

An Unusual Presentation of Merkel Cell Carcinoma

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ABSTRACT

We describe a 71-year-old male patient admitted to the hospital with posterior chest pain. Following the detection of a paravertebral mass at the level of the 2nd thoracic vertebra, the patient underwent a surgical en bloc resection of the mass. The histopathologic examination revealed a Merkel cell carcinoma. One month after the operation, magnetic resonance imaging showed an inoperable mass in the same location, which indicated a rapid progression of the tumor. The patient died of progressive respiratory failure due to pneumonia on the 6th day after the onset of radiochemotherapy. Although this appears to be an isolated case, Merkel cell carcinoma must be included in the differential diagnosis of intrathoracic masses.

Key Words: Merkel cell carcinoma, intrathoracic, extracutaneous

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Introduction

Merkel cell carcinoma (MCC) is an uncommon primary cutaneous neoplasm of neuroendocrine cells with a predilection for the head and neck and distal extremities in elderly patients. It is principally a disease of the Caucasian race with an incidence of 0.44 per 100,000 and is very high (8%) among immunosuppressed patients (1, 2). The disease course is difficult to predict and ranges from relatively indolent to highly aggressive, often spreading to local, regional, and distant sites (3, 4).

MCC very rarely arises outside the skin. In the literature, the salivary glands, nasal cavity, lymph nodes, and subcutaneous fat have been reported as the most common extracutaneous sites (5-8). We describe a 71-year-old man with Merkel cell carcinoma, which presented as an intrathoracic mass. To the best of our knowledge, this is the first described case in the English-language literature of such a lesion located intrathoracically with no detectable primary site.

Case Report

A 71-year-old male presented to the Thoracic Surgery department with an 11-month history of left-sided posterior chest pain. He had smoked one packet of cigarettes daily for 35 years but had given up the habit one year before admission. On physical examination, no rash or lymphadenopathy was detected. Laboratory results and chest radiography were normal. Computed tomography of the thorax showed a paravertebral mass (41x21 mm in diameter), extending to the neural foramen of the 2nd and 3th thoracic vertebrae in the

apical-posterior segment of the left upper lobe. The transthoracic fine-needle aspiration biopsy revealed a malignant tumor. Positron emission tomography scan showed a hypermetabolic malignant lesion in the apical-posterior segment of the left upper lobe, with no hypermetabolic lesions in the mediastinum (Figure 1). No other lesions, primary or metastatic, were demonstrated.

The patient underwent en bloc chest wall resection with parietal pleura, facets and transverse processes of the thoracic vertebrae (2nd and 3th), and intercostal muscles. On exploration, the lesion with a lobulated contour appeared to invade the thoracic vertebrae and an intrathoracic but extra-pulmonary location.

The histopathological examination showed a tumor characterized by small indefinite nests and solid areas consisting of small and round cells with narrow cytoplasm. Tumor necrosis and tumor thrombi were also recognised. Macroscopically, the tumor did not show bone invasion. At first glance, malignant small round cell tumors namely; metastasis of small cell carcinoma, metastasis of melanoma, PNET/Ewing sarcoma and Merkel cell carcinoma were considered histologically. By means of immunohistochemistry, some possibilities were excluded. Cytokeratin 7 and TTF-1 were negative for metastasis of small cell carcinoma, S-100 and HMB-45 were negative for malignant melanoma and CD-99 was negative for PNET/Ewing sarcoma. Specific cytokeratin 20 positivity with specific globular pattern enabled us to label the tumor as Merkel cell carcinoma (Figure 2).

