Accepted Manuscript online: 2022-05-22 Article published online: 2022-06-24

Malignant Transformation of Recurrent Residual Cerebellopontine Angle Epidermoid Tumor: Significance of Clinical Vigilance and Long-Term Surveillance

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J Neurol Surg Rep 2022;83:e63–e66.

Abstract

Epidermoid tumors (ET) are slow-growing masses where malignant transformations occur extremely rarely. Malignant transformation warning signs are the rapid-onset, progression, and recurrence of symptoms. The radiologic evidence for malignant transformation is contrast enhancement with rapid growth, observed with magnetic resonance imaging (MRI) or computed tomography scans. Here, we provide a case report of a 68-year-old woman with a long-standing history of left-sided cerebellopontine angle ET who presented with a recent worsening of symptoms, and MRI observation of new ET contrast enhancement. Surgical re-exploration and histopathologic confirmation are mandatory in this setting of recent symptom worsening and MRI observation of rapid mass growth.

Keywords

- brain tumor
- cerebellopontine angle
- epidermoid tumor
- malignant transformation
- rapid progression
- recurrence
- squamous cell carcinoma

Introduction

Epidermoid tumors (ET) are rare slow-growing masses[1] that comprise just 0.2 to 1.8% of all intracranial tumors.[2–4] The duration of symptoms varies from several months to several years.[1] Malignant transformations (MTs) of ETs are extremely rare[1–3] and have a very poor prognosis.[4] The first report of MT of an ET was published in 1912.[1]

The MT interval after primary diagnosis varies from 3 months[3] to 33 years.[2–4] Symptoms are related to the location of the MT, with symptom duration ranging from a few weeks to several years.[3] The warning signs and most important clinical indicators of MT are rapid symptom onset, progression, and recurrence.[2,3] MT is considered likely when magnetic resonance imaging (MRI) or computed tomography (CT) of the radiological feature indicates rapid growth combined with contrast enhancement of over 87.8% of the radiological feature,[3] since no contrast enhancement is expected with an ET that has not transformed.

received
May 5, 2022
accepted
May 12, 2022

DOI https://doi.org/10.1055/a-1858-7483.
ISSN 2193-6358.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

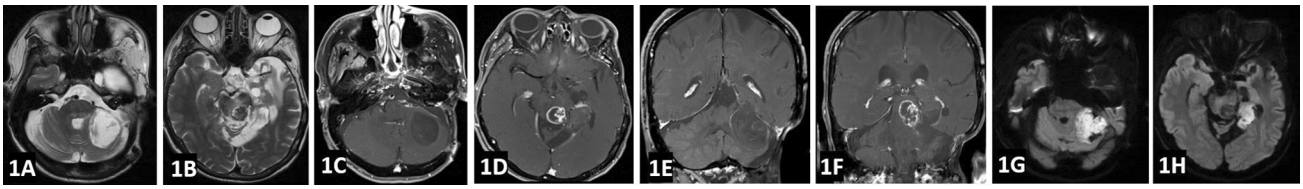

Fig. 1 Presurgical magnetic resonance imaging (MRI). (**A, B**) Axial T2-weighted MRI with a predominantly hypointense 2.3 × 1.9 × 1.9 cm solid mass in the left dorsal midbrain, and left-sided hyperintense 4.2 × 3.8 × 3.2 cm cerebellar cystic mass. Axial (**C, D**) and coronal (**E, F**) MRI show a heterogeneous rim-enhancing mass in the left dorsal midbrain and pons with nonenhancing cerebellar mass. (**G, H**) Axial diffusion-weighted images show cerebellar cystic mass with diffusion restriction, and nonrestricted mass in the left dorsal midbrain.

Case Report

The patient was a 68-year-old woman with a long-standing history of a left-sided cerebellopontine angle (CPA) ET that was first resected 37 years ago, at the age of 31. She underwent multiple middle and posterior cranial fossa procedures in the intervening years as well as radio frequency radiation treatment (25 years ago, at the age of 43) of this recurrent and slowly growing ET. This left her with left-sided hemifacial paresthesia and mild facial weakness. She recently (18 months ago, at the age of 66) underwent a retrosigmoid approach for resection of ET at an outside hospital, which left her with high-grade facial nerve palsy and left-sided hearing loss. She was referred for facial nerve rehabilitation and tarsorrhaphy to the rehabilitation clinic at our hospital, where she then reported recent imbalance and blurred vision. At that time, a new MRI revealed a heterogeneous rim-enhancing 2.3 × 1.9 × 1.9 cm solid mass in the left dorsal midbrain and pons that was causing mass effect on the cerebral aqueduct. It was predominantly hypointense on T2-weighted images without diffusion restriction on diffusion-weighted imaging (DWI). There was an additional left-sided 4.2 × 3.8 × 3.2 cm cerebellar cystic mass with diffusion restriction on DWI, and extensive postsurgical changes, presumably related to prior left middle and posterior cranial fossa tumor resections over the last several decades. This appeared compatible with the recurrent ET, as well as gliosis and encephalomalacia (►**Fig. 1A–H**).

