CASE REPORT

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Carcinoma ex-pleomorphic adenoma of the nasal septum with adenoid cystic and squamous carcinomatous differentiation*

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SUMMARY

Carcinoma ex-pleomorphic adenoma of the nose or paranasal sinuses is extremely rare. We report the first histopathologically confirmed case with adenoid cystic carcinomatous differentiation to present arising from the nasal septum.

Key words: carcinoma ex-pleomorphic adenoma, mixed tumour, adenoid cystic carcinoma, nose, nasal septum

INTRODUCTION

Pleomorphic adenoma of the nasal septum is a rare but well-recognised entity (Jassar et al, 1999). Carcinomatous differentiation is extremely rare with only three cases having been reported (National Cancer Institute, Monograph 57, 1981; Cho et al., 1995). We report such a case and discuss the pathological findings.

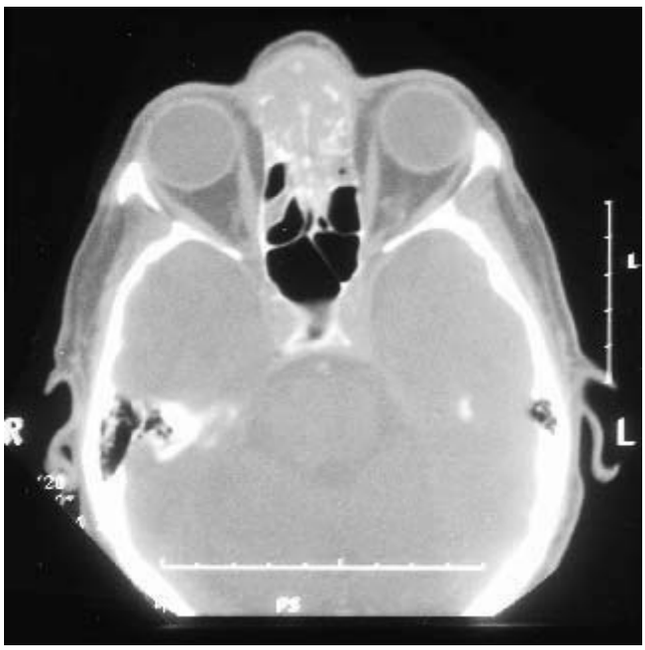

Figure 1. Axial CT scan showing tumour involving the anterior nasal cavity, nasal septum and right ethmoid cells.

CASE REPORT

A 66-year-old Caucasian female presented to the otolaryngology department with a twelve-month history of right-sided nasal obstruction. On examination she was found to have widening of the lower two-thirds of her nose externally with a large ulcerated mass filling the right nasal vestibule. The nasal septum was deflected to the left. A computed tomographic (CT) scan of the paranasal sinuses showed a large soft tissue lesion extending from the nasal septum to the right anterior ethmoid cells, the frontal sinus and filling the right nasal cavity (Figure 1). Some bony destruction of the right nasal bone was noted, but there was no intra-cranial extension seen. To obtain tissue for histology, the lesion was debulked piecemeal under general anaesthetic. It was found to be hard and rubbery in consistency and involving most of the septum.

The fragments showed a variety of histological appearances. Some had features of invasive, glandular adenoid cystic carcinoma, including typical cribriform arrangements, with microcysts containing alcian blue-positive and diastase-resistant PAS-negative stromal mucin (Figure 2). Perineural invasion was also present in one piece of tissue. Other areas contained sheets of cytologically atypical squamous epithelium (Figure 3). Abundant hyaline stroma was present and one area showed islands and strands of epithelial and myoepithelial cells in chondromyxoid stroma, consistent with a pleomorphic adenoma 'ghost' (Figure 4). A pathological diagnosis of carcinoma ex pleomorphic adenoma (CePA), with multiple differentiation patterns was made.

Magnetic resonance imaging (MRI) showed intracranial extension through the cribriform plate on the right side (Figure 5).

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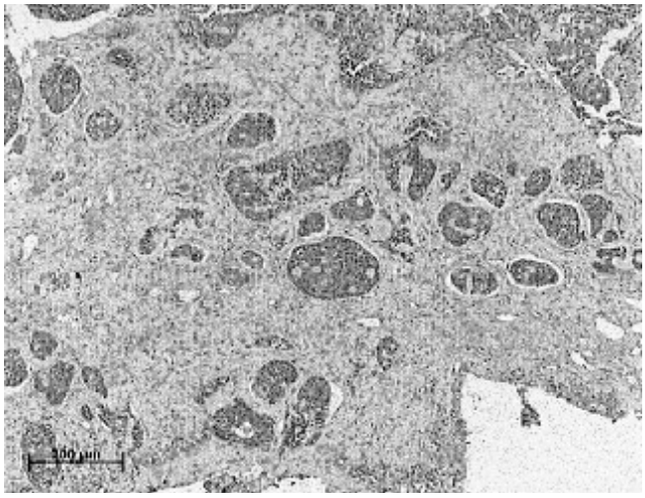

Figure 2. Initial biopsy histology from the right side of the nasal septum showing islands of basophilic cells with a cribriform pattern typical of adenoid cystic carcinoma. The majority of the resection specimen showed this pattern.

