

Ameloblastoma of the Mandible With Intracranial Metastasis

A Case Study

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- Ameloblastoma is an aggressive locally recurring neoplasm of odontogenic epithelium. We describe a case of a mandibular ameloblastoma with a 17-year history of local recurrences followed by two metachronous intracranial metastases. Central nervous system metastasis without pulmonary involvement is previously unreported in a living patient with ameloblastoma. The behavior of this tumor qualifies it as a malignant ameloblastoma.

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A meloblastoma is a benign tumor of odontogenic epithelium that seldom metastasizes, although the local recurrence rate is high.¹ These tumors are thought to be derived from several possible sources, including remnants of the dental lamina or the enamel organ, the epithelial lining of odontogenic cysts, and basal cells of the oral mucous membrane.² The ameloblastomas are considered the most common epithelial odontogenic neoplasm; however, they represent only 1% of all oral tumors. About 80% of ameloblastomas occur in the mandible and the remainder in the maxilla. Recent literature has emphasized that this tumor rarely metastasizes,^{3,4} and fewer than 35 cases with metastasis have been reported.⁵ The tumor metastasizes most frequently to the lungs (75%); lymph nodes and bone are less common sites for tumor spread.⁶ Metastases to the brain have been reported but are exceedingly rare⁷ and have occurred only in the presence of lung metastasis or from direct extension of the tumor.^{3,8} We describe a patient who had multiple recurrences of a mandibular ameloblastoma over a period of 17 years with subsequent metastasis to the brain without evidence of other systemic metastases.

REPORT OF A CASE

In 1972, a 65-year-old white man presented to his local physician with swelling in the area of the left mandible. The tumor was locally excised, and diagnosed histopathologically as an ameloblastoma. In the following 13 years, he had five recurrences treated with local excisions. In November 1985, he underwent a completion left hemimandibulectomy, maxillectomy, and radical resection of the infratemporal space. The patient remained asymptomatic for 2 years.

In December 1987, the patient noticed swelling of his scalp in the left parietal area after bumping his head. Plain films and a computed tomographic scan showed a lytic lesion of the left parietal skull (Figs 1 and 2). Surgical excision was performed after aspiration cytology revealed the presence of ameloblastoma. The biopsy specimen of the dura was positive for tumor but the brain



Fig 1.—Lateral skull roentgenogram showing lytic defect.



Fig 2.—Axial computed tomographic scan showing extradural tumor.

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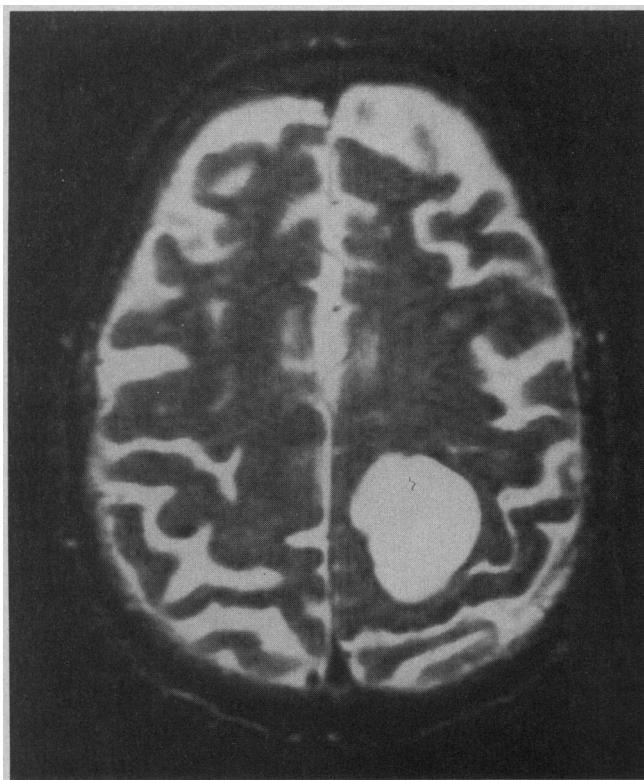


Fig 3.—Axial magnetic resonance imaging scan showing intraparenchymal tumor (contrast gadolinium enhanced).



Fig 4.—Parasagittal magnetic resonance imaging scan showing depth of intraparenchymal invasion.