No suspected skin lesion or lymph nodes were detected after careful physical examination of the patient. The patient had no history suggesting an immuno-compromised status

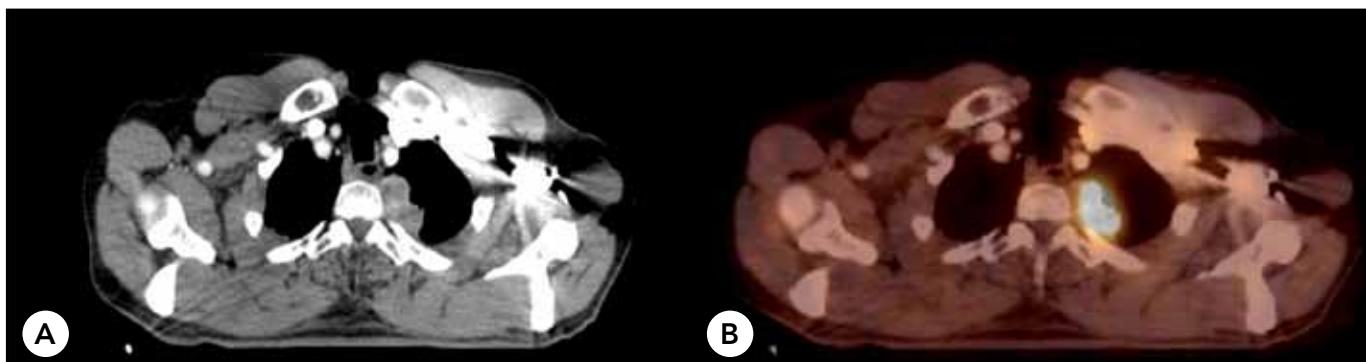


Figure 1. A: Computed tomography scan shows the left intrathoracic mass B: Positron emission tomography and superimposed computed tomography scan shows the left intrathoracic hypermetabolic malignant mass

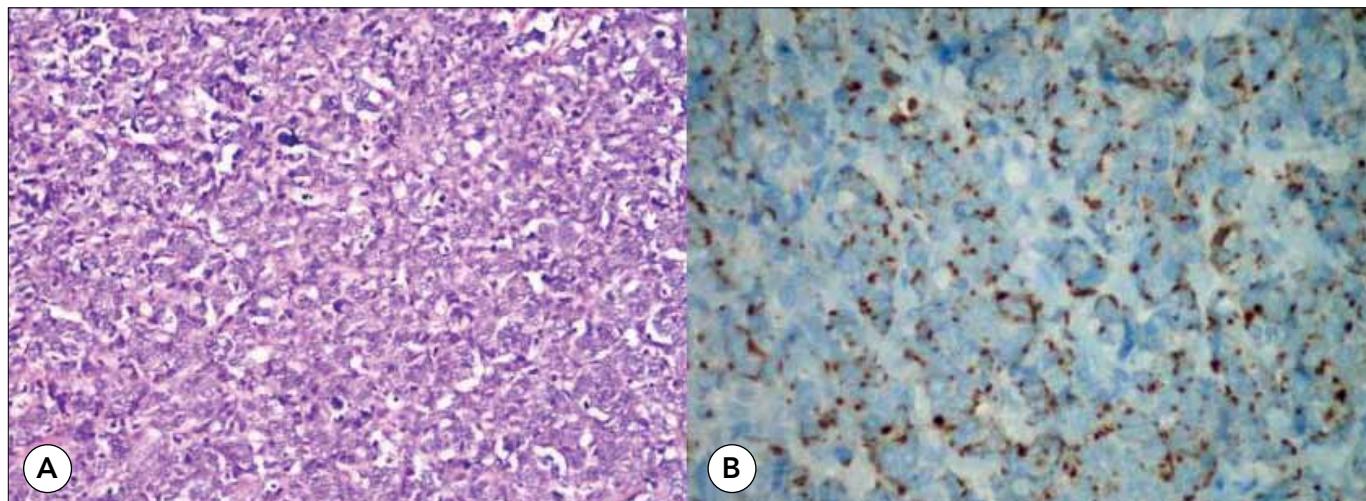


Figure 2. A: Solid tumor areas composed of atypical small round cells (HEx200). B: Globular cytokeratin 20 positivity in cytoplasms of tumor cells (Immunoperoxidase cytokeratin 20 x 400)

and human immunodeficiency virus infection was excluded by the appropriate laboratory tests.

