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Malignant myoepithelioma of the parotid gland: case report and review of the literature

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Abstract
A 62-year-old male with a myoepithelioma of the right parotid gland was treated with surgical excision followed by adjuvant radiation therapy. Prior to the completion of radiation therapy, the patient developed progressive disease at local, regional, and distant metastatic sites. Combined modality treatment with radiation and chemotherapy resulted in a significant but transient shrinkage of the tumours at all sites. The patient succumbed to metastatic disease 212 days following the diagnostic biopsy. This case illustrates several of the distinctive clinical and pathological characteristics of this rare tumour.

Key words: Head and neck neoplasms; Parotid gland; Myoepithelioma

Introduction

Myoepitheliomas of the salivary gland are relatively unusual, comprising only about one per cent of all salivary gland tumours (Barnes *et al.*, 1985; Dardick *et al.*, 1989a; Sciubba and Brannon, 1982).

Malignant myoepitheliomas of the salivary gland are even less common, and comprise only about 10 per cent of myoepitheliomas (Sciubba and Brannon, 1982; Barnes *et al.*, 1985; Dardick, 1985; Di Palma *et al.*, 1991; Takeda, 1992; Di Palma and Guzzo, 1993). We describe a patient with a myoepithelioma of the right parotid gland that metastasized to the lung, mediastinal lymph nodes, and other tissues. The metastases responded, albeit transiently, to combination chemotherapy and radiation therapy, which to our knowledge has not been previously reported. In addition, this case illustrates some of the characteristic clinical and pathological features of this rare tumour.

Case report

A 62-year-old male presented with the gradual onset of painless swelling of the right cheek. His past medical history was unremarkable. He occasionally consumed alcoholic beverages in small quantities, and had never smoked. Physical examination revealed a 4 × 5 cm mass in the area of the right parotid gland. There was no accompanying adenopathy, and the remainder of the physical examination was within normal limits.

Routine blood chemistries and a chest X-ray were negative. Magnetic resonance imaging revealed that the tumour had almost entirely replaced the parotid gland; there was no radiographical evidence of invasion of adjacent structures. Light microscopic examination of a biopsy specimen (Figure 1a, b, and c) revealed pleomorphic spindle and polygonal cells with relatively abundant cytoplasm, pleomorphic nuclei with prominent nucleoli, and frequent mitoses. Glandular architecture was not observed. An immunoperoxidase panel was positive for cytokeratin but negative for S100, CEA, HMB 45, CD45, L26, HHF35, vimentin, glial fibrillary acidic protein, and UCHL1. Electron microscopic examination (Figure 2) revealed a sheet-like growth pattern of tumour cells with moderately abundant cytoplasm containing ribosomes, rough endoplasmic reticulum, and mitochondria. Occasional desmosomes were observed. In addition, unequivocal myofilaments were appreciated beneath the plasma membrane (Figure 2). Tonofibrils, secretory granules, microvilli, and tight junctions were absent. The overall light and electron microscopic appearances were most consistent with a diagnosis of poorly differentiated malignant myoepithelioma.

A superficial and deep parotidectomy and mastoidectomy were performed. At the time of the surgery it was noted that the diameter of the tumour had increased by approximately 2 cm since the time of the diagnostic biopsy 15 days earlier. Sacrifice of the facial nerve was necessary because of grossly apparent facial nerve invasion.

Histological examination of the resected material revealed tissue identical to that seen in the previous specimen. Microscopic invasion of the facial nerve trunk was present. The margins of the surgical specimen, including the peripheral facial nerve branches, were free of tumour. Because of the tumour's rapid growth and malignant pathological appearance, adjuvant radiation treatment was initiated. The treated field included the operative bed with generous margins as well as the mastoid area and the ipsilateral neck. Doses of 200 cGy were administered in single daily fractions.

