Malignant squamous degeneration of a cerebellopontine angle epidermoid tumor

Case report

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Typically, an epidermoid tumor of the posterior fossa appears initially as a slowly enlarging mass, compressing the cranial nerves and brainstem. The rate of growth is linear rather than exponential, and the duration of symptoms before diagnosis and treatment usually ranges from several months to several years. Leakage of the cyst contents may result in repeated bouts of chemical meningitis and subsequent hydrocephalus. When malignant degeneration to a squamous cell cancer occurs, the course is more aggressive clinically and radiologically than that of epidermoids. Treatment of such a malignancy can be problematic, particularly if there is intimate involvement of the brainstem.

We report on the case of a woman with a CPA epidermoid tumor that subsequently degenerated into a squamous cell carcinoma. The neuroimaging identification, surgical management, subsequent adjuvant therapy, and follow-up care of this patient with this unusual pathological entity are discussed.

Case Report

History and Examination. This 57-year-old woman initially presented in July 1996 with a 10-year history of left trigeminal neuralgia involving V3, which was controlled with carbamazepine, and a progressive left-sided hearing loss and facial weakness of 3 weeks’ duration. Initial magnetic resonance (MR) imaging revealed a left CPA mass, consistent with an epidermoid. There was faint contrast enhancement where the tumor was in contact with the lateral brainstem.

A subtotal resection was performed. Histopathological findings were consistent with an epidermoid tumor. One year after initial presentation, the patient’s neurological deficit had increased, and follow-up MR imaging demonstrated a large contrast-enhancing tumor filling the left CPA and compressing the brainstem. At repeated surgery a squamous cell carcinoma arising from the previous epidermoid was found. The patient was subsequently treated with external-beam radiotherapy and stereotactic radiosurgery. Her tumor stabilized. Three years and 8 months after the patient’s initial presentation, a new area of tumor developed at the torcular Herophili. The patient died shortly thereafter.

Malignant squamous degeneration is a rare cause of enhancement on MR images, as is progressive neurological deficit in a patient with an epidermoid. The combination of subtotal resection, external-beam radiotherapy, and stereotactic radiosurgery may be useful for local tumor control but the long-term prognosis is guarded.

KEY WORDS • cerebellopontine angle • epidermoid cyst • squamous cell carcinoma • trigeminal neuralgia

Abbreviations used in this paper: CPA = cerebellopontine angle; CSF = cerebrospinal fluid; MR = magnetic resonance.
and a facial sling (W. L. Gore & Associates, Newark, DE) for cosmesis. She also noted further decreased hearing in the left ear and decreased sensation in the third division of the trigeminal nerve. Her trigeminal neuralgia completely resolved, and her regimen of carbamazepine was tapered and stopped.

Second Operation and Postoperative Course. The patient did well until July 1997, when she experienced an acute onset of transient vertigo and generalized weakness with near syncope. She reported slightly increased difficulty swallowing solids and a left hemicranial pressure headache. An MR image revealed a 2.5-cm enhancing lesion in the left pons and CPA (Fig. 3). The differential diagnosis included malignant degeneration of an epidermoid, collision brainstem glioma adjacent to a previous epidermoid, or abscess. The patient was monitored clinically, and serial MR images were reviewed. On the basis of progressive symptoms and tumor growth seen on MR images, a left posterior petrosectomy approach was performed, and her previous suboccipital craniotomy was reopened. The tumor was markedly adherent to the brainstem, the lower cranial nerves, and the basilar artery and its branches. Therefore, only a limited resection was possible. The histopathological findings were consistent with squamous cell carcinoma (Fig. 4). The patient tolerated the procedure well with no new neurological deficits.

Adjuvant external-beam radiotherapy to treat the residual tumor was administered at 45 Gy in 28 fractions between August 14, 1997 and September 10, 1997. The patient tolerated radiotherapy with no new complaints. On October 7, 1997, she underwent stereotactic boost radiosurgery to the residual contrast-enhancing mass. A dose of 15 Gy was delivered to the 80% isodose line by using a single isocenter with a 22.5-mm collimator. Unequally weighted arcs were used to draw the dose radiant away from the brainstem (Fig. 5).

Third Operation and Postoperative Course. The patient did well until March 2000, when recurrent headache, neck pain, and fatigue developed. Follow-up MR imaging revealed a new area of tumor in the posterior fossa midline and in the torcular Herophili (Fig. 6), which was presumed to be metastasis from her CPA squamous cell carcinoma. A subtotal resection of this new lesion was performed. The pathological features of this lesion were consistent

Fig. 1. Preoperative axial MR images (T1 [upper] and proton-density weighted [lower]) revealing a tumor involving the left CPA. The tumor signal is similar to that of CSF, which is consistent with an epidermoid. There is a faint area of contrast enhancement adjacent to the brainstem.
with the patient’s known squamous cell carcinomas. The patient and her family elected no further adjuvant treat-
ment, and she died shortly thereafter.

