Surgical management of brain metastasis as a part of systematic metastases from adenoid cystic carcinoma of the external auditory canal: illustrative case

Shunichiro Kuramitsu, MD, PhD, Kazuya Motomura, MD, PhD, Yasuhiro Nakajima, MD, PhD, Takashi Tsujiuchi, MD, PhD, Ayako Motomura, MD, PhD, Mamoru Matsuo, MD, Nobuhisa Fukaya, MD, Akinori Kageyama, MD, Iori Kojima, MD, Masasuke Ohno, MD, PhD, and Ryuta Saito, MD, PhD

1Department of Neurosurgery, National Hospital Organization Nagoya Medical Center, Nagoya, Japan; 2Department of Neurosurgery, Nagoya University School of Medicine, Nagoya, Japan; Departments of 3Neurosurgery and 4Pathology, Daido Hospital, Nagoya, Japan; and 5Department of Neurosurgery, Aichi Cancer Center Hospital, Nagoya, Japan

BACKGROUND  Adenoid cystic carcinoma (ACC) of the external auditory canal (EAC) is a rare tumor that accounts for approximately 5% of all EAC tumors. ACC is generally known as a slow-growing tumor, but patients often experience recurrence or distant metastasis in the long clinical course. While the major pattern of recurrence is pulmonary metastasis, brain metastasis of ACC of the EAC is rare.

OBSERVATIONS  The authors describe the case of a 72-year-old male who was diagnosed with ACC of the EAC. Approximately 7 years later, brain magnetic resonance imaging revealed an intra-axial homogenously enhancing mass lesion that had no direct connection with the skull base in the left frontal lobe. The patient underwent tumor resection and histopathological examination revealed a mixture of cribriform and tubular patterns. The image and pathological characteristics of the tumor were similar to those of primary ACC or ACC from other sites of origin.

LESSONS  While patients with ACC of the EAC often experience recurrence or distant metastasis in the long clinical course, they survive for a relatively long period of time, even though an optimal treatment has not been established. The authors therefore recommend surgical resection for brain metastasis of ACC of the EAC to improve neurological symptoms.

Illustrative Case  A 72-year-old right-handed male was initially diagnosed with ACC of the left EAC (TNM staging; T1 N0 M0), following partial resection of the tumor at a nearby hospital (Fig. 1A–C). Two years later, multiple pulmonary nodules were identified using 2-deoxy-2-[fluorine-18] fluoro-D-glucose-positron emission tomography/computed tomography (CT). A CT-guided percutaneous lung biopsy was performed and revealed lung metastases of ACC (Fig. 1D and E). Almost a year later, a metastatic lesion was found in the left parotid lymph node, and a superficial parotidectomy was performed at the same hospital. Subsequently, the patient was treated with adjuvant chemotherapy including tegafur, gimeracil, oteracil, and docetaxel. He was followed up in the outpatient ward and did not receive any further treatment.

KEYWORDS  adenoid cystic carcinoma; external auditory canal; brain metastasis

ABBREVIATIONS  ACC = adenoid cystic carcinoma; CT = computed tomography; EAC = external auditory canal; MRI = magnetic resonance imaging.

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chemotherapy after January 2014. Approximately 1 year later, the patient presented with facial palsy and dysarthria, both of which he had experienced for several weeks already. Brain magnetic resonance imaging (MRI) revealed an intra-axial homogeneously enhancing mass lesion in the left frontal lobe (31 × 34 mm in size), which had no direct connection with the skull base (Fig. 2A–D). The patient was referred to...
our department and underwent resection of the tumor a month later. The tumor fit into the precentral sulcus, and the boundary between the normal brain and the tumor was relatively clear (Fig. 3A). Thus, complete resection of the tumor was achieved (Fig. 3B and C). Histopathological examination of the resected tumor revealed a mixture of cribriform and tubular patterns (Fig. 4A). Cribriform structures displayed variably sized pseudocysts filled with Alcian blue-positive mucinous material surrounding basaloid cells with hyperchromatic nuclei (Fig. 4B). Tumor cells were positive for AE1/AE3 (Fig. 4C), with a subset of cells stained for p63 (Fig. 4D), suggesting that the tumor was mainly composed of both epithelial and myoepithelial neoplastic cells. p53 (Fig. 4E) and Ki-67 (Fig. 4F) expression were detected in the tumor cell nuclei. Based on these pathological analyses, the patient was finally diagnosed with metastatic ACC tumor. He experienced no postoperative neurological complications and was discharged after 17 days. Although the patient had an uneventful course after the surgery without recurrence for 1.5 years, multiple brain metastases were found in September 2016, and his clinical neurological status deteriorated eventually (Fig. 1C). It has been reported that surgery does not improve survival outcomes for intracranial solitary metastasis with no evidence of leptomeningeal metastasis. Importantly, low-intensity lesions on T2-weighted MRI are correlated with high tumor cellularity (solid subtype) and a poor prognosis.13 In our case, brain metastatic lesions exhibited a homogenously high signal on T2-weighted MRI, and pathological findings revealed that a major part of the tumor showed a mixture of cribriform and tubular patterns. These data are consistent with the characteristics of primary ACC.