She underwent a left-sided paramedian suboccipital approach and microsurgical gross total resection of both components of the mass (►**Fig. 2A–H**). The pathology report for an intraoperative frozen section for the brain stem lesion described shards of keratin with epithelium and reactive peripheral nervous system changes consistent with ET. The surgery and postoperative course were uneventful, and the patient was discharged to home.

Forty-five days after discharge, the patient presented with worsening imbalance and dysmetria. MRI revealed a large recurrent heterogeneous rim-enhancing mass within the dorsal left midbrain measuring 3.1 × 2.3 × 2.3 cm, with resultant mass effect on the cerebral aqueduct and inferior third ventricle (►**Fig. 3A–H**). She underwent a paramedian posterior fossa craniotomy with a supracerebellar approach for microsurgical subtotal (90%) resection of the rapidly growing recurrent midbrain mass (►**Fig. 4A–H**). The surgery was uneventful but the patient's postoperative course was complicated with increased frequency of her pre-existing seizures. Eventually these were controlled with increased dosage of her medications. The histopathologic diagnosis was squamous cell carcinoma (SCC) arising in the ET (►**Fig. 5A** and **B**). A re-review of the initial pathology revealed nuclear atypia that was attributed to postradiation

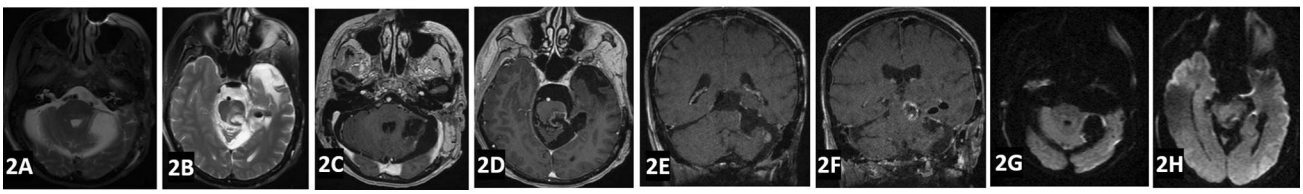

Fig. 2 Immediate postsurgery magnetic resonance imaging (MRI). (**A, B**) Axial T2-weighted MRI. Axial (**C, D**) and coronal (**E, F**) MRI and axial diffusion-weighted imaging (**G, H**) revealed microsurgical gross total resection of both components of the mass.

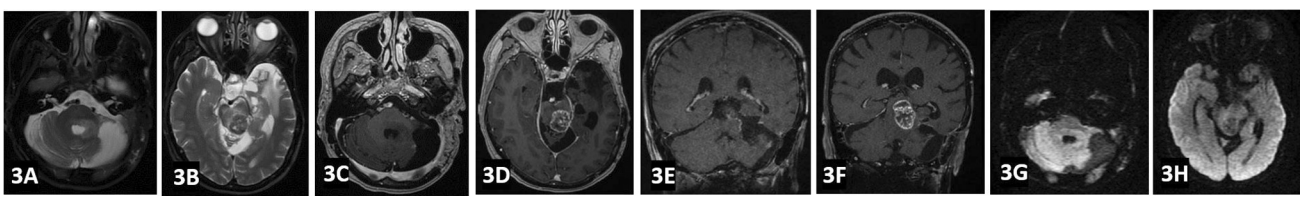

Fig. 3 Forty-five days postsurgery magnetic resonance imaging (MRI). (**A, B**) Axial T2-weighted MRI. Axial (**C, D**) and coronal (**E, F**) MRI and axial diffusion-weighted imaging (**G, H**) revealed a large recurrent heterogeneous rim-enhancing mass within the dorsal left midbrain measuring 3.1 × 2.3 × 2.3 cm, with resultant mass effect on the cerebral aqueduct and inferior third ventricle.

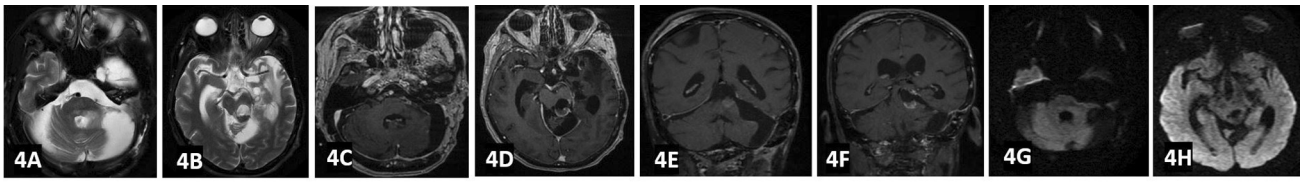

Fig. 4 Immediate post second surgery magnetic resonance imaging (MRI). (**A, B**) Axial T2-weighted MRI. Axial (**C, D**) and coronal (**E, F**) MRI and axial diffusion-weighted imaging (**G, H**) revealed subtotal 90% resection of malignant squamous transformation of the midbrain epidermoid tumor.