Discussion

Epidermoid Cysts

Epidermoid and dermoid cysts are thought to arise from misplaced epithelial elements that become trapped in the
meninges, ventricles, or brain parenchyma. Rarely, an epidermoid tumor arises after epithelial cells are introduced by percutaneous puncture for CSF aspiration. Epidermoid tumors constitute 0.2 to 1.8% of all brain tumors. Most epidermoids develop eccentrically in the region of the CPA, although occurrence has been reported in various locations, including suprasellar, intraventricular, and thalamic regions, and the brainstem. Pathologically, the wall of epidermoids consists of a layer of stratified squamous epithelium surrounded by a thin

Fig. 2. Photomicrograph showing keratin debris and squamous epithelium, which is consistent with an epidermoid cyst. H & E, original magnification × 500.

Fig. 3. Contrast-enhanced axial T1-weighted MR images obtained in July 1997 (1 year after the initial surgical procedure), demonstrating an intensely contrast enhancing mass in the left CPA, with compression and possible invasion into the adjacent pons.
layer of connective tissue. The cyst or tumor contents consist of desquamated epidermal cellular debris, often in concentric layers.

Neuroimaging Appearance

Epidermoids appear, on imaging, to conform to the subarachnoid space in which they grow and to compress the surrounding brain. Their external surface may be lobulated compared with the smooth surface of an arachnoid cyst. On computerized tomography scans, they are hypodense and do not enhance with administration of contrast medium. Using MR imaging, these tumors can usually be distinguished from CSF because they demonstrate mild hypointensity, usually between CSF and the brain parenchyma, on short TR/TE images. On long TR/TE sequences the tumors are markedly hyperintense, similar to or greater than that seen for CSF, and they are almost never isointense to CSF on long TR/short TE images. No enhancement is expected after Gd administration.

Malignant Transformation of Epidermoids

On serial imaging, malignant transformation of an epidermoid is evidenced by enhancement after administration of contrast medium and with rapid growth. When we retrospectively reviewed our patient’s initial MR imaging study, we found a tiny area of contrast enhancement in the tumor, an indication that the epidermoid was atypical; however, a retrospective review of the initial pathological specimen did not uncover any evidence of squamous cell carcinoma. Subsequent MR images revealed intense enhancement, and squamous cell cancer was discovered during repeat operation.

In another case, a foreign body giant cell reaction created a similar appearance on computerized tomography and MR images but no malignant degeneration was found. Thus, in cases of previously resected epidermoids when new contrast-enhancing lesions are seen, surgical reexploration.
Malignant degeneration of epidermoid

TABLE 1
Cases of malignant degeneration of a benign epithelial tumor into a squamous cell carcinoma*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Patient Age (yrs), Sex</th>
<th>Location of Tumor</th>
<th>Symptom Duration</th>
<th>Interval to Malignancy</th>
<th>Original Diagnosis</th>
<th>Final Diagnosis</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ernst, 1912</td>
<td>52, M</td>
<td>rt CPA</td>
<td>10 yrs</td>
<td>EC &amp; SCC</td>
<td>diagnosis at autopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davidson &amp; Small, 1960</td>
<td>46, M</td>
<td>rt frontal polar</td>
<td>5 mos</td>
<td>epidermoid carcinoma</td>
<td>XRT; “recovered”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Landers &amp; Danielli, 1960</td>
<td>73, M</td>
<td>cerebellum</td>
<td>1.5 mos</td>
<td>EC &amp; SCC</td>
<td>diagnosis at autopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fox &amp; South, 1965</td>
<td>50, M</td>
<td>lt subtemporal</td>
<td>8.5 yrs</td>
<td>EC</td>
<td>died 6 wks postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toglia, et al., 1965</td>
<td>54, M</td>
<td>base of brain</td>
<td>1 yr</td>
<td>EC</td>
<td>died 6 wks postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wong, et al., 1976</td>
<td>4, M</td>
<td>rt CPA</td>
<td>3 mos</td>
<td>epidermoid carcinoma</td>
<td>diagnosis at autopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scully, et al., 1977</td>
<td>59, M</td>
<td>rt CPA</td>
<td>2 yrs</td>
<td>SCC</td>
<td>local XRT; died 2 yrs postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nosaka, et al., 1979</td>
<td>46, M</td>
<td>rt CPA</td>
<td>10 yrs</td>
<td>SCC</td>
<td>died 7 mos postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dunn, et al., 1981</td>
<td>53, M</td>
<td>4th ventricle</td>
<td>4 mos</td>
<td>EC &amp; SCC</td>
<td>XRT; died 2 mos postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lewis, et al., 1983</td>
<td>53, F</td>
<td>rt parasellar region</td>
<td>&lt;12 mos</td>
<td>epidermoid carcinoma</td>
<td>diagnosis at autopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bondeson &amp; Falt, 1984</td>
<td>56, F</td>
<td>lt CPA</td>
<td>2 mos</td>
<td>EC &amp; SCC</td>
<td>died postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goldman &amp; Gandy, 1987</td>
<td>56, M</td>
<td>rt lat ventricle</td>
<td>33 yrs</td>
<td>SCC</td>
<td>XRT; alive 3 yrs postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abramson, et al., 1989</td>
<td>37, M</td>
<td>rt CPA</td>
<td>7 yrs</td>
<td>SCC</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nishiura, et al., 1989</td>
<td>38, M</td>
<td>rt CPA</td>
<td>8 mos</td>
<td>SCC</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tognetti, et al., 1991</td>
<td>67, F</td>
<td>rt temporal lobe</td>
<td>31 yrs</td>
<td>SCC</td>
<td>died 1 mos postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acciarri, et al., 1993</td>
<td>62, M</td>
<td>rt parasellar region</td>
<td>2 mos</td>
<td>EC &amp; SCC</td>
<td>died 1 wk postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nishio, et al., 1995</td>
<td>58, M</td>
<td>rt CPA</td>
<td>1 yr</td>
<td>EC &amp; SCC</td>
<td>XRT; stable at 2.5-yr FU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ogata, et al., 1996</td>
<td>63, F</td>
<td>dorsolateral pons</td>
<td>18 mos</td>
<td>SCC</td>
<td></td>
<td></td>
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</tbody>
</table>

