Metastatic Large Cell Neuroendocrine Carcinoma of the Lung Mimicking a Merkel Cell Carcinoma

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Large cell neuroendocrine carcinoma (LCNEC) of the lung is a newly recognized entity of pulmonary neuroendocrine carcinoma. Histologically, it is very difficult to differentiate LCNEC from other pulmonary carcinomas and the prognosis is significantly poor. The cutaneous metastasis of LCNEC of the lung shares some features with a Merkel cell carcinoma of the skin in light microscopy and yet it is negatively stained with cytokeratin 20. We report a case of cutaneous metastasis of LCNEC of the lung, previously misdiagnosed as squamous cell carcinoma. Our patient showed a poor response to the chemotherapy and also revealed a brain metastasis on follow-up brain CT scan. (Ann Dermatol 14(2) 121-123, 2002).

Key Words : Large cell neuroendocrine carcinoma, Cutaneous metastasis

Large cell neuroendocrine carcinoma (LCNEC) of the lung is a newly recognized clinicopathologic entity and defined as a poorly differentiated and high-grade neuroendocrine tumor that stands morphologically and biologically between atypical[1] carcinoid and small cell lung carcinomal. Histopathologically, most LCNECs revealed a marked decrease in or a loss of organoid architecture and could be mistaken for poorly differentiated adenocarcinoma or squamous cell carcinoma[2,3]. Cutaneous metastasis of pulmonary cancer is common as shown in its rate up to 1.5 to 2.6% and may be presented as a first sign of cancer[4,5]. Furthermore, the neuroendocrine features of cutaneous metastasis of LCNEC of the lung may be similar to Merkel cell carcinoma and other neuroendocrine carcinomas and therefore, it should be differentiated from them by histological and immunohistochemical studies. Thus, we herein report a case of cutaneous metastasis of LCNEC of the lung, previously misdiagnosed as squamous cell carcinoma.

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CASE REPORT

A case of a 72-year-old man presented with a 2 × 1cm sized slowly enlarging subcutaneous nodule on his back of 1-month duration. Three months before admittance to our clinic, he was diagnosed as squamous cell carcinoma of the lung (T2N1M0, stage Ib) and operated with right lower lobectomy and with a wedge resection and ligation of right upper lobe bullae. There were no metastasis on the bronchus, pleura and peripheral lymph nodes on operational biopsy findings. With a provisional clinical diagnosis of metastatic carcinoma, we biopsied the skin lesion. The specimen showed a dermal tumor in which tumor cells were arranged in variously sized nests, broad and irregular strands, or solid sheets with prominent stromal lymphoid infiltration and focal necrosis (Fig. 1, 2). At higher magnification, the tumor cells usually were large and polygonal with an abundant, finely granular and eosinophilic cytoplasm, coarse or salt and pepper chromatins, and frequent nucleoli and high mitotic rate. Further observation revealed rosette-like structure in variously sized tumor cell nests (Fig. 3). Tumor cells were stained diffusely

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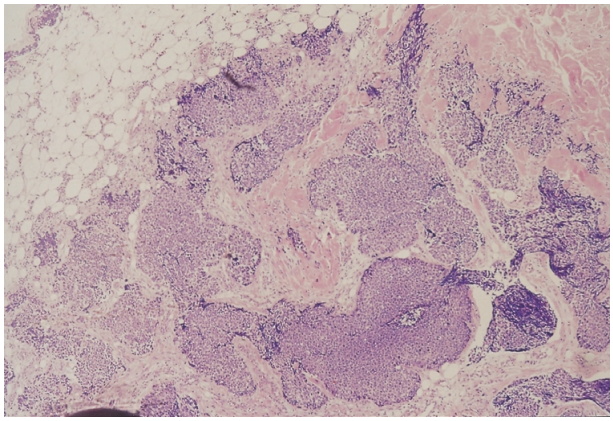

Fig. 1. Tumor cells are arranged in variously sized nests, broad and irregular strands, or solid sheets with prominent stromal lymphoid infiltration and focal necrosis (H × E (40).

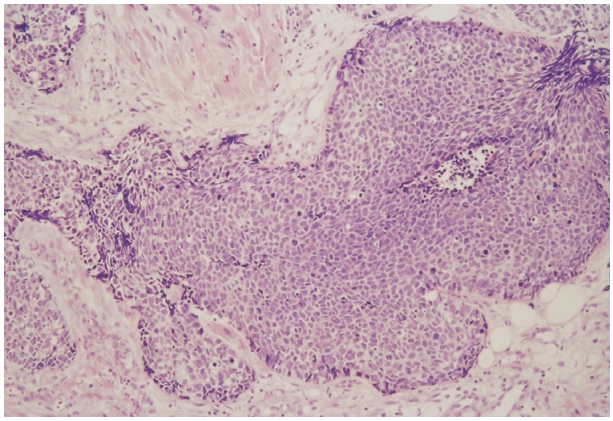

Fig. 2. Tumor cells form variously sized nests (Hematoxylin & eosin stain (100).

