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Clinical Study

Clinical features of brain metastasis from salivary gland tumors

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ABSTRACT

Salivary gland tumors comprise a group of 24 tumor subtypes with a wide range of clinical behaviors and propensities for metastasis. Several prognostic factors have been identified that help predict the development of systemic metastases, most commonly to the lung, liver, or bone. Metastases to the brain are rare. To better understand the behavior of salivary gland tumors that metastasise to the brain, we performed a retrospective cohort analysis on a series of patients to highlight features of their medical and surgical management. From 2007 to 2011, a database of 4117 elective craniotomies were queried at a single institution to identify patients surgically treated for salivary gland metastases to the brain. Three patients were identified. Histologic subtypes included salivary duct carcinoma, poorly differentiated carcinoma, and papillary mucinous adenocarcinoma. They had all undergone previous treatment for their primary malignancy. The mean time to intracranial metastasis was 48 months from initial diagnosis (range, 14–91 months). Treatment for intracranial metastases included surgical resection, whole brain radiation, stereotactic radiosurgery, and chemotherapy. Intracranial metastases from salivary gland tumors are rare, present years after diagnosis of the primary tumor, and are treatable with multimodality therapy.

1. Introduction

Salivary gland malignancies comprise a heterogeneous group of tumors with different propensities for metastasis. Salivary gland malignancies have an estimated incidence of 0.5–2.5 per 100,000 people.[1–3] In the US, incidence of salivary gland cancer has increased significantly towards the end of the 1990s, from 6.3% in 1974–1976 to 8.1% of all head and neck cancers in 1998–1999.[4] Most arise from the parotid glands (70–80%), with the remainder arising from submandibular gland (10%) or sublingual and minor salivary glands (5%).[3] Survival in adults is approximately 83% at 1 year, 69% at 3 years and 65% at 5 years. Prognostic factors include sex and age. Women typically have higher survival rates than men (72% *versus* 58%), and the 5 year survival is higher among patients aged 15–45 *versus* those older than 75 years (87% and 59%, respectively).[5]

Since the majority of patients have long survival times following initial diagnosis, the development of metastatic disease is relatively common. For example, high-grade salivary ductal carcinoma eventually metastasizes in 46% of patients, often with indolent courses.[6] The most common sites for metastases are lung (80%), bone (15%), and liver and other sites (5%). Metastases to the brain are very rare with only limited data available in the literature.[7–15] Surgery and radiation are traditionally the mainstays for therapy both for primary as well as metastatic lesions. We report a series of salivary gland malignancy with metastases to the brain to highlight this rare clinical entity and review the medical and surgical management.

2. Methods

Following Institutional Board approval, a retrospective analysis was performed during the period of 2007–2011 at a single, quaternary-level care neurosurgical center. Four thousand, one hundred and seventeen craniotomies were identified during the period that were subsequently queried for histopathology consistent with salivary gland metastases. Each case was reviewed by a neuropathologist (MS) and diagnosis was confirmed. The electronic medical record was queried for treatment history including clinic notes, hospital notes, operative notes, radiation treatment dosimetry plans, and neuroimaging.

3. Results

3.1. Patient 1

A 60-year-old woman presented with a lump under the angle of her right mandible. She underwent resection and neck dissection and was found to have a primary 1.5 cm salivary duct carcinoma of the right submandibular gland with vascular and perineural

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invasion. Metastases were found in three of 19 regional lymph nodes. Immunohistochemistry was positive for amplification of HER2/Neu. Postoperatively, she completed a concurrent course of cisplatin and radiotherapy. Follow-up surveillance CT scans performed 6 months later demonstrated multiple pulmonary nodules consistent with metastatic disease. Two years following the original diagnosis, MRI of the spine demonstrated vertebral body metastases from T8 to T12 causing lower thoracic pain that was palliated with radiotherapy (35 Gy) and concurrent chemotherapy (taxol and trastuzumab).

She continued on trastuzumab monotherapy for 1 year without symptoms until she presented with unsteady gait. Brain MRI revealed a contrast enhancing 1.5 cm right cerebellar mass (Fig. 1a–c), as well as right parietal and left frontal masses. She underwent a suboccipital craniotomy to resect her cerebellar mass, followed by 35 Gy whole brain radiation administered in 14 fractions, followed by a boost of 18 Gy with stereotactic proton radiosurgery to the right parietal lesion. Four years following the initial diagnosis, she had a generalized seizure that began with left arm and leg twitching. A CT scan of the brain demonstrated hemorrhage into the right parietal lesion (she was being treated with low molecular weight heparin at the time for an incidentally discovered pulmonary embolism). Anticoagulation was discontinued and an inferior vena cava filter was placed. She underwent right parietal craniotomy for tumor resection. Histopathological review confirmed an adenocarcinoma with extensive necrosis consistent with metastasis from her salivary gland tumor (Fig. 1d and e). Her postoperative course was complicated by intermittent seizure activity despite high-dose levetireacetam.

