Clinical Case Report

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Intracranial squamous cell carcinoma arising in a cerebellopontine angle epidermoid cyst

A case report and literature review

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Abstract

Rationale: Most of the intracranial epidermoid cysts are benign, but malignant lesions are occasionally reported. These lesions appear as squamous cell carcinoma and carry a dismal prognosis. Here, we report a case of a primary intracranial squamous cell carcinoma arising in a cerebellopontine epidermoid cyst. The relevant literatures were also reviewed.

Patient concerns: A 53-year-old woman presented with dizziness and diplopia 9 months in duration. Magnetic resonance imaging revealed an epidermoid cyst in the left cerebellopontine angle and prepontine region with a focal enhancing lesion on T1-weighted gadolinium-enhanced images.

Diagnoses: Histopathologic diagnosis revealed squamous cell carcinoma on a background of epidermoid cyst. Imaging studies excluded metastases.

Interventions: The tumor was removed subtotally through a lateral suboccipital approach. The patient received intensity modulated radiation therapy (6720 cGy total) postoperatively.

Outcomes: The patient was free from recurrence of the tumor until 3 years after surgery, at which point she was lost to follow-up. The patient died 4 years after the surgery.

Lessons: The epidermoid cyst may occasionally become malignant. Finding an area of enhancement through preoperative magnetic resonance imaging can help to make a correct diagnosis. Based on the review of previous reports, surgical removal followed by radiotherapy shows the best result to treat malignant epidermoid cysts.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, PET = positron emission tomography, SCC = squamous cell carcinoma, WBBS = whole body bone scan.

Keywords: brain neoplasms, cerebellopontine angle, epidermoid cyst, malignant transformation, squamous cell carcinoma

1. Introduction

Intracranial epidermoid cysts are rare congenital lesions that account for 0.2% to 1.8% of brain tumors.[1,2] They are slow-growing benign tumors, thought to arise from misplaced epithelium.[3] They occasionally degenerate into squamous cell carcinoma (SCC), although this is extremely rare. We report the case of a woman with primary intracranial squamous cell carcinoma arising from an epidermoid cyst. The relevant literature for this rare disease is also reviewed.

2. Case report

2.1. History and examination

A 53-year-old woman presented with a 9-month history of dizziness and diplopic vision. She had no relevant past medical history. Ophthalmologic examination revealed lateral gaze palsy of the left eye, suggesting cranial nerve VI palsy. Cranial nerve examination revealed no other cranial nerve abnormalities other than left cranial nerve VI palsy. The patient was awake, alert, and oriented; motor, sensory and cerebellar functions were normal.

2.2. Imaging studies

A non-contrast computed tomography (CT) scan of the head revealed an extra-axial low-density mass in the left cerebellopontine angle cistern extending to the prepontine region. The density of the mass was similar to that of cerebrospinal fluid. The pons and the basilar artery were slightly deviated toward the right due to compression by the mass.

Magnetic resonance imaging (MRI) also revealed an extra-axial mass in the same region (Fig. 1). T1-weighted images without enhancement showed a low-intensity signal and T2-weighted images showed a high-intensity signal, which were consistent with an

