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Malignant Transformation of an Intracranial Large Epidermoid Cyst With Leptomeningeal Carcinomatosis

—Case Report—

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Abstract

A 64-year-old female presented with rapid onset of left ophthalmoplegia and truncal ataxia, after experiencing diplopia due to left abducens nerve palsy for a year. She had undergone surgery twice for left trigeminal neuralgia caused by a large intracranial epidermoid cyst at the age of 48 and 52 years. The intracranial epidermoid cyst grew and became predominantly enhanced by contrast medium on computed tomography (CT) and T_1-weighted magnetic resonance (MR) imaging, which had not been observed earlier. The tumor was partially removed and the histological diagnosis was squamous cell carcinoma (SCC). Radiation therapy was administered, but she presented with paraplegia of the bilateral lower extremities and anesthesia due to spinal multiple metastases of SCC one year later. Radiation therapy was administered for the spinal lesions, but she died of multiple metastases to the cerebellum and medulla oblongata with hydrocephalus 2 years after the third surgery. Transformation of intracranial epidermoid cysts to SCC appears as predominant enhancement on CT or T_1-weighted MR imaging with rapid deterioration of neurological features. All reported cases of malignant transformation of intracranial epithelial cysts to SCC with leptomeningeal carcinomatosis have occurred in intracranial epidermoid cysts.

Key words: intracranial epidermoid cyst, squamous cell carcinoma, malignant transformation, leptomeningeal carcinomatosis, brain neoplasm

Introduction

Intracranial epidermoid cysts (IECs) account for approximately 0.2–1% of brain tumors,[29] and develop from aberrant ectodermal embryonic tissue in the neural groove at 4 or 5 weeks of fetal development. IECs are generally thought to be benign and potentially curable by surgery. Malignant transformation of an IEC to squamous cell carcinoma (SCC) is rare, and such malignant transformation associated with leptomeningeal carcinomatosis

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Table 1 Cases of malignant transformation of intracranial epithelial cysts with leptomeningeal carcinomatosis

Author (Year)	Age (yrs)/ Sex	Location	Original diagnosis	Final diagnosis	Notes
Ernst-Heidelberg (1912)[7]	52/M	CPA		EC, SCC	CSF cytology, autopsy
Yamanaka et al. (1955)[36]	57/M	base of brain		EC, SCC	autopsy
Landers and Danielski (1960)[21]	73/F	cerebellar vermis		EC, SCC	autopsy
Fox and South (1965)[8]	50/M	temporal	EC	SCC	autopsy, Op(+)
Koempf and Menges (1977)[19]	57/F	parapontine		EC, SCC	CSF cytology, autopsy
Takado et al. (1982)[32]	53/F	parapontine		EC, SCC	autopsy
Bondeson and Faelt (1984)[5]	56/F	CPA		EC, ECa	CSF cytology, autopsy
Maffazzoni et al. (1986)[24]	45/M	fronto-basal		EC, ECa	surgery
Ishimatsu et al. (1988)[15]	40/M	CPA		EC, SCC	myelography, autopsy, Op(+)
Gi et al. (1990)[10]	39/M	CPA		EC, SCC	myelography, Op(+)
Mohanty et al. (1996)[25]	20/M	midline PF		EC, SCC	autopsy, Op(+)
Ishikawa et al. (2000)[14]	65/M	CPA		EC, SCC	autopsy
Asahi et al. (2001)[3]	55/F	CPA		EC, ECa	MR imaging, Op(+)
Khan et al. (2001)[16]	53/M	prepontine		EC, SCC	MR imaging
Shirabe et al. (2003)[31]	49/M	ventral pons		EC, SCC	autopsy
Hamlat et al. (2003)[11]	54/F	medial temporal	EC	SCC	MR imaging, cytology, autopsy, Op(+)
Kodama et al. (2007)[18]	67/M	CPA, MO	EC	SCC	MR imaging, autopsy, Op(+)
Pagni et al. (2007)[28]	65/F	pineal		EC, SCC	MR imaging, cytology, Op(+)
Present case	64/F	parapontine, lt medial temporal	EC	SCC	MR imaging, Op(+)

CPA: cerebellopontine angle, CSF: cerebrospinal fluid, EC: epidermoid cyst, ECa: epidermoid carcinoma, MO: medulla oblongata, MR: magnetic resonance, Op(+): operation suspected to cause leptomeningeal carcinomatosis, PF: posterior fossa, SCC: squamous cell carcinoma.