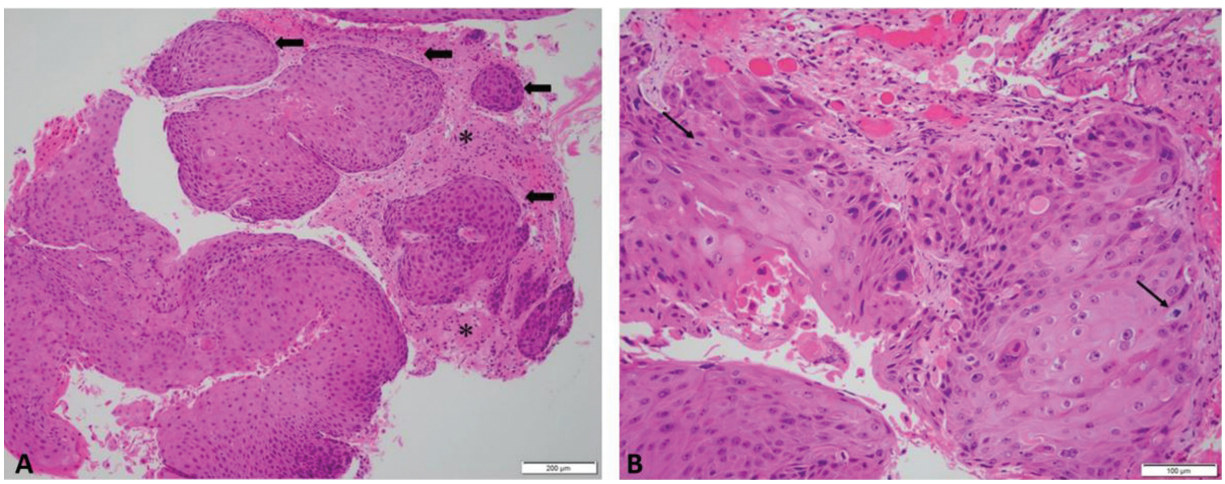

Fig. 5 (**A**) At low magnification, infiltration of gliotic central nervous system marked with * is evident by finger-like projections of squamous cell carcinoma (arrows; hematoxylin and eosin stain, original magnification 4x). (**B**) At higher magnification, malignant squamous cell is recognized by their abundant pink cytoplasm, atypical nuclei, enlarged nucleoli, and presence of atypical mitotic activity (arrows; (hematoxylin and eosin stain, original magnification 10x).

changes. The patient was discharged to a rehabilitation hospital and was elected to receive palliative radiotherapy (RT). However, due to the patient's declining general health palliative RT was not possible, and she passed away 5 months later.

Discussion

Primary intracranial SCCs are extremely rare, with the majority originating from MT of ETs or dermoid cysts.[1–3,5] Infratentorial MTs have a better prognosis than supratentorial ones, while both supra- and infratentorial MTs have a tendency for rapid local reoccurrence.[3]

When malignant degeneration occurs, the clinical and radiologic course is more aggressive.[1] Progressive neurological deficit and new contrast enhancement in a patient with ET are warning signs of malignant SCC transformation.[1,2] In a recurrent ET with new contrast enhancement, surgical exploration is mandatory to document malignant degeneration.[1] The surgical resection may be limited to maximal safe resection because the tumor capsule may be firmly adherent to critical structures, including the brain stem, cranial nerves, and perforating vessels.[4]

The exact mechanism of MT is unknown. One suggested pathogenic mechanism is chronic inflammation in the setting of repeated tumor ruptures, subtotal resection, and tumor wall remnants.[4] A second is the long-term existence of an in situ tumor,[3] which introduces a foreign material from the contents of the ET to the normal brain spaces, and which then might be a trigger for cellular atypia and subsequent neoplasia.[1–3] The tumor capsule rupture and introduction of squamous cells into the central nervous system and subarachnoid space elicits severe inflammatory response that in a chronic setting may underlie MT within the epidermoid epithelium. Furthermore, such chronic inflammations may demonstrate MRI enhancement adjacent to the ET. Given that enhancement in ET may also represent MT, surgical re-exploration and histopathologic confirmation is paramount and mandatory before adjuvant therapy in recurrent cases.[2,4]