Six days after the initiation of radiation therapy, a new

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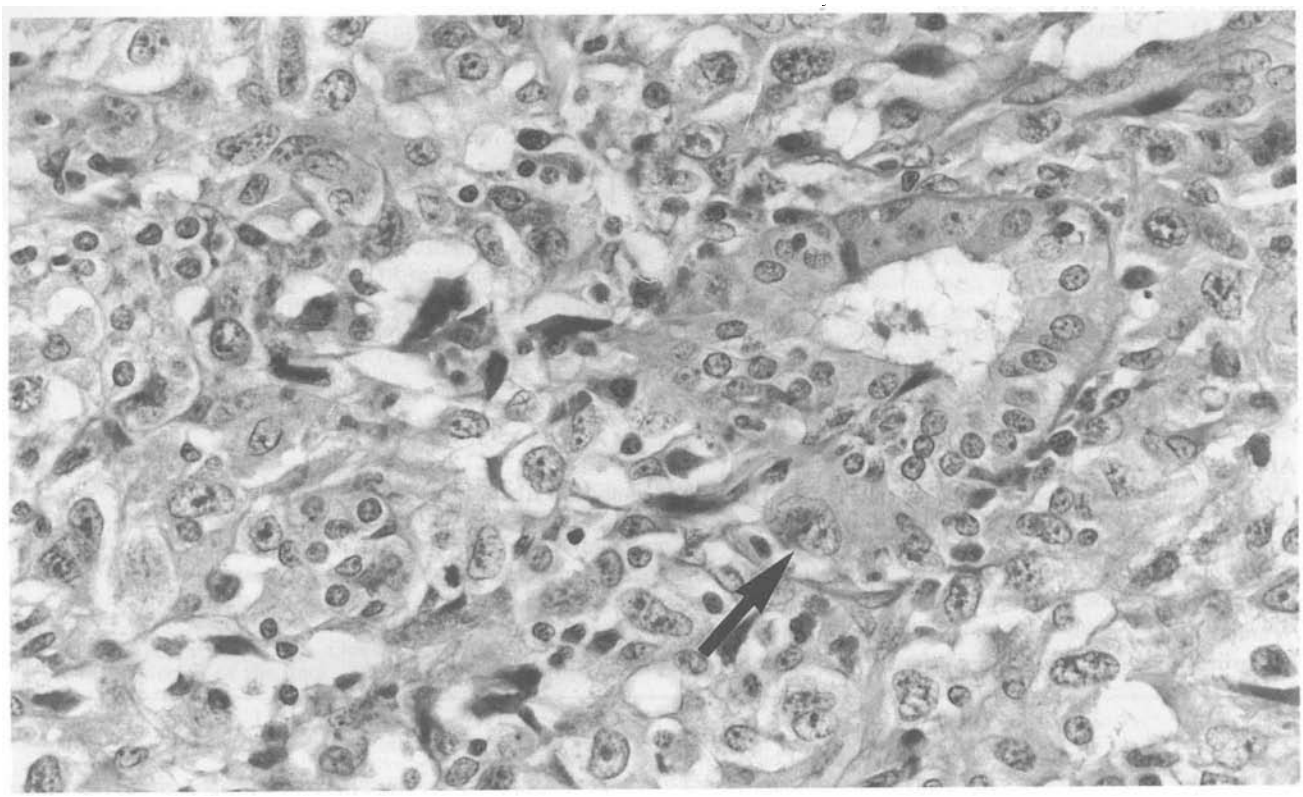
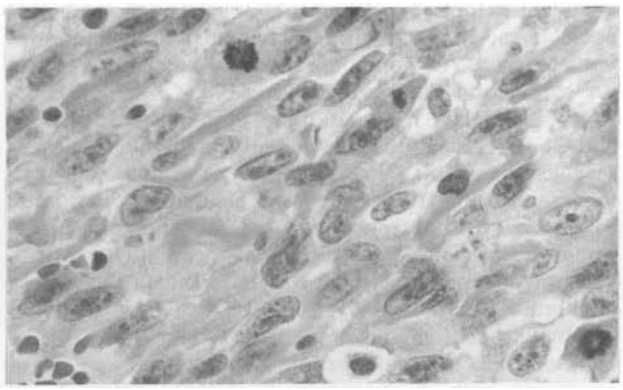


(a)



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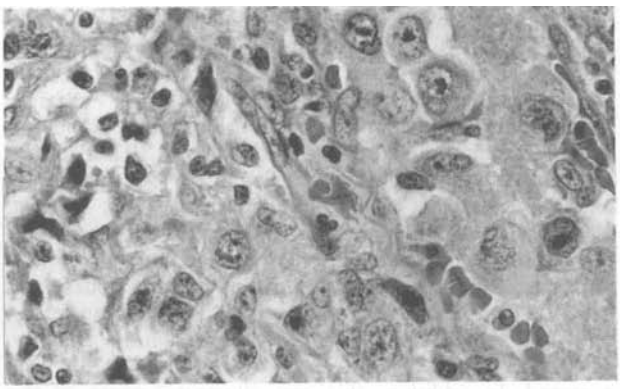

(c)

FIG. 1

The tumour is composed of polygonal, spindle, and round cells replacing most of the normal salivary gland tissue. (a) In one of the residual ducts, a tumour cell is seen in intimate contact with the adjacent normal epithelial cells (arrowed). The tumour cells possess abundant cytoplasm and large nuclei with prominent nucleoli. Vacuolization of the cytoplasm is seen in some tumour cells. (b) Some tumour cells are characterized by prominent spindle-cell morphology, resembling that of a sarcoma. (c) Some tumour cells show plasmacytoid features. (H&E; × 500).

exophytic mass in the right external auditory canal was discovered. Biopsy revealed neoplastic tissue histologically identical to the two previous specimens. A repeat physical examination revealed new adenopathy in the right supraclavicular area and recurrent swelling in the area of the original tumour bed. CT scanning revealed the appearance of multiple bilateral pulmonary nodules consistent with metastatic tumour, new mediastinal and hilar adenopathy, extensive submandibular lymph node metastasis, and recurrent local tumour invading the right mastoid and temporal bones.