We speculate that the mechanism of spread of this tumor is hematogenous metastasis, because the tumor in this case was a solitary metastasis with no evidence of leptomeningeal metastasis on MRI and intraoperative findings such as thickening of the dura mater or arachnoid membrane. Merchesini et al.15 reported that in their case, the mechanism of dissemination of ACC of the EAC seemed to be direct invasion to the brain surface and subsequent spreading by cerebrospinal fluid seeding. The lesion we observed was inconsistent with direct invasion and the primary lesion in the EAC was stable. Therefore, this mechanism does not seem to apply to our case.

Important factors related to improved survival outcomes after surgery in patients with a single brain metastatic lesion are good Karnofsky performance status and a limited number of extracranial metastases.16 In our case, the patient had already been diagnosed with multiple progressive lung metastases and pleural dissemination of the ACC (Fig. 1C). It has been reported that surgery does not improve survival outcomes for intracranial solitary metastasis with
progressive and multiple extracranial metastases of other carcinomas, such as lung cancer and breast cancer. Therefore, radiation therapy may be a good treatment option for these patients. Surgical resection is often not indicated for brain metastasis as a part of systematic metastases because it is considered a radical approach. However, ACC has an uncommon clinical course. Although data suggest that 40% of patients diagnosed with ACC of the EAC experience tumor recurrence in the protracted clinical course (median time to recurrence: 8 years), they survive for more than 2.8 years even after tumor recurrence; these unique characteristics of ACC therefore need to be considered when selecting therapeutic strategies.8

Marchesini et al.15 recently reported intramedullary spinal cord metastases of the ACC of the EAC with multiple disseminated lesions in the brain. The patient underwent spinal cord tumor removal despite the advanced stage of the disease to improve their neurological symptoms. Our patient also underwent brain tumor resection even after multiple lung metastases had been detected. As a result, his neurological status improved after the surgery, and he survived 1.5 years without recurrence.

**Lessons**

We report a rare case of ACC of the EAC with a metastatic brain tumor. To date, there are no reports of brain metastasis of ACC of the EAC that provide detailed imaging and pathological findings due to the rarity of this tumor. It has thus not been clarified whether brain metastasis of ACC of the EAC can be managed the same way ACC of other origins is managed. Here, we show that the pathological and imaging characteristics of ACC of the EAC are

**TABLE 1. Cases of central nerve system metastases from ACC of the EAC**

| Authors & Year | Age | Sex | Location            | Other Distant Metastases | Main Histology | Previous Treatment                          | Time to CNS Metastases (yrs) | Symptoms                   | Therapy Following CNS Metastases Diagnosis |
|----------------|-----|-----|---------------------|--------------------------|----------------|--------------------------------------------|-------------------------------|---------------------------|-------------------------------------------|
| Conlin et al., 200214 | 38  | Male| Parietal lobe       | None                     | Solid          | Surgery                                    | 1                            | Headache                  | Biopsy                                    |
| Marchesini et al., 202115 | 54  | Male| Cerebellum, parietal lobe, intramedullary conus | Lung, parotid gland | Cribriform & tubular | Surgery, radiotherapy (70 Gy), chemo (adriamycin/cisplatin) | 11                           | Gait disturbance sphincter impairment | Surgery (intramedullary conus lesion) |
| Current case | 72  | Male| Frontal lobe        | Lung, parotid lymph node | Cribriform & tubular | Surgery, chemo (tegafur/gimeracil/otracil) | 7                            | Facial palsy & dysarthria       | Surgery                                   |

chemo = chemotherapy; CNS = central nervous system.
similar to those of primary ACC or ACC originating from other sites. In this case, we showed the pathological and image characteristics are similar to those of primary ACC or ACC originating from other sites. Patients with ACC of the EAC often experience recurrence or distant metastasis in the long clinical course, but they survive for a relatively long period of time, even though an optimal treatment has not been established. Therefore, surgical resection for brain metastasis of ACC of the EAC to improve the patient’s neurological symptoms is recommended.

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Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: K Motomura, Kuramitsu, Kageyama. Acquisition of data: Kuramitsu, Tsujiuchi, A Motomura, Kageyama, Kojima, Ohno. Analysis and interpretation of data: Kuramitsu, Kageyama, Kojima. Drafting the article: K Motomura, Kuramitsu, Kageyama. Administration/technical/material support: Nakajima, Matsuo, Fukaya. Study supervision: K Motomura, Saito.

Correspondence
Kazuya Motomura: Nagoya University School of Medicine, Nagoya, Japan. kmotomura@med.nagoya-u.ac.jp.