In a report by Link et al,[1] in a retrospective review of a 57-year-old woman with an MT of an ET, they observed a tiny area of contrast enhancement in the tumor. This was an indicator of an atypical ET, although the initial pathological specimen did not reveal SCC. Follow-up images exhibited an intense enhancement, and the histopathology of the resected mass was compatible with SCC.[1] In the present case report, contrast enhancement warned us about the possibility of MT. However, the brain stem lesion had been reported as ET. In contrast, the rapid progression of symptoms combined with rapid growth on MRI was suggestive of MT (as was the observation of contrast enhancement) and the second resection by us confirmed SCC. These findings indicate that the initially observed nuclear atypia was indeed part of MT in the

ET, as was supported by our first MRI enhancement. In a report by Nakao et al,[2] another feature of MT seen in our case was that the malignant part of the ET is hypointense (dark) on DWI (►**Fig. 1G–H**), in contrast to the hyperintense (bright or restricted diffusion) for a benign ET.

MTs have a poor prognosis[3] and their treatment is troublesome, especially where there is brain stem involvement.[1] Surgery is the treatment mainstay,[3] and surgery followed by RT may be the best therapeutic option.[3] In most situations, the surgical aim is gross total resection; however, some authors have suggested that leaving capsule remnants avoids complications since MT of such remnants after a first surgery is extremely rare.[2] Nakao et al[2] reported a 74-year-old woman with a history of ET resection 20 years ago who presented with sudden onset of oculomotor nerve paresis. Detailed evaluation revealed an enhancing paraclinoid mass with involvement of the CPA and basal cistern. The histopathology of the resected mass was compatible with MT within the ET. This long interval between the initial surgery to MT was reported in nine cases with intervals that varied from 2 to 33 years (mean: 15.5 years).[2] In our reported case, the interval between the initial surgery to the MT was an even longer 37 years.

In a report by Chon et al,[5] a 43-year-old man with facial weakness and a right CPA ET underwent subtotal resection via a retrosigmoid approach and gamma knife radiosurgery (GK-RS) 5 months after surgery. Two years later, he presented with a new neurological deficit and underwent MRI evaluation that showed a large contrast-enhancing mass in the left CPA. Aggressive resection of an ET with SCC transformation that involves the brain stem may cause a dismal outcome due to unacceptable morbidity and mortality,[1,4] while adjuvant RT might offer better control of the disease. Close follow-up and frequent imaging are, therefore, mandatory in the setting of incomplete resection.[4] In our case, we believe that repetitive subtotal resections, RT, and the long-term existence of the tumor resulted in the MT.

Reports on the survival of surgery for MT alone ranged from 1 day to 7 months, but it has been suggested that adjuvant RT, with and without chemotherapy, promises to provide better tumor control.[1–4] However, the characteristics of RT and tumor response have yet to be well established.[3] Subtotal resection and subsequent RT may not improve survival rates, and maximal safe resection with adjuvant RT appears more effective. In a report by Link et al,[1] a patient underwent partial resection to verify the diagnosis and then received external-beam RT that was boosted by a stereotactic radiation. But ultimately, the tumor spread by intracranial metastasis and resulted in patient's death. Short-term follow-up results of patients with recurrent SCC transformation within ETs, who underwent stereotactic radiosurgery after conventional fractionated external-beam focal RT failure, have been promising.[1] Some reports have showed the efficacy of GK-RS as adjuvant therapy.[2] Tamura et el[4] reported that GK-RS might be efficacious in short-term control, but long-term effectiveness has yet to be shown.[4,6] In our case report, the patient first underwent microsurgical gross total resection, but with rapid regrowth of the tumor, she then underwent subtotal (90%) resection. However, due to the patient's general health, palliative RT was not possible, and she passed away 5 months later.

Some authors have suggested RT to treat recurrent benign ETs, which cause tumor shrinkage and symptom relief over 2-year follow-ups, but longer follow-ups are needed since these tumors are slow growing. Other authors have reported the recurrence of ET after adjuvant RT. In the present report, the patient received RT several years ago but had a recurrent mass with SCC transformation.[1]

Conclusion

Neurosurgeons should be aware of MT of ETs and thus consider the necessity for close long-term follow-up of these patients, especially in the setting of subtotal resection. The onset of new neurologic deterioration warrants appropriate imaging with MRI or CT scan with contrast. Rapid progression of symptoms and new contrast enhancement are characteristic warning signs of MT. Maximal safe resection is important for survival, and histopathologic confirmation and close follow-up are mandatory. Finally, when MT occurs, RT is an effective adjuvant therapy if allowed by the patient's condition.

Disclosure
The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Conflict of Interest
None declared.

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