Unfortunately, widespread brain disease progression was found on routine surveillance imaging 3 months after the second craniotomy. After discussion with the patient and her family about her goals of care, she was transitioned to hospice care.

3.2. Patient 2

A 52-year-old woman presented with neck swelling and progressive trismus over 3 months. MRI of the head and neck revealed a deep parotid mass measuring 1.4 cm, with involvement of the mandible and pterygoids at the skull base. Positron emission tomography demonstrated intense uptake of the parotid mass and a level II neck lymph node. She underwent open biopsy for definitive diagnosis, which showed a poorly differentiated carcinoma that was positive for keratin staining but negative for S100. Due to the unresectability of the primary lesion, she underwent concurrent chemoradiation with carboplatin and taxol. The left neck field received 60 Gy over 3 months with a 10 Gy boost to the primary lesion and involved lymph node. One year later, routine surveillance MRI of the neck revealed an asymptomatic ring-enhancing left temporal lobe lesion (Fig. 2a–c). She underwent left temporal craniotomy for surgical resection of the enhancing mass. Pathologic analysis of the temporal lobe specimen demonstrated poorly differentiated carcinoma with similar morphological and immunohistochemical features to the parotid primary tumor (Fig. 2d and e). She was subsequently treated with stereotactic radiosurgery of 15 Gy to the residual disease in the left temporal resection cavity. Surveillance imaging of the parotid and temporal lesions have shown a good response thus far. The most recent brain MRI a year following the craniotomy demonstrated a slight increase in size of the remaining enhancing lesion in the left temporal lobe.

3.3. Patient 3

A 48-year-old man presented with a several year history of gradually enlarging mass in the posterior mouth. A biopsy demonstrated papillary mucinous adenocarcinoma arising from a minor salivary gland. Staging CT scans and MRI demonstrated the primary mass with extension to the soft palate, anterior pillar, and retromolar trigone but no lymphadenopathy. He was treated by surgical resection and postoperative radiotherapy.

Surveillance imaging 1 year later identified bilateral pulmonary metastases that were managed by surgical resection and radiofrequency ablation. Pathology demonstrated a mucinous adenocarcinoma, which was a progesterone receptor positive, estrogen

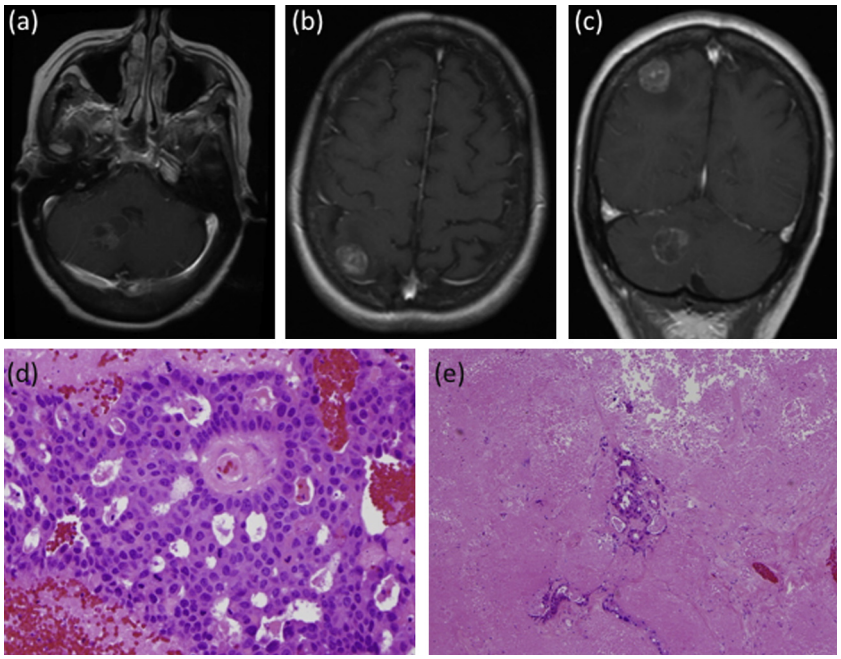

Fig. 1. Patient 1 with brain metastasis from salivary duct carcinoma. Upper row, post-contrast Ti-weighted MRI (a) axial section showing the right cerebellar lesion, (b) axial section showing the right parietal lesion, (c) coronal section showing both the right cerebellar and parietal lesions. Lower row, histopathological examination of the surgical samples (hematoxylin and eosin stain) showing (d) adenocarcinoma with extensive necrosis (original magnification × 400), with (e) scattered glands present in an otherwise entirely necrotic background (original magnification × 100). (This figure is available in colour at www.sciencedirect.com).