(LC) is extremely rare, with only 18 reported cases (Table 1).[3,5,7,8,10,11,14–16,18,19,21,24,25,28,31,32,36] We describe a case of malignant transformation of an IEC to SCC associated with LC, originating as a large cystic lesion, located in the left parapontine to left medial temporal region, which underwent malignant transformation 16 years after the first surgery or 17 years after the onset of clinical symptoms, and showed LC 2 years later.

Case Report

A 64-year-old female had first presented with severe left trigeminal neuralgia at the age of 48 years. Magnetic resonance (MR) imaging revealed a large cystic lesion extending from the left parapontine to the left medial temporal regions, with partial enhancement of the capsule after intravenous administration of gadolinium-diethylenetriaminepenta-acetic acid (Fig. 1A, B). The tumor was removed through combined subtemporal and lateral suboccipital approaches on May 17, 1989. The tumor contained soft cheesy yellow materials and compressed the left trigeminal nerve. The tumor in the cerebellopontine angle (CPA) region was removed, but the tumor in the medial temporal region was not completely resected. The histological diagnosis was epidermoid cyst (Fig. 2A). She again presented with severe left trigeminal neuralgia at age 52 years, about 3 years after the first surgery. MR imaging suggested regrowth of the tumor extending to the upper medulla oblongata. Second subtotal resection of the recurrent tumor was performed on April 7, 1992. After the second surgery, her left trigeminal neuralgia was well controlled by administration of 300 mg/day carbamazepine and 6 mg/day diazepam.

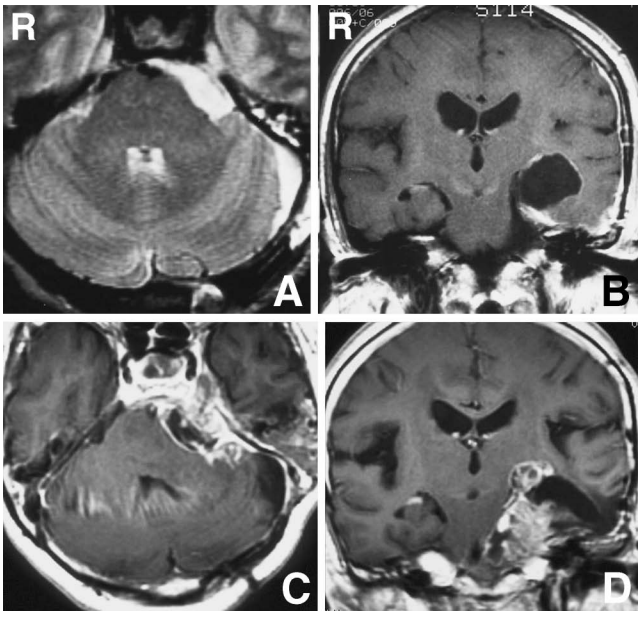

Fig. 1 A: Axial T_2-weighted magnetic resonance (MR) image before first surgery revealing a cystic lesion in the left parapontine region. B: Coronal T_1-weighted MR image with gadolinium before first surgery revealing a large cystic lesion extending to the left parapontine region, measuring 3.5 × 2.5 cm in the left medial temporal region with rim enhancement in the tumor capsule. C, D: Axial (C) and coronal (D) T_1-weighted MR images with gadolinium about 12 years after second surgery revealing growth of the cystic lesion with predominant enhancement and severe compression of the pons, mainly located in the left upper portion of the pons and invading the surrounding structures.

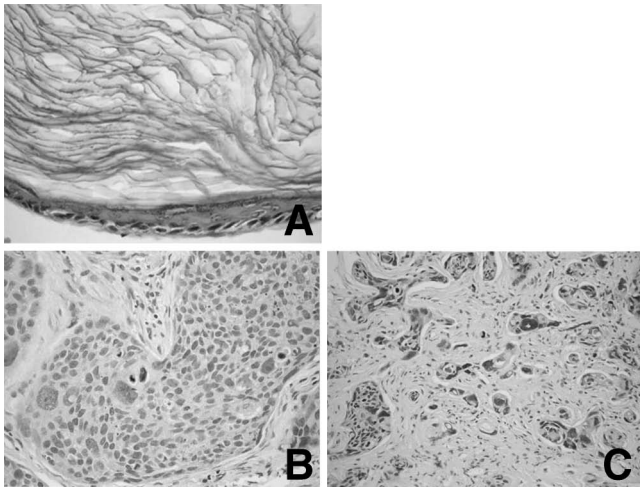

Fig. 2 A: Photomicrograph of the first surgical specimen showing well differentiated squamous cell epithelium with multilayered keratin debris, consistent with an epidermoid cyst. Hematoxylin and eosin stain, original magnification × 400. B, C: Photomicrographs of the third surgical specimens showing proliferation of anaplastic epithelial neoplasm consisting of anaplastic cells with pleomorphic nuclei and many mitotic figures, consistent with squamous cell carcinoma (B), and islands of squamous cell carcinoma infiltrating into the surrounding tissues (C). Hematoxylin and eosin stain, original magnification B: ×400, C: ×200.