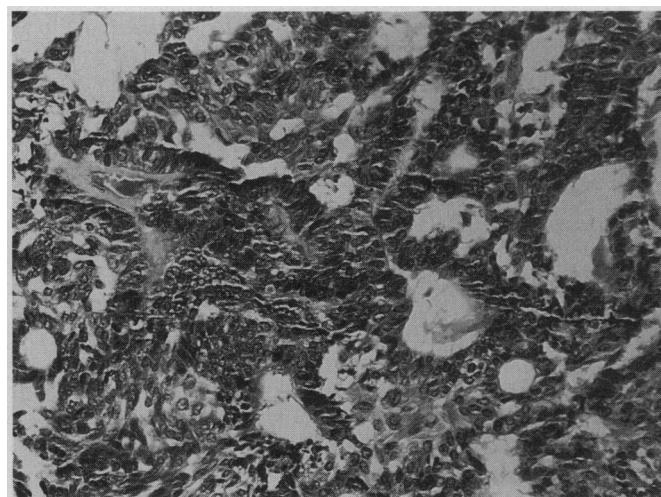


Fig 6.—Metastatic intracranial tumor. Brain tissue histopathologic findings show ameloblastoma with greater cellular atypia suggestive of ameloblastic carcinoma (magnification, $\times 280$).

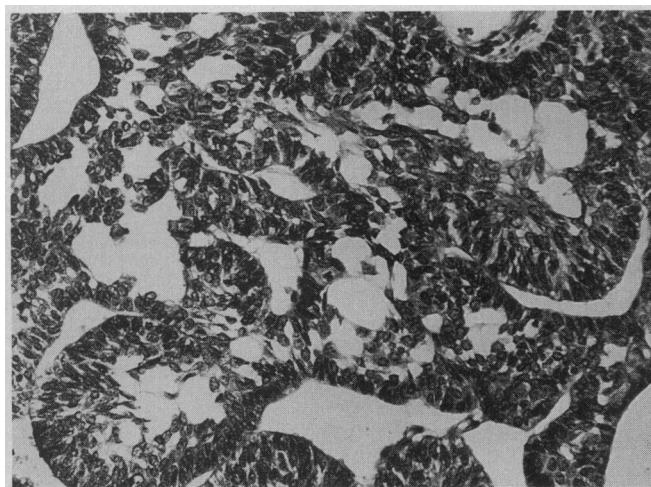


Fig 5.—Mandibular tumor specimen from 1985 shows a mixed follicular and plexiform ameloblastoma pattern with mild cellular atypia (magnification, $\times 280$).

tissue itself was without tumor. The diagnosis was metastatic ameloblastoma.

In March 1989 the patient developed a right upper extremity hemiparesis, focal seizures on the right side, and a positive Babinski sign on the right side. Magnetic resonance imaging showed an intraparenchymal tumor in the left parietal region (Figs 3 and 4). This lesion was separated from the previous intracranial lesion by 5 cm and was not a direct extension of that tumor. He underwent a left parietal craniectomy, with gross resection of subgaleal, epidural, and intracranial metastases. On opening the scalp, the lesion was found to be a soft tumor, which created a 1.5-cm hole in the skull. The tumor appeared to originate from the dura, extending both above and through the bone and below deep

into the parietal cortex. The brain tissue was found to be positive for metastatic ameloblastoma. A distinct plane was around the tumor, separating it from the rest of the brain. Gross total resection was accomplished, and the bone was removed with a 1- to 3-cm margin. The patient was treated with postoperative radiation therapy. Follow up chest roentgenograms and computed tomographic studies of the chest failed to show any lung metastases. In July 1990, the patient returned with a 1.5×2 -cm mass in the region of the left carotid bifurcation. This was removed and diagnosed as ameloblastoma. Since this last operation, no further tumor recurrences have been noted.

PATHOLOGIC FINDINGS IN SURGICAL SPECIMENS

Microscopic examination of the lesion specimens from the mandible and temporal fossa in 1985 showed ameloblastoma with follicular and plexiform patterns (Fig 5). Many areas within the neoplasm exhibited cytologic atypia, as characterized mainly by hypercellularity and nuclear hyperchromatism of the ameloblastic cells.