The patient was referred to the Oncology department for adjuvant treatment one month after the operation. Magnetic resonance imaging of the thorax showed a mass with dimensions of 28x15 mm in the same location, which was apicomediadially adjacent to the corpus of the 2nd thoracic vertebra, and the mass was also expanding into the neural foramen. It was thought to be a rapid progression of the tumor. The tumor was inoperable and concomitant radiochemotherapy was planned. He developed severe pneumonia six days after the onset of the radiochemotherapy and died despite the rapid onset of broad spectrum antibiotic therapy two days after the diagnosis of pneumonia.

Discussion

MCC is rare, with an estimated annual incidence of 0,2 and 0,45 cases per 100,000 (9). MCC is extremely rare before the age of 50 years, after which the incidence increases steeply with age. The incidence is increased approximately 11-fold for people with AIDS and five-fold for people who have undergone an organ transplantation (9, 10). The risk of MCC may be particularly high with prior psoralen and UV-A treatment,

which reinforces the likely etiologic role of UV radiation (11). In the current case, there was no such history.

Fredrick Merkel first described Merkel cells in 1875 as mechanoreceptors in the basal layer of the epidermis. An epithelial origin is possible, but some data suggest that Merkel cells may have a neural-crest origin (12). Cyril Toker first published a series of skin neoplasms of the elderly with special histologic characteristics between 1966-1970 (13).

Microscopically, the tumor nodule of MCC is comprised of small cells with scant neoplasm, large nuclei and finely granular chromatin. Accurate diagnoses of neuroendocrine carcinoma is difficult due to its similarity to other poorly differentiated "small blue cell tumors", like small cell carcinoma of the lung. Immunohistochemistry is an essential tool in the routine diagnosis of MCC. MCC cells stain negatively for S-100 protein which is positive in melanoma, for TTF-1 and CK-7 which is positive in small-cell lung carcinoma, and for LCA which is positive in lymphoma. Combined immunostaining for TTF-1 and CK20 can be used for differentiating MCC from small cell lung carcinoma (14). A CK20 positive and TTF-1 negative result in a tumor morphologically consistent with MCC establishes the diagnosis (15). In the present case, diffuse globular CK20 positivity and TTF-1 negativity were detected. Additionally, MCC cells stain positively for neuroendocrine markers chromogranin and synaptophysin.

MCC almost always arises from the dermis. It occurs extremely rarely outside the skin. In the literature, the salivary glands, lymph nodes, subcutaneous fat and nasal cavity, are the reported extracutaneous sites with no detectable skin primary (6-8, 16). However, no case of MCC located intrathoracically with no detectable skin primary have been reported. Actually, it is very difficult to decide that the intrathoracic mass is primary or metastatic in the current case. The hypothesis that MCC may originate from a pluripotent cell has gained recent support. This hypothesis could help to explain the origins of both skin and non-skin tumors (17).

Currently, there is no a standard therapy protocol for MCC. The treatment of choice depends on the extension of the disease. Local excision is preferred in localized disease, whereas a wide excision with 2 to 3 cm of tumor free surgical margin is preferred for primary lesions smaller than 2 cm. Adjuvant radiotherapy is suggested for tumors greater than 2cm after surgical excision. The mortality rate could be decreased in cases with lymphatic metastasis through irradiation of the primary tumor bed and lymph node site after wide local excision and complete lymphatic node dissection. Chemotherapy is the most common preferred modality for the treatment of metastatic disease. In stage IV MCC, cisplatin, doxorubicin, and vincristine or the combination of etoposide and platinum are the most common agents used for chemotherapy (18-20).

MCC is a rare, neuroendocrine cancer of the skin. Primaries in other sites may also be seen. MCC from an unknown primary site is an extremely rare entity. Although the presented patient appears to be an isolated case, MCC should be kept in mind in the differential diagnosis of intrathoracic extrapulmonary malignant masses even without an identifiable primary site.

Conflict of Interest

No conflict of interest was declared by the authors.

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