Therefore, a combined modality approach was instituted. Cisplatin (60 mg/m^2 × 1), 5-fluorouracil (500 mg/m^2/day × 5 by continuous infusion) and external beam radiation therapy 160 cGy b.i.d. utilizing 16 MeV electrons were administered. The radiation field was enlarged to encompass the new areas of disease. Within four days there was an obvious reduction in the size of the involved lymph nodes. The recurrent swelling and induration in the area of the original tumour bed was also markedly improved. The treatment was complicated by severe oral mucositis primarily involving the ipsilateral buccal mucosa and oropharynx.

Repeat CT scans following the administration of a second cycle of combined modality therapy confirmed improvement in the cervical adenopathy as well as greater than 70 per cent reduction in the diameter of the pulmonary nodules and mediastinal nodes. Many of the pulmonary nodules had disappeared entirely. However, the response was considered mixed because CT scanning of the abdomen performed at the same time revealed a

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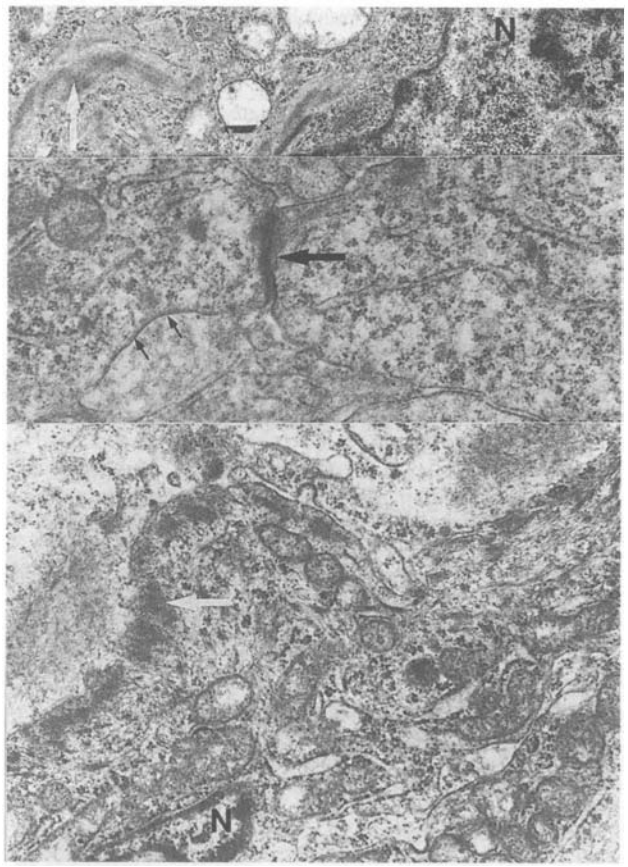

FIG. 2

Composite electron micrograph demonstrating portions of several tumour cells. Sub-plasma membrane filaments (white arrows), junctions (thick black arrows), and dense plaques (thin black arrows) are characteristic features of myoepithelial cells. (× 10 500).

new hypodense lesion, consistent with a metastasis, in the liver.

Following the completion of radiation therapy, the patient was switched to a regimen of cisplatin, 5-fluorouracil, leucovorin, and doxorubicin. A total of three cycles of the latter regimen were administered. Initially there was continued modest improvement in the cervical disease as assessed by clinical examination and serial CT scanning. However, later cycles were accompanied by progression of the hepatic and pulmonary disease as well as the appearance of new areas of disease in the bones and bone marrow. The patient died of progressive disease 212 days after the original diagnostic biopsy.

Discussion

Myoepithelial cells are present in a number of secretory organs including the breast, the lacrimal glands, the sweat glands, and the salivary glands (Batsakis *et al.*, 1983; Redman, 1994). Although myoepithelial cells have characteristics of both mesenchymal and ectodermal tissue, most authors feel that the weight of the histological and ultrastructural evidence suggests that they are derived from ectoderm (Dardick *et al.*, 1982; Batsakis *et al.*, 1983; Batsakis, 1985). The presence of contractile elements and their location in the acinar and ductal tissues have led to the hypothesis that they are responsible for the contractile expulsion of glandular secretions. In the salivary gland, myoepithelial cells are located in the acini and the intercalated ducts. They are in contact with the abluminal surface of the secretory epithelial cells, and are within the confines of the basement membrane (Batsakis *et al.*, 1983).