The surgical specimens from the first intracranial lesion showed that the dura was positive for tumor. The brain as well as the skin and subcutaneous tissue were negative. The dural specimen consisted of fibrous tissue with an adherent soft gray tumor mass. The tumor mass appeared to be grossly confined to one side of the dura. Microscopic study of the tumor showed that the morphologic features were very similar to the primary lesion in the mandible. Anastomosing cords and islands of cells resembling odontogenic epithelium were seen. Peripherally placed cells were of the columnar type with polarization of nuclei and arranged in a palisading orientation. The ameloblastoma demonstrated both follicular and plexiform patterns with focal areas of cytologic atypia.

The surgical specimens from the second craniotomy showed metastatic ameloblastoma in the brain tissue. The tumor specimen consisted of focally hemorrhagic tan-gray and tan-white tissue. Microscopically, the tumor again was arranged in a palisading configuration, with both follicular and plexiform patterns with some areas of atypia and increased cellularity. There were also pleomorphic cells with hyperchromic nuclei (Fig 6).

COMMENT

Treatment of ameloblastomas is difficult because of their well-known propensity to recur.⁹ Metastases are uncommon but have been reported after several local recurrences.⁶ This patient's history is typical in that he had several local excisions followed by a radical en bloc resection several years after the original diagnosis. He had several recurrences even after en bloc surgical resection, emphasizing the perplexing challenge faced by the physician who must choose an effective mode of therapy. When surgery has been ineffective, radiation therapy or chemotherapy has been considered. Some have found chemotherapy to be beneficial.¹⁰ Atkinson et al¹¹ found that radiation therapy could be useful in certain specific situations, such as with the elderly or patients who are not otherwise good surgical candidates.

Intracranial metastases of ameloblastoma are rare and have not been reported in the absence of pulmonary metastasis.¹² We found a single reference to a patient with intracranial metastasis at autopsy. Several reports describe direct tumor extension into the skull base, but these cannot be considered metastatic.^{3,8} The route of tumor metastasis has been proposed to be one of three types: lymphatic, hematogenous, or in the case of lung involvement, aspiration.¹³ Most authors believe that the hematogenous route is most likely.^{14,15}

Histopathologically, the ameloblastomas can have different patterns: plexiform, follicular, granular cell, basal cell, or acanthomatous. Most ameloblastomas will show either a follicular or plexiform pattern, and frequently a combination of the two. Ueno et al¹⁴ found that 62% of the primary ameloblastomas were of the follicular type and 38% of the plexiform type. There is no evidence to support the possibility of one pattern being more likely to metastasize than another. However, Hartman¹⁶ reported 20 cases of granular cell ameloblastoma and emphasized that this histologic variant of ameloblastoma is more aggressive with greater tendency to recur. In addition, ameloblastomas of this type have been reported as metastasizing.

Classification of the malignant potential ameloblastomas is controversial. A malignant ameloblastoma is defined by the World Health Organization as "a neoplasm in

which the features of an ameloblastoma are shown by the primary growth in the jaws and by any metastatic growth."¹⁷ Recent literature has attempted to offer a more specific method of classification.^{18,19} Following Slootweg and Muller's²⁰ scheme, Lee et al¹⁸ describe malignant ameloblastomas and ameloblastic carcinomas as two separate entities. A malignant ameloblastoma is defined by some investigators as an ameloblastoma that has metastasized but in which the metastatic tumor has shown no significant histologic differences from the primary tumor. The ameloblastic carcinoma, on the other hand, is an ameloblastoma that has exhibited histologic malignant transformation of the ameloblastic component and in which the metastatic deposits exhibit poor microscopic differentiation. The case that we have presented demonstrated atypical ameloblastic changes in the primary, recurrent, and metastatic tumor. By definition, this malignant ameloblastoma most likely represents an ameloblastic carcinoma.

Ameloblastomas are slow-growing tumors, but the effect of multiple recurrences and malignant transformation can be devastating. Early en bloc surgical resection is the treatment of choice to avoid recurrence. Other forms of therapy such as chemotherapy and radiation therapy have been tried but with mixed results. The site of metastasis is a unique feature of this case. The lungs are the most frequent site of metastasis, and initial metastasis to the intracranial cavity is unreported. This case illustrates the importance of close monitoring of these patients for local and distant disease.

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