Skull Metastases From Atypical Pulmonary Carcinoid Tumor in a 19-Year-Old Man
—Case Report—

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Abstract
A 19-year-old man presented with a rare skull metastasis from atypical pulmonary carcinoid tumor (APCT) manifesting as headache, diplopia, and cough. Head magnetic resonance imaging showed a skull base tumor extending from the posterior clinoid process to the clivus, and calvarial tumors in the right temporal and occipital bones. Chest and abdominal computed tomography showed a round tumor, 4 cm in diameter, in the lower lobe of the right lung and multiple small tumors in the liver. Surgery for the calvarial tumor in the right temporal bone was performed on June 27, 2003. The histological diagnosis was skull metastasis of neuroendocrine tumor. Gamma knife radiosurgery was performed for the residual skull metastases. Partial resection of the right lower lobe was performed for the lung tumor on August 22, 2003. The histological diagnosis was atypical carcinoid tumor. Subsequent adjuvant systematic chemotherapy was performed. The patient died of progression of the tumors in the lung and liver on April 19, 2004. We must consider APCT in the differential diagnosis of pulmonary tumors in adolescents, and perform follow-up observation or treatment, including surgery, if APCT is suspected.

Key words: skull metastasis, atypical carcinoid, pulmonary neuroendocrine tumor, adolescent

Introduction
Atypical pulmonary carcinoid tumor (APCT) is a neuroendocrine lung tumor arising from the Kulchitzky cells of the bronchus, and the diagnosis is based on the histological criteria proposed by the World Health Organization (WHO). The 5-year survival rate for patients with APCT ranges from 25% to 69%, which shows that APCT is essentially a malignant neoplasm. APCT has a high potential for local and/or distant metastasis, frequently to the lymph nodes, liver, lungs, and bone. Skull metastasis is a rare type of bone metastasis.

We recently treated a 19-year-old man with skull metastases from APCT which were controlled by treatment, but he died of progression of the primary tumor.

Case Report
A 19-year-old man was referred to our hospital with complaints of headache, diplopia, and cough, all developing within 3 weeks, on June 11, 2003. Physical examination showed no abnormalities. Neurological examination showed bilateral abducens nerve palsy, but no papilledema. Laboratory studies revealed that the serum levels of CYFRA21.1, neuron-specific enolase (NSE), and progastrin-releasing peptide were elevated, but those of carcinoembryonic antigen and alpha-fetoprotein were normal. Pituitary function was normal. His medical history revealed that chest radiography at a medical checkup 1 year prior to our examination had detected a mass lesion, approximately 2 cm in diameter, in the lower lobe of the right lung.

Skull radiography showed osteolytic coin lesions in the right temporal and occipital bones. Head computed tomography (CT) and head magnetic resonance (MR) imaging showed that the lesions were calvarial tumors. The calvarial tumors were chiefly present extradurally and compressed the
brain under the tumor. Both T₁ and T₂-weighted MR images showed the calvarial tumors as isointense, with homogeneous enhancement by gadolinium-diethylenetriaminepenta-acetic acid (Fig. 1). MR imaging showed, in addition to the calvarial tumors, another skull base tumor extending from the posterior clinoid process to the clivus (Fig. 2A).

Chest radiography showed a solitary round mass lesion, approximately 4 cm in diameter, in the lower lobe of the right lung. This lesion had markedly increased in size since the medical checkup 1 year earlier. Chest CT showed that the lesion was a bronchial tumor (Fig. 3). In addition, a pleural tumor was found. Abdominal and pelvic CT showed multiple small tumors in the liver, but no abnormal tumors in other organs. Technetium-99m bone scintigraphy showed increased uptake only in the skull tumors. Whole body scintigraphy using gallium-67 citrate and metaiodobenzylguanidine showed no abnormal uptake in any organ.

Although the tumor in the lower lobe of the right lung was thought to be the primary tumor, diagnosis and treatment for the skull metastases were given the higher priority. Surgery for the calvarial tumor in the right temporal bone was performed on June 27, 2003. The tumor consisted of a red, gelatinous, and easily bleeding mass, and had proliferated expansively in the temporal bone, as well as invaded the dura mater. The tumor was completely resected together with the invaded dura mater. Macroscopically, no subdural tumor invasion was detected, and the brain surface was normal in appearance, despite compression by the tumor.