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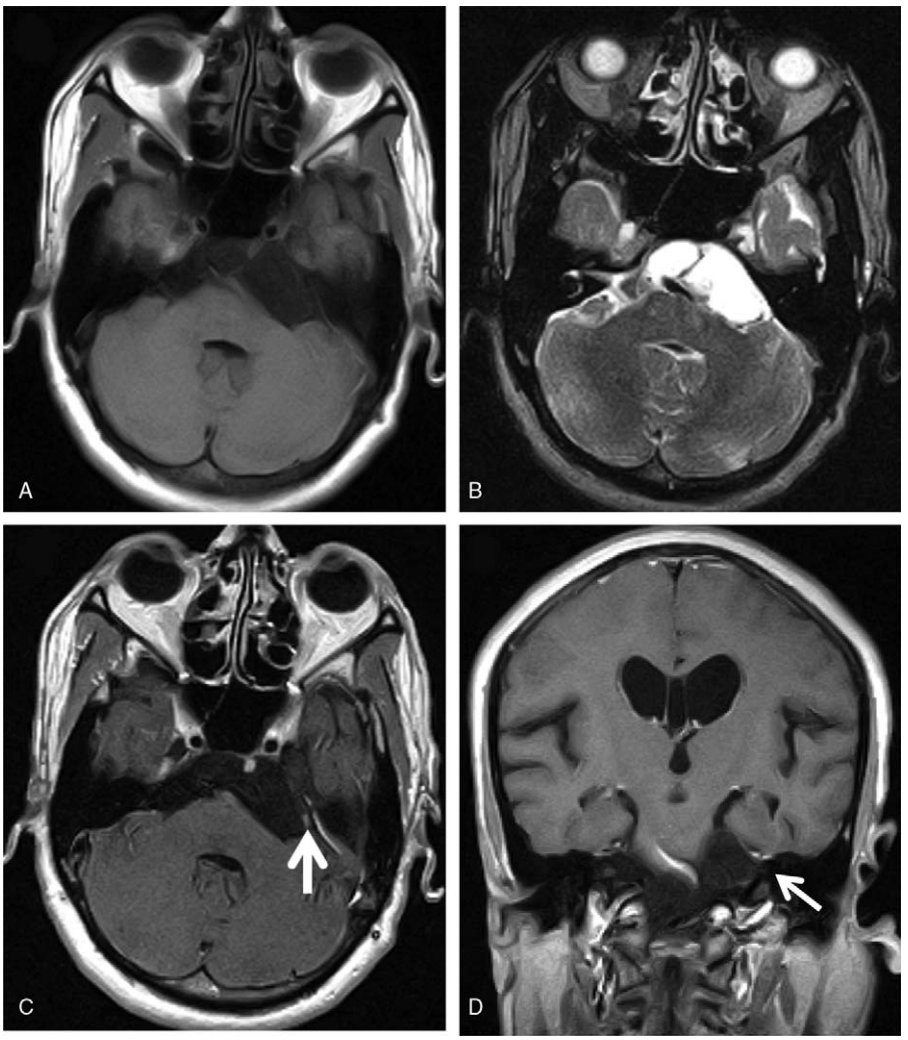

Figure 1. Preoperative MRIs show a cyst-like lesion in the left cerebellopontine and prepontine cistern on (A) T1-weighted axial image, and (B) T2-weighted axial image. On contrast enhanced (C) axial and (D) coronal images, the lesion shows a faint enhancement in its lateral portion (arrows). MRI = magnetic resonance imaging.

epidermoid cyst. There was no peritumoral edema; however, the T1-weighted images with enhancement by gadolinium-diethylene triamine pentaacetic acid showed a small, enhanced portion in the mass, which is not a typical feature of epidermoid cysts.

2.3. Surgical treatment and outcome

A left suboccipital craniotomy was performed and the tumor was gross totally resected. The tumor was pearly white, and appeared to have the typical gross appearance of an epidermoid cyst. Cranial nerves were identified and preserved.

Postoperatively, the patient had mild facial weakness, which improved gradually. Sixth cranial nerve palsy and hearing impairment remained the same.

One month after surgery, the patient began to receive intensity-modulated radiotherapy for a total dose of 67.2 Gy in 28 fractions. The patient tolerated the radiotherapy well.

2.4. Pathological findings

Histologic examination of the resected tumor specimen revealed the histological features of a poorly differentiated squamous cell carcinoma. However, in some portions, the tumor contained multiple layers of squamous epithelium lining and lamellar keratin, which are consistent with an epidermoid cyst (Fig. 2).

In order to rule out an extra-cranial primary tumor, abdominopelvic CT, chest CT, positron emission tomography (PET), and whole-body bone scan (WBBS) were performed, and all were normal. Given the histopathological features and the absence of extra-cranial malignancy, the SCC was thought to have arisen from a pre-existing epidermoid cyst.

2.5. Result of treatment

An MRI taken 3 months after the surgery showed a small enhancement in the left tentorium, which was thought to be a radiotherapy-induced change or a postoperative change. Nine months later, the enhanced volume had decreased. The 20-month follow-up MRI revealed that the enhanced portion had nearly disappeared, and showed no evidence of recurrence.