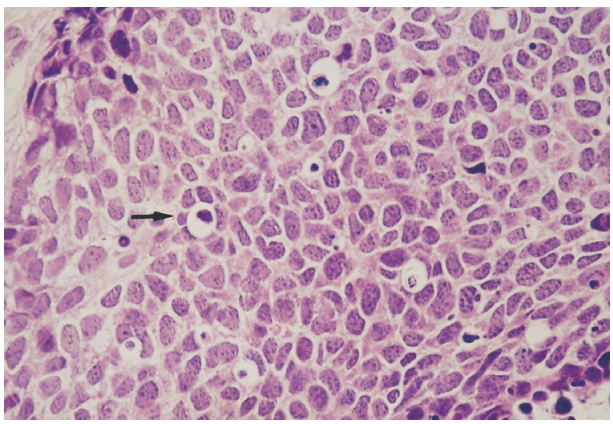

Fig. 3. Tumor cells usually are large and polygonal with an abundant, finely granular and eosinophilic cytoplasm, coarse or salt and pepper chromatins, and frequent nucleoli and high mitotic rate. Some rosette-like structures(arrow) are founded (H × E (400).

with neuron-specific enolase (NSE) and chromogranin A (Fig. 4A, B) and not with cytokeratin (CK) 20. After confirmation of these histological findings, our patient was rediagnosed as pulmonary LCNEC because of the metastatic cancer on his back. The patient was re-hospitalized to perform follow-up radiological examinations and to take chemotherapy. There was no evidence of metastasis on follow-up whole body bone scan and chest CT but brain CT scan revealed the metastatic lesion on right cerebellum.

DISCUSSION

Large cell neuroendocrine carcinoma (LCNEC) is very difficult to differentiate in light microscopy, especially in cases that are decreased in or loss of organoid architecture. In one study, 18 of 22 cases di-

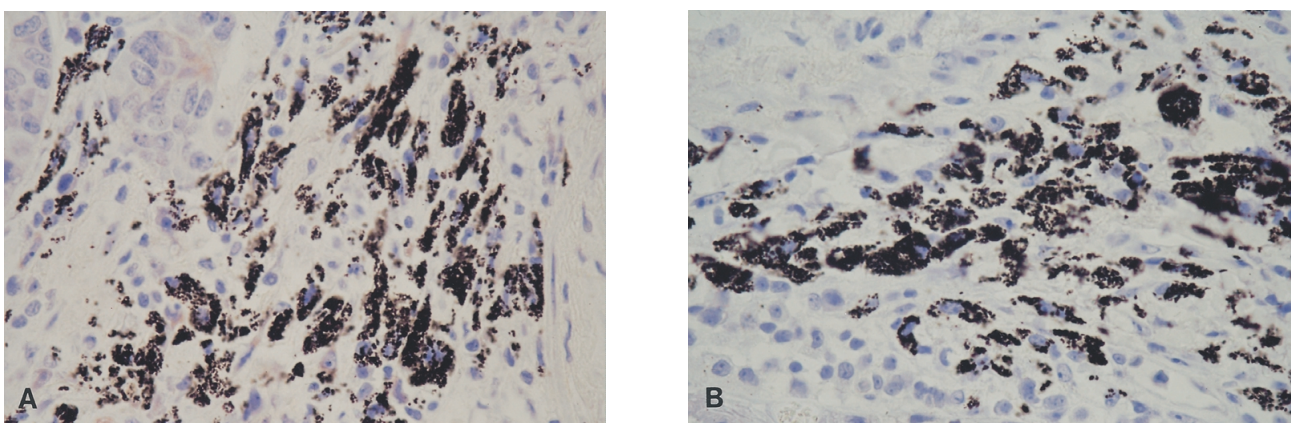

Fig. 4. Tumor cells are stained diffusely with NSE and chromogranin A (A: NSE, B: chromogranin A × 400).

agnosed as LCNEC were misdiagnosed previously and 9 of these 18 cases were squamous cell carcinoma like our case[7]. Cutaneous metastatic neuroendocrine carcinoma must be differentiated from Merkel cell carcinoma and metastatic carcinoma from other visceral disease. Rosette-like structure, suggested by Jiang SX et al.[7] as the best marker for recognition of neuroendocrine differentiation is described as the small and regular, oval or round lumina, deeply eosinophilic luminal surfaces, and the absence or rare accumulation of nonmucous-secreted material but frequent apoptotic debris in the lumina. Some histologic features of our case resembled the Merkel cell carcinoma. However the cell size and the rosette-like structures were different and rather close to the features of pulmonary neuroendocrine carcinoma. To confirm these neuroendocrine features, NSE, chromogranin A were used as immunohistochemical staining and to differentiate from a Merkel cell carcinoma CK 20 was used[8]. Although some features were similar to the Merkel cell carcinoma, the result elucidated that the tumor contained significant neuroendocrine natures but it could be differentiated from the Merkel cell carcinoma by its negative staining for CK 20. Cutaneous metastasis from visceral organ was usually from hematogenous spreading but in our case, direct extension of tumor cell was doubted because the location of skin lesion was near that of previous diagnostic fine needle aspiration biopsy site. We also found similar immunohistochemical features in the previous surgically resected lung cancer sections. It represents that previous squamous cell carcinoma was a misdiagnosis and resected lung cancer was infact pulmonary neuroendocrine carcinoma. In various pulmonary neuroendocrine carcinoma, these histological findings corresponded with the histologic criteria for LCNEC proposed by Travis et al[1]. Clinically, the prognosis of LCNEC is significantly worse than that for stage-comparable non-small cell lung cancer and our patient had a poor response to chemotherapy and a brain metastasis on follow-up brain CT scan.

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