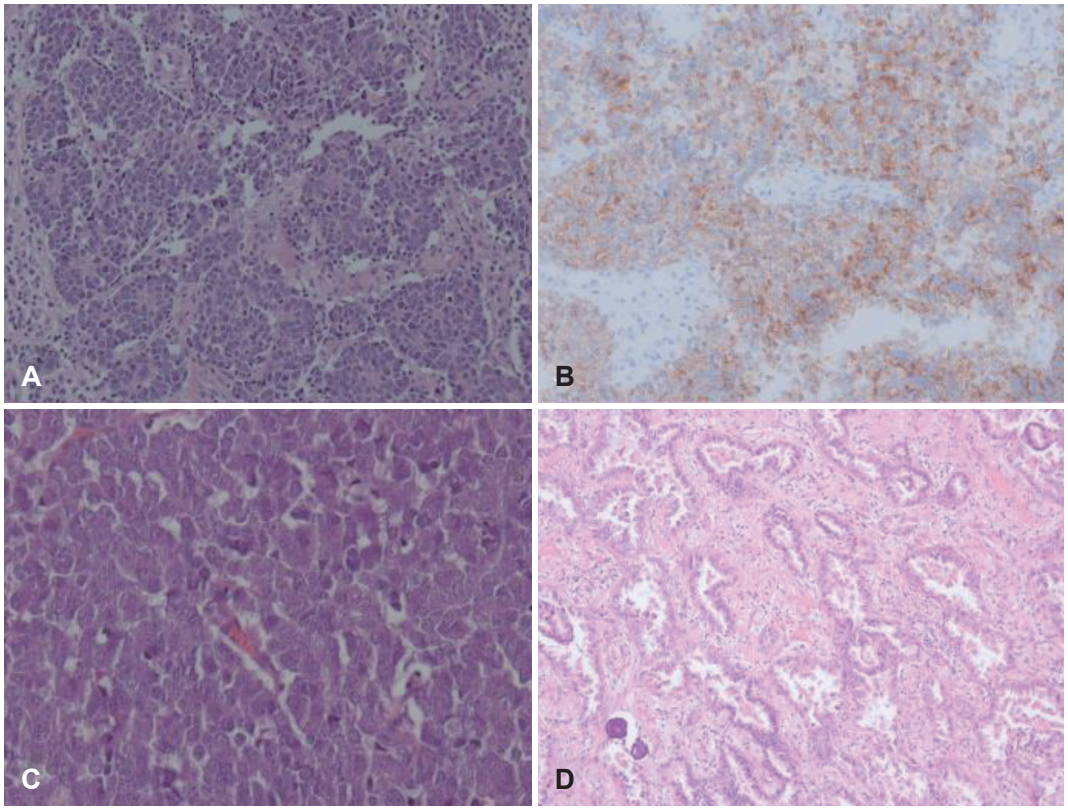

Fig. 4. Histopathological examination of excised mass in the earlobe (A and B). A: Hematoxylin and eosin staining. Small, round tumor cells with high nuclear/cytoplasmic ratio. B: Immunohistochemistry staining for CD56. Tumor cells staining positive for CD56. C: Hematoxylin and eosin staining of excised intraparotid lymph node. Monotonous round tumor cells with high nuclear/cytoplasmic ratio. D: Hematoxylin and eosin staining of excised lung mass. Irregularly-shaped glands are present in a fibrotic stroma (original magnifications: A, ×200; B, ×200; C, ×400; D, ×100).

idence of recurrence (Fig. 5).

DISCUSSION

In our case, the patient presented to our outpatient clinic with a confirmed diagnosis of earlobe MCC following an excisional biopsy performed by other orthopedic surgery clinic. Most MCC lesions are usually asymptomatic, red-to-violet nodules that might be clinically misconstrued as benign lesions or other malignant lesions. Therefore, it is important to identify the initial lesions to suspect the possibility of malignancy, and to determine the need for further examination. Heath, et al. [5] reported 5 most common clinical features of MCC at diagnosis in 195 patients using an acronym: AEIOU (Asymptomatic/lack of tenderness, Expanding rapidly [≤3 months], Immunosuppression, Older than age 50, location on a UV-exposed site). These features may serve as a basis for suspicion of MCC in the diagnosis process.