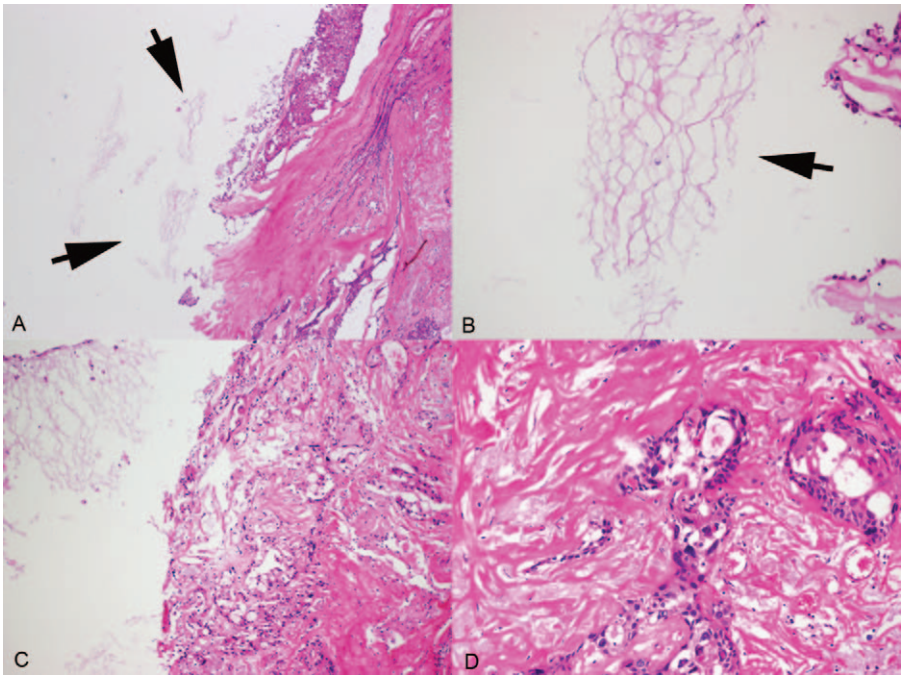

Figure 2. Pathologic findings of squamous cell carcinoma arising epidermoid cyst. Low power view showing thick fibrous tissue (right side) with scattered squames (arrows) (A: ×40, H-E) (B: ×200, H-E). In thick fibrous tissue, the carcinoma cell infiltration is noted (C: ×100, H-E). High power view showing definite infiltrating squamous cell carcinoma cells (D: ×200, H-E).

The patient's sixth nerve palsy had not improved after the radiotherapy, and the hearing impairment was aggravated, resulting in left ear deafness; facial weakness had resolved.

Forty-six months after the surgery, the patient was stable without any new symptoms, and MRI at last follow-up evidenced no recurrence. However, mild ventricular enlargement was suspected. The patient was lost to further follow-up, but was found to have died 4 years after surgery.

3. Methods

A systematic literature review was conducted using PubMed, Medline, and Google Scholar databases to search for relevant English language articles published up to March 2016. The following search terms were used: "malignant epidermoid cyst" OR "intracranial squamous cell carcinoma" OR "epidermoid cyst degeneration." All eligible studies were reviewed, and the references were checked for additional relevant publications. Information and data were extracted from all included literature. Data include patients' age, sex, treatment modality, overall survival, and recurrence-free survival. The ethical approval was not necessary, because this is a retrospective case report. The informed consent of the patient was given.

4. Results

We found 43 previously reported literature cases describing a malignant transformation from an epidermoid cyst (Table 1).[4,5–46] There were 23 men and 21 women in these reports, with a mean age of 54 years (range, 4–74 years), including our patient. Their features do not differ from those of benign epidermoid cysts. Primary intracranial squamous cell carcinomas were present initially in 32 cases, while 12 cases were developed following an interval after the resection of a previous epidermoid cyst.[8,10,23,27,30]

5. Discussion

Most squamous cell carcinomas involve the brain as a manifestation of metastases primarily originating from elsewhere in the body or as a result of direct invasion from head and neck cancer.[47,48] Malignant transformation of an epidermoid cyst is extremely rare, but it has been well documented since Ernst[4] first reported a case in 1912.

Garcia et al[34] defined the criteria for such a malignant transformation as follows: the tumor had to be restricted to the intracranial, intradural compartment without invasion of or extension beyond the dura or cranial bones, and there must be no extension or invasion through intracranial orifices, no communication or connection with the middle ear, air sinuses, or sella turcica, and no evidence of nasopharyngeal tumor.

Hamlat et al[49] reviewed 52 cases fulfilling Garcia's criteria and their additional criteria, as follows: presence of a benign squamous cell epithelium within the malignant tumor, and metastasis of carcinoma were excluded. Their review included SCC arising from other benign cysts rather than an epidermoid cyst, such as dermoid cysts, epithelial cysts, endodermal cysts, and craniopharyngiomas.

The present case fulfills Garcia and Hamlat criteria. No other malignancy found by systemic evaluation. Given that the epidermoid cyst was the only squamous epithelial tissue in the brain, we concluded that the squamous cell carcinoma had developed from a pre-existing epidermoid cyst.