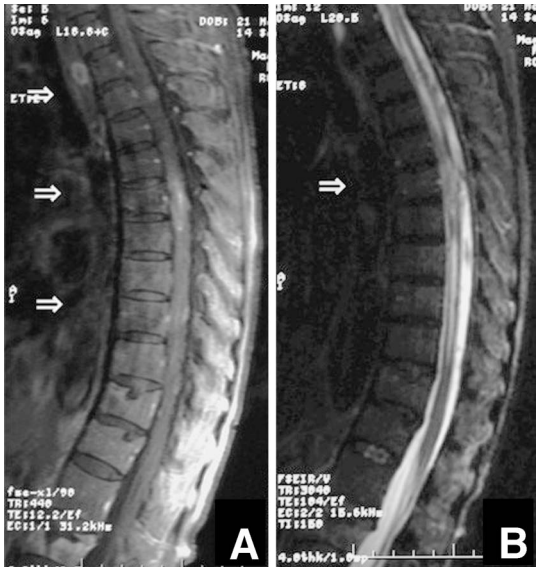

Fig. 3 A: Sagittal T_1-weighted magnetic resonance (MR) image with gadolinium about one year after first radiation therapy showing multiple spinal enhanced lesions and compressed pathologic fractures in T6, T11, T12, and L2 vertebrae. The *arrows* indicate the metastatic spinal lesions at T3, T6, and T9 levels. B: T_2-weighted MR image about one year after first radiation therapy showing metastatic lesions with syrinx. The *arrow* indicates the metastatic lesion at T6 level.

She presented with double vision due to left abducens nerve palsy at age 63 years, about 11 years after the second surgery. MR imaging did not reveal any responsible lesion. She presented with left ophthalmoplegia and truncal ataxia at age 64 years. Computed tomography (CT) and T_1-weighted MR imaging revealed the enlarged tumor predominantly enhanced by contrast medium (Fig. 1C, D), located in the left parapontine to left medial temporal regions with cystic lesions, and severely compressing the pons. Third subtotal removal of the recurrent tumor was performed through a left lateral suboccipital approach on June 16, 2004. The tumor had grown to involve the fifth, seventh, and eighth cranial nerves, and severely compressed the pons, so only a small part of the tumor could be resected. Histological examination of the third surgical specimen revealed SCC in the lesion (Fig. 2B, C) that had been previously diagnosed as IEC. Whole body CT failed to identify any possible primary lesion for the intracranial SCC. Radiation therapy (local 50 Gy) was administered for the residual tumor following the third surgery.

She presented with gait disturbance aged 65 years in August 2004, about one year after the radiation therapy. Neurological examination disclosed paraplegia of the bilateral lower extremities and anesthesia under the T8 level in September 2004. MR imaging revealed multiple spinal metastases of the tumor and multiple spinal fractures (Fig. 3). Additional radiation therapy (whole spine 50 Gy) was administered for the spinal lesions. However, she died on July 12, 2006 of multiple metastases to the cerebellum and medulla oblongata with hydrocephalus.

Discussion

Malignant transformation of intracranial epithelial cysts to malignant tumors appears as predominant enhancement by contrast medium on CT and T_1-weighted MR imaging.[17,20,22,34] In the present case, the rapid deterioration of symptoms was concomitant with predominant enhancement of the tumor on CT and T_1-weighted MR imaging, thus suggesting extremely rare malignant transformation of an IEC. The malignant transformation of the IEC in the present case was thought to arise from the lesion in the upper CPA, because the enhanced lesion was mainly located in the upper portion of the CPA with extension to the left medial temporal region (Fig. 1C, D).