Since MCCs are highly invasive tumors that have a strong tendency for regional and distant metastases (greater than 50% and 20%–40%, respectively) and local recurrence (30%–40%), it is important to not only remove the primary tumor, but also to evaluate the area for further invasion or metastasis through diligent history-taking, physical examinations, and radiologic studies. Once the primary MCC and other sites of

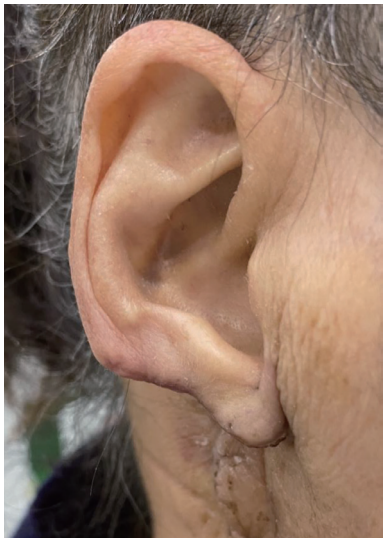

Fig. 5. Postoperative image of patient's right ear at 1 month.

invasion or metastasis are confirmed, a histopathologic diagnosis is needed for final confirmation. Other diseases for differential diagnosis include basal cell carcinoma, squamous cell carcinoma, malignant melanoma, hidradenocarcinoma, lymphoma, neuroblastoma, metastatic oat cell carcinoma, and carcinoid tumors [6,7]. Approximately 5% of MCCs are observed in the lymph nodes without a primary tumor on the skin. Since MCCs are rare and difficult to diagnose through clinical examination, biopsy is necessary to establish a pathologic diagnosis. The histopathological features include small-blue-round cell tumors and dermal and/or subcutaneous nodules or sheets. Immunohistochemical demonstration of neuron-specific enolase, CD56, chromogranin A, synaptophysin, low molecular weight cytokeratins (CK8, CK18, CK19, CK20), and absence of thyroid transcription factor-1 (TTF-1), CK7, S100 protein and leukocyte common antigen are enough to confirm the diagnosis [8-11].

Although there is no single established algorithm for treatment of MCCs, surgery is considered the most important treatment modality. The current National Comprehensive Cancer Network (NCCN) guidelines recommend 1- to 2-cm resection margins. In recent, Perez, et al. [12] reported surgical outcomes of 240 patients who underwent resection of primary MCC, and concluded 1-cm resection margins did not increase the risk of local recurrence and margin width did not make a significant difference in disease-specific survival. Since most of the patients who were node-free eventually developed lymph node metastases, Goepfert, et al. [13] recommended elective treatment of the regional lymph node. Therefore, regional lymph node treatment is recommended for patients with high risk factors. If lymph node metastasis is evident at the time of diagnosis, both surgery and adjuvant radiotherapy should be considered for better outcomes [3,4,8] since postoperative radiotherapy has been shown to be effective in lowering local and regional recurrence rates [10,13,14].

According to other studies reporting double primary cancers, the most commonly recognized primary cancers were melanoma, prostate cancer, breast cancer, and colorectal cancer [3,15]. These patients went through either one or a combination of treatment modalities involving surgery, radiotherapy, chemotherapy, or no therapy depending on various factors such as stage, site, and general condition. People with MCCs exhibited more than double the risk of subsequent primary cancer compared with the general population [3].

This case report highlights the importance of conducting a thorough examination and close follow-up not only for a metastasis but also for double primary cancer should be considered when a patient is diagnosed with MCC. In cases of double primary tumors, it is also important that the clinician participates in a tumor board meeting to discuss the treatment plan with members of other departments such as radiology, oncology, and radiotherapy.

Ethics Statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review Board of Incheon St. Mary's Hospital, The Catholic University of Korea (OC18RESI0067) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient.

Conflicts of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Hyun Jin Lee. Data curation: So Yun Lim. Formal analysis: Kyung Il Jang. Funding acquisition: Hyun Jin Lee. Investigation: Hyun Jin Lee. Methodology: So Yun Lim, Hyun Jin Lee. Project administration: Hyun Jin Lee. Resources: So Yun Lim. Software: Jeon Mi Lee. Supervision: Eun-Ju Jeon, Jeon Mi Lee. Validation: Hyun Jin Lee. Visualization: Hyun Jin Lee. Writing—original draft: Kyung Il Jang. Writing—review & editing: Hyun Jin Lee. Approval of final manuscript: all authors.

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