The typical CT appearance of a benign intracranial epidermoid cyst is a low-density lesion in the subarachnoid space without contrast enhancement,[50–53] although the margin of the cyst may exhibit minimal enhancement.[7,54] An enhancement within an epidermoid cyst on CT or MRI suggests malignant transformation.[12] Almost all of the cases we reviewed showed enhancement

Table 1

Reported cases of intracranial squamous cell carcinoma.

Reported cases of intracranial squamous cell carcinoma

Y	Authors	Age	Sex	Location	Treatment	Follow up	LC	Interval from epidermoid cyst
1912	Ernst[4]	52	M	R CPA	Medical	Dead 12 mo	LC	
1960	Davidson and Small[44]	46	M	R Frontal	S + Rx	UD		
1965	Toglia[45]	54	F	Base of brain	S	Dead POD 1 d		1 y
1965	Fox and South[5]	50	M	L Subtemporal	S	Dead 1.5 mo	LC	7 y
1976	Wong[32]	4	M	R CPA	Medical	–		
1977	Kompf and Menges[33]	57	F	Cerebellar	Medical	Dead	LC	
1981	Garcia[34]	61	M	R CPA	S + Rx	Dead 25 mo		
1981	Dubois[46]	53	M	Fourth ventricle	S + Rx	Dead 2 mo		
1983	Lewis[6]	53	F	R Parasellar	S	Dead 1 mo		
1984	Bondeson and Fält[35]	56	F	L CPA	Medical	Dead 21d (Dx)	LC	
1987	Goldman and Gandy[8]	56	F	R Lateral Ventricle	S + RX	Alive 36 mo		33 y
1987	Matsuno[9]	43	M	CPA	S + Ch + Rx	Dead 28 mo		
1987	Salazar[7]	49	M	CPA and Pons	S + Rx	Alive 10 mo		3 mo
1989	Nishiura[36]	38	M	R CPA	S + Ch	Alive 24 mo		6 mo
1991	Tognetti[10]	67	F	R Temporal Lobe	Surgery alone	Dead 1 mo		1 y
1993	Acciari[11]	62	M	R Parasellar	Surgery alone	Dead 1 wk		
1995	Mori[14]	42	M	R CPA	S + Ch + Rx	Dead 26 mo		
1995	Nishio[13]	58	M	R CPA	S + Rx	Alive 30 mo		
1995	Uchino[12]	57	M	CPA	S + Rx	Alive 4 mo		
1995	Fuse[37]	74	F	CPA	S + Rx	Dead 12 mo		
1996	Mohanty[16]	20	M	Cerebellar	S + Rx	Dead 13 mo	LC	
1996	Bayindir[15]	67	F	Intra ventricular	S	Alive 26 mo		
1999	Murase[38]	50	F	R CPA	S + Ch + Rx	Alive 60 mo		10 y
2000	Ishikawa[39]	65	M	CPA	Ch + Rx	Dead 10 mo	LC	
2000	Sawan[40]	66	M	Pre pontine	Shunt	Dead 9 mo		
2001	Asahi[17]	55	F	CPA	S	Dead 3 mo	LC	13 y
2001	Nawashiro[18]	46	M	Temporal	S	UD		
2001	Khan[41]	53	M	Pre pontine	Shunt	Dead 10 mo	LC	
2002	Link[42]	57	F	L CPA	S + Rx	Dead 35 mo		12 mo
2003	Monaco[57]	36	M	Cysterna magna	Surgery alone	Alive 24 mo		
2003	Shirabe[43]	49	M	Ventral pons	S + Rx	Dead 42 mo		
2004	Hamlat[20]	62	F	temporal	Ch	Dead 7 mo	LC	
2003	Park and Park[29]	65	F	R CPA	S + Rx	Alive, 6 mo		
2003	Akar[19]	UD	F	–	S	Dead, 5 mo	–	
2004	Guan[58]	42	F	Temporal	S + Rx	Alive, 12 mo		
2005	Michael[21]	45	M	L CPA	S + Rx	Dead 12 mo	LC	
2006	Ge[25]	50	M	temporal lobe	S	UD		6 y
2007	Pagni[23]	65	F	pineal region	S	UD	LC	
2007	Agarwal[22]	45	M	posterior fossa	S	UD		
2008	Hao[28]	63	F	prepontine	S	Dead 1.2 mo		
2008	Kim[24]	72	F	R CPA	S + Rx	Alive 12 mo		
2010	Kano[26]	64	F	L CPA	S + Rx	Dead 25 mo	LC	16y
2010	Nakao[27]	74	F	Base of brain	S + Rx	Alive 17 mo		20y
2012	Present case	53	F	L CPA	S + Rx	Dead 48 mo		