Histological examination of the surgical specimen showed that the tumor consisted of diffuse cellular nests of polygonal tumor cells with oval to spherical hyperchromatic nuclei and scant cytoplasm, supported by abundant vascular stroma, and (B) organoid solid nests (arrows) and punctate foci of necrosis (arrowheads) within the nests. Hematoxylin and eosin stain, A: ×400, B: ×75.
ported by abundant vascular stroma (Fig. 4A). These nests had invaded the skull bone and dura mater. Organoid solid nests and punctate foci of necrosis within the nests were sometimes found, but mitotic figures were rare (Fig. 4B). Connective tissue reaction against the nests was abundant in the dura. Immunohistochemical study confirmed that most tumor cells were positive for chromogranin A (CgA), NSE, and epithelial membrane antigen (Fig. 5). Some tumor cells were positive for somatostatin. The histological diagnosis was skull metastasis of neuroendocrine tumor.

The postoperative course was uneventful, but neurological symptoms including headache and diplopia continued. The residual skull metastases, including the calvarial tumor in the occipital bone and the skull base tumor from the posterior clinoid process to the clivus, were treated with gamma knife radiosurgery in another hospital on July 28, 2003 (Fig. 2). After treatment, progression of these tumors was completely controlled, and the neurological symptoms, including headache and diplopia, gradually improved.

Partial resection of the right lower lobe was performed for the tumor in the right lung on August 22, 2003. The histological diagnosis was atypical carcinoid tumor, based on the 1999 WHO criteria for the diagnosis of pulmonary neuroendocrine tumors26) (Fig. 6). Two courses of combined chemotherapy using cisplatin and etoposide were performed as adjuvant therapy. Although the chemotherapy succeeded in controlling the progression of the tumors in the lung and liver, no marked reductions were achieved. The patient was transferred to another hospital, in accordance with his desire to undergo treatment nearer his birthplace on November 10, 2003.

We were subsequently informed that the patient died of multiple organ failure resulting from the progression of the tumors in the lung and liver on April 19, 2004.

**Discussion**

Our present patient, a 19-year-old man, had skull metastases of APCT, and died 10 months after initial diagnosis, despite various types of treatment. The diagnosis for the skull tumor was a metastasis from a neuroendocrine tumor, based on neuroendocrine morphology and neuroendocrine properties, such as positive staining for CgA and NSE.14,24,27,30) The diagnosis for the pulmonary tumor was atypical carcinoid tumor, based on the 1999 WHO criteria for the diagnosis of pulmonary neuroendocrine tumors.26,27) The pulmonary tumor had increased in size by approximately eight-fold since the medical checkup 1 year earlier, and no other possible primary tumors were found by systematic examination, so we believed that the pulmonary tumor was the primary in this case. In addition, the histological appearances of the pulmonary tumor and the skull tumor were similar. Therefore, we believe that the skull tumor was a metastasis from APCT.

Skull is a rare site of a metastasis from APCT.19,21,22,29) Only one other case of skull metastasis associated with neurological complications has been reported with similar cranial nerve palsies caused by a skull base metastasis.21) The reason for the low incidence of skull metastasis as a clinical manifestation of APCT is not clear. However, we found that the mitotic figures in the skull metastasis specimen were obviously fewer than in the primary tumor of the present case. This difference may be related to the low incidence.

In the present case, both the pulmonary tumor and skull tumors were found on admission. Partial resection of the right lower lobe including the tumor was appropriate for the diagnosis and treatment of
the pulmonary tumor. This was thought to be more invasive than removal of the right temporal calvarial tumor. In addition, the complaints of headache and diplopia were intense. Therefore, we first treated the skull tumor by surgery and gamma knife radiosurgery, which were very effective. However, treatment for the primary pulmonary tumor was delayed, which might have contributed to the fatal progression.

Pulmonary tumors in children and adolescents are extremely rare.\(^2\)\(^,\)\(^3\)\(^,\)\(^10\)\(^,\)\(^12\)\(^,\)\(^13\)\(^,\)\(^31\) Local and/or distant metastases are found in approximately 20% to 27% of cases of bronchial tumors in children: institutional experience and perform follow-up observation or treatment, including surgery, if APCT is suspected.

APCT in the differential diagnosis of pulmonary carcinoid tumors is related to tumor size, and the prognosis is poor. The metastatic potential of carcinoid tumors is related to tumor size, and tumors larger than 2 cm in diameter have high malignant potential.\(^6\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^17\)\(^,\)\(^18\)

In this case, a pulmonary mass lesion of approximately 2 cm in diameter was identified during a medical checkup when the patient was 18 years of age. If he had undergone the surgery at that time, he might have survived. Therefore, we must consider APCT in the differential diagnosis of pulmonary tumors in adolescents, and perform follow-up observation or treatment, including surgery, if APCT is suspected.

References


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