Sheldon is credited with the first description of a salivary gland myoepithelioma (Sheldon, 1943). Since his original description, over 50 additional cases have been reported in the medical literature (Barnes *et al.*, 1985; DiPalma and Guzzo, 1993). Nevertheless, the precise pathological definition of myoepithelioma remains a matter of controversy. In part, this is because myoepithelial elements have been found in varying numbers in pleomorphic adenomas, clear cell tumours, and other salivary gland tumours (Batsakis *et al.*, 1983). Some authors have insisted that the presence of any discernable ductal structure excludes the diagnosis of myoepithelioma. However, the current consensus is that the presence of isolated areas of ductal structure may be seen in otherwise clear-cut cases (Dardick *et al.*, 1989a). Myoepitheliomas are most commonly categorized as either 'spindle cells' or 'plasmacytoid', (Barnes *et al.*, 1985; Dardick, 1985; Dardick and van Nostrand, 1987), corresponding to the appearance of the normal myoepithelial cell in the salivary gland acinus or intercalated duct, respectively. Other histological variants have also been described (Dardick, 1985; Dardick *et al.*, 1989b).

Myoepitheliomas usually present as slowly enlarging, painless masses arising in the parotid gland. Other sites of origin include the palate, the larynx, the gingiva, and the breast. The average age at diagnosis is approximately 55 years, but examples in patients as young as age 14 and as old as 81 years have been reported (Barnes *et al.*, 1985). Males and females are affected with approximately equal frequency. In most cases the tumour is less than 5 cm in diameter, is well-encapsulated, and does not recur following surgical excision. Only a few cases of histologically invasive or clinically metastatic disease have been reported (Sheldon, 1943; Stromeyer *et al.*, 1975; Crissman *et al.*, 1977; Sciubba and Brannon, 1982; Dardick, 1985; Batsakis *et al.*, 1986; Toto and Hsu, 1986; Singh and Cawson, 1988; Dardick *et al.*, 1989a; Dardick *et al.*, 1989b; El-Naggar *et al.*, 1989; DiPalma *et al.*, 1991; DiPalma and Guzzo, 1993).

The immunohistochemical and ultrastructural features of myoepithelial cells have been extensively studied in normal salivary glands, in myoepitheliomas, and in other salivary gland tumours (Dardick *et al.*, 1982; Sciubba and Brannon, 1982; Batsakis *et al.*, 1983; Barnes *et al.*, 1985; Singh and Cawson, 1988; Dardick *et al.*, 1991).

The most characteristic feature of myoepithelial cells is the presence of myofilaments (Dardick *et al*, 1992; Dardick and Burford-Mason, 1994). The filaments may appear in well-aligned bundles or as disordered arrays, and may be diffusely present throughout the cytoplasm or concentrated in the sub-plasma membrane region. Cytokeratins, muscle-specific actin, myosin, and, occasionally, glial fibrillary acidic protein, are detected immunohistochemically. Desmosomes are also commonly present. These features are almost invariably present in native myoepithelial cells, but may be variably expressed or absent in the neoplastic state (Dardick and van Nostrand, 1987; Mori *et al*, 1987; Ibrahim *et al.*, 1991; Dardick *et al.*, 1992). Most authors agree that although the *sine qua non* for the identification of the native myoepithelial cell is the presence of the characteristic cytoplasmic filaments, these may or may not be clearly identifiable in myoepitheliomas (Franke *et al.*, 1980; Sciubba and Brannon, 1982; Tanimura *et al.*, 1985). The presence of myofilaments in the tumour cells of our patient, as well as the absence of glandular elements, the presence of characteristic spindle-shaped cells, and the positive immunostaining for cytokeratin, are all consistent with the diagnosis of myoepithelioma. As was

seen in the present case, limited expression of muscle-specific actin coupled with formalin fixation may result in negative immunostaining for this protein (Dardick *et al.*, 1992). The clinical and histological evidence of local invasion and the eventual appearance of local and distant metastases strongly support the malignant nature of the tumour in our patient.

In patients with malignant myoepithelioma, surgical excision has usually resulted in long-term disease-free survival. To our knowledge, only three previously reported patients have developed distant metastases, (Crissman *et al.*, 1977; El-Naggar *et al.*, 1989; Ibrahim *et al.*, 1991), only one of whom was treated with chemotherapy. The latter patient (Ibrahim *et al.*, 1991) did not respond to treatment with either radiation therapy or chemotherapy, and died of metastatic disease within three months of diagnosis. In contrast, our patient responded, albeit transiently, to combined modality treatment with chemotherapy and radiation therapy.

Conclusion

Our patient had a malignant myoepithelioma arising in the parotid gland. Surgery and radiation therapy failed to control the tumour, and the patient eventually succumbed to wide spread metastatic disease. The case illustrates some of the clinical and pathological features of this interesting and rare entity.

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