Rim enhancement of the capsule of the IEC on T_1-weighted MR imaging[13] in this case (Fig. 1B) suggests that trigeminal neuralgia at the onset may have been caused by chemical meningitis caused by inflammation in the surrounding tissues due to rupture of the IEC. Acute, or very rapid, deterioration in symptoms is usually observed at the onset of malignant transformation of benign epithelial cysts.[12] Our patient had experienced chronic left trigeminal neuralgia for over 15 years, and left ophthalmoplegia and cerebellar ataxia rapidly appeared following left abducens nerve palsy over a year. Therefore, malignant transformation of the IEC was associated with rapid deterioration of her neurological symptoms, and was suspected to have arisen at the onset of left abducens nerve palsy. The series of neurological changes in our patient and the location of the enhanced lesion on CT and MR imaging sug-

Table 2 Criteria for diagnosis of malignant transformation of intracranial epithelial cysts

Garcia's criteria[9]:
1. Tumor restricted to the intracranial and intradural compartment
2. No extension beyond the dura, cranial orifices, or connection with the middle ear, air sinuses, or sella turcica
3. No evidence of nasopharyngeal tumor
Additions by Hamlat et al.[12]:
4. Presence of benign squamous cell epithelium within the malignant tumor
5. Metastasis of carcinoma excluded

Table 3 Classification of malignant transformation of intracranial epithelial cysts into five groups[12]

1. Initial malignant transformation of epidermoid cyst
2. Malignant transformation from remnant epidermoid cyst
3. Malignant transformation of dermoid and epithelial cyst
4. Malignant transformation with leptomeningeal carcinomatosis
5. Other malignancies arising from benign cysts

gest that the malignant transformation might have arisen in the lesion near the CPA.

Benign squamous cell epithelium in the malignant tumor is important under Garcia's criteria[9] (Table 2), which strictly define primary intracranial SCC, as to when the malignant transformation of IEC to SCC occurs.[30] Malignant transformation of intracranial epithelial cysts can be divided into five groups under Hamlat's classification (Table 3),[12] suggesting that only 18 reported cases were malignant transformations of IECs with LC (Table 1). Although Hamlat's classification is very useful to understand the malignant transformation of the IEC, two types of cases must still be considered, primary intracranial SCC and malignant transformation of remnant IEC.

All 19 reported cases, including the current case, originated from epidermoid cysts. This may be related to the clinical finding that almost all cases of malignant transformation originated from IECs, with only 6 cases of malignant transformation arising from dermoid cysts of 44 cases of IECs.[12] There were 11 males and 8 females aged from 20 to 73 years (mean 53.4 years). Fourteen of the 19 cases were under the cerebellar tent, and 4 of 19 cases were above the cerebellar tent. Such lesions occur under the cerebellar tent because the CPA or parapontine region is the most common site of IECs.[2,12,35]

LC is thought to form due to wide dissemination of tumor cells from an intradural primary lesion, leptomeningeal seeding by tumor cells in the cerebrospinal fluid, or both. A leptomeningeal metastatic lesion may develop far from the primary lesion without continuity to the primary lesion through leptomeningeal seeding of tumor cells in the cerebrospinal fluid. Therefore, surgery might also cause LC. Nine of the 19 cases were related to surgery, indicating that surgery for IECs might carry the risk of LC through seeding. LC is usually only identified at autopsy, but recently MR imaging has also established the diagnosis in patients.

The mechanisms of malignant transformation of IECs are controversial, and may involve inflammation caused by reaction to foreign bodies or in situ carcinoma. Materials contained within the cyst may cause repeated inflammation during over a long period and trigger malignant transformation of the intracranial epithelial cysts.[1,27,37] In contrast, in situ carcinoma might grow and infiltrate around the tissues after a long period of no tumor growth and trigger malignant transformation of the intracranial epithelial cyst.[4,6,27] In the present case, trigeminal neuralgia was caused by inflammation due to the rupture of the IEC, based on the rim enhancement observed on MR imaging before the first surgery, so the malignant transformation of the IEC in the current case cannot be explained by only inflammation, because long-standing inflammation[37] was not observed in the current case.

Radiation therapy for intracranial SCC has been effective over a short period, and radiation therapy for remnant SCC is widely used. Stereotactic radiation therapy following the surgery is also effective in some cases, with disease-free survival of more than 5 or 8 years[26,33] or local tumor control for 29 months[23] following stereotactic radiation therapy. However, no effective therapies for LC have been reported. In addition, almost all cases of LC have been associated with rapid deterioration of the patients' general condition, ending in death.

Malignant transformation of IEC to SCC with LC is extremely rare. The intracranial epithelial cysts were all IECs in the 19 reported cases. Therefore, malignant transformation from IECs to SCC is more likely than from other intracranial epithelial cystic lesions.

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