Ch = Chemotherapy, CPA = cerebellopontine angle, F = female, L = left, LC = leptomeningeal carcinomatosis, M = male, R = right, Rx = Radiotherapy, S = surgery, Sx = symptom.

within the tumor, and, in some cases, malignant transformation of the enhanced portion was proven.[6,13,16,46] In Kodama's case, the enhanced nodule was not resected during surgery and the pathological findings revealed an epidermoid cyst without malignant change[31]; however, a follow-up MRI 2 months after the surgery revealed growth of the enhanced region. The patient underwent stereotactic radiosurgery, but died 13 months after the first MRI evaluation. An autopsy revealed a poorly differentiated SCC originating from the epidermoid cyst. This case emphasizes that enhancement within an epidermoid cyst should be considered a sign of malignancy, and should be removed as possible.

Sudden development of symptoms or a growing epidermoid cyst seen on imaging study also suggests a malignant change.[49] Epidermoid cysts grow linearly, thus, if they show exponential growth, malignant change should be considered.[55]

Diffusion-weighted MRI could be useful for the differential diagnosis of epidermoid cysts and SCC. A normal epidermoid cyst shows diffusion restriction on diffusion-weighted MRI, whereas transformed squamous cell carcinoma may not.[18,31]

The ideal treatment of epidermoid cysts is complete removal of the tumor and capsule[2]; however, this may result in unacceptable morbidity and mortality.[7] The remnant tumor could lead to cyst recurrence or malignant transformation. If a patient has a

remnant epidermoid cyst, follow-up to check for possible recurrence or a malignant transformation is necessary. The enhanced portion of the tumor should be removed to as great an extent as possible for accurate diagnosis and proper treatment. However, whether total resection of the tumor raises the survival rate compared with subtotal resection has not yet been investigated. Aggressive resection sometimes results in postoperative mortality.[6,10,11]

Postoperative radiotherapy has been used for the treatment of intracranial SCC and has been proven to improve short-term survival. Nagasawa et al[56] reviewed 36 cases of malignant epidermoid tumors and compared survival outcomes between the surgery-alone group and the surgery plus radiotherapy group. Patients treated with surgery alone had an overall survival of 6.6 months, whereas those treated with postoperative radiotherapy demonstrated a statistically significant increase in survival of 12.7 months (log-rank test, $P < .003$). The mean dosage used during radiotherapy for the malignant epidermoids was 52.2 Gy. There was no significant correlation detected between the radiation dose and the survival outcome.

Radiosurgery can be used as an alternative or adjuvant to radiotherapy. There have been 4 reported cases in which stereotactic radiosurgery was applied to the treatment of malignant epidermoid cysts. Tamura et al[30] performed a meta-analysis for the survival of 24 intracranial malignant epidermoid cysts. The median survival time for patients treated with surgery alone (n = 9), surgery plus external-beam radiation (n = 11), and surgery plus stereotactic radiosurgery (n = 4) were 1, 18, and 44 months, respectively (log-rank test, $P < .004$). However, this study was insufficient to advocate radiosurgery as a standard treatment. Because it was a retrospective study, there may have been selection bias, and the number of cases was small.

The prognosis of malignant epidermoid cyst is poor. Of the 43 cases of malignant epidermoid cysts we reviewed, 13 patients were reportedly alive, only 1 patient survived to 5-year follow-up, while 26 patients eventually died.[38] All 11 patients with leptomeningeal carcinomatosis died.

The unique point of our patient is that the preoperative MRI showed the appearance of a typical epidermoid cyst, with only a small enhancement. Unless the possibility of a malignant epidermoid cyst has been considered in advance, it may not have been found in squamous cell carcinoma in pathologic results. An accurate diagnosis enabled adjuvant radiotherapy of this patient and resulted in relatively long survival period compared with the cases reported so far.

6. Conclusion

Malignant transformation of an epidermoid cyst is rare, and exhibits poor prognosis. The standard treatment for malignant epidermoid cyst is surgery and radiotherapy. Radiosurgery may replace or reinforce radiotherapy. Malignant transformation should be considered when the cyst exhibits contrast enhancement.

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