* EC = epidermoid cyst; FU = follow up; SCC = squamous cell carcinoma; XRT = radiotherapy.

reration is necessary to document malignant transformation before adjuvant therapy is considered.

The first reported case of malignant transformation of an epidermoid into a squamous cell carcinoma was published in 1912.17 Since then, several cases have been reported of the malignant degeneration of a benign epithelial tumor, such as an epidermoid or dermoid, with pathological verification intraoperatively or at autopsy.1,2,12,34

Cases in the English-language medical literature are summarized in Table 1. The 12 male and six female patients described in these reports ranged in age from 4 to 73 years (mean 51 years; median 55 years). Among the patients who initially underwent a surgical procedure for a benign epithelial tumor, the interval before malignant transformation ranged from 6 months to 33 years. Some authors have suggested that introduction of a foreign material intraoperatively in combination with the inflammation-inducing contents of the epidermoid cyst, may be a cause of cellular atypia leading to neoplasia.1,34

Treatment Options

We chose to reexplore the CPA and lateral brainstem through a posterior petrosectomy approach to optimize exposure. We did not attempt an aggressive resection of the tumor because of the histopathological diagnosis of squamous cell carcinoma and because of the tumor’s adherence to the brainstem, cranial nerves, and vasculature of the posterior fossa. Many authors treating epidermoids involving the brainstem and cerebrovasculature have found that attempts to remove these adherent tumors completely may result in unacceptable morbidity and should be avoided.3,23,30 The surgical results reported in the medical literature are dismal: after attempted aggressive resection of squamous cell carcinomas, three patients died postoperatively29,44 and survival was limited to between 6 weeks and 7 months in the other patients who received only surgical treatment.19,37,46 Radiotherapy seems to offer better tumor control. Doses of 20 to 50 Gy for external-beam radiotherapy have been used with good tumor control, with up to 3 years’ follow up.12,22,35,41 One patient died 2 months after undergoing subtotal resection and subsequent radiotherapy with 50 Gy.44

Our patient had good clinical and local MR imaging–confirmed responses to external-beam radiotherapy and subsequent stereotactic boost radiosurgery. The benefit of radiotherapy for squamous cell cancer located elsewhere in the body has been well demonstrated.4,8,32 Stereotactic radiosurgery has been used to treat squamous cell cancer of the hard palate25 as well as to treat intracranial metastases with acceptable short-term results.9,10 Mori, et al.,34 also used stereotactic radiosurgery to treat a recurrent squamous cell cancer arising in an epidermoid after conventional fractionated external-beam focal radiotherapy failed to control the tumor. Only short-term follow up was available but the results were encouraging. Radiotherapy has also been used to treat recurrent benign epidermoids with reported shrinkage of the tumor and resolution of the patient’s symptoms over a 2-year follow up;29 however, with the slow growth of these tumors, much longer follow up is needed, and other authors have reported recurrence of epidermoids after postoperative radiotherapy.25

Conclusions

We report a case of an epidermoid tumor degenerating into a squamous cell carcinoma. Our patient had a good response to conservative debulking to establish the diagnosis and subsequent external-beam radiotherapy accompanied by a stereotactic boost, but ultimately the tumor spread by intracranial metastasis, resulting in her death. The diagnosis of squamous cell cancer arising from a previously subtotaly resected epidermoid is strongly suggested by development of new contrast enhancement and an enlarging tumor on serial MR images. Tissue diagnosis is necessary before proceeding with adjuvant therapy be-
cause foreign body giant cell reaction can mimic the neuroimaging appearance of a carcinoma. We do not believe that aggressive surgical resection is beneficial for tumor control. As in treating epidermoid tumors, overly aggressive attempts to remove squamous cell tumors can result in significant morbidity and mortality. External-beam radiotherapy with a subsequent stereotactic boost appears to provide good short-term tumor control with acceptable morbidity. We do not believe that radiotherapy is indicated for residual benign epidermoids, but continued clinical and neuroimaging follow up at yearly intervals is necessary. The long-term outlook for squamous cell carcinomas arising within a previously subtotally resected epidermoid is guarded.

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Malignant degeneration of epidermoid


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