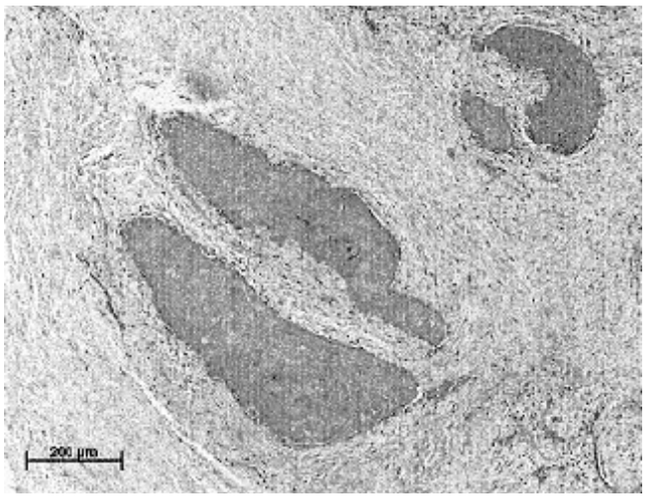

Figure 3. Initial biopsy from the left side of the nasal septum. Islands of atypical squamous epithelium are seen together with myxoid stroma.

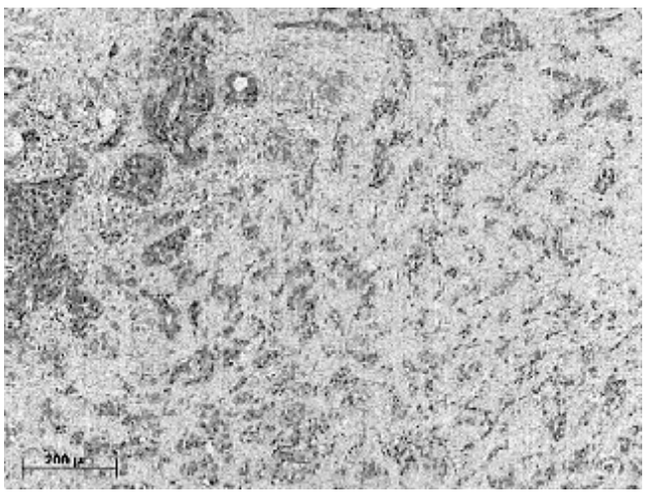

Figure 4. Resection specimen showing a small focus of cells resembling residual pleomorphic adenoma in continuity with solid adenoid cystic carcinoma (left).

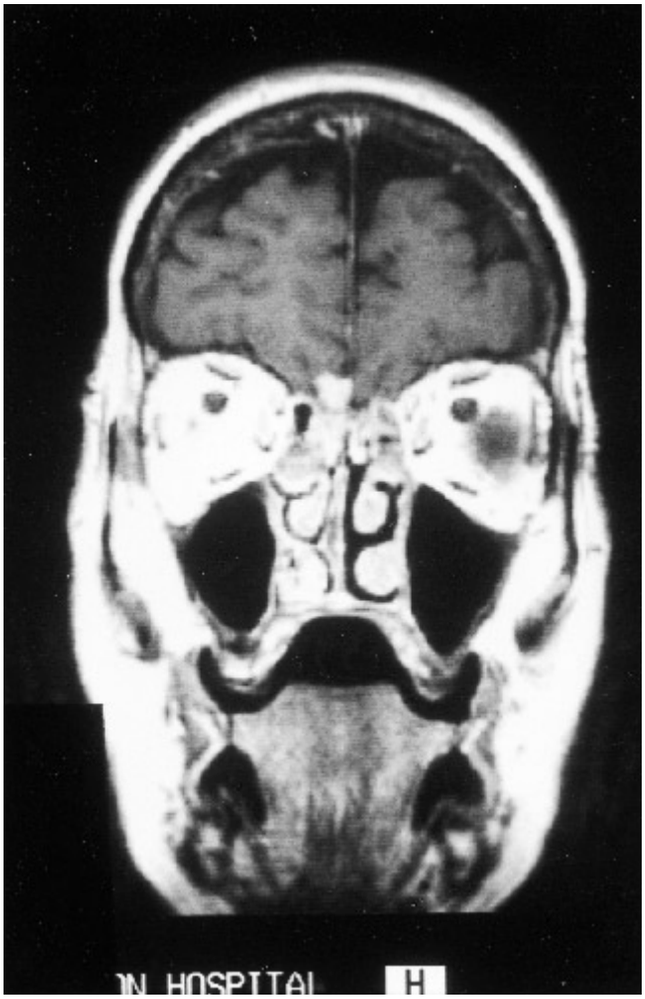

Figure 5. Coronal MR scan T1-weighted with gadolinium contrast showing intracranial extension of the tumour.

Computerised tomography (CT) scanning of the brain, thorax and abdomen found no evidence of metastases. A craniofacial resection of the nasal tumour and subdermal rhinectomy were performed jointly by the otolaryngological and neurosurgical teams. The tumour was found to be extending through the cribriform plate, which was unusually soft. It had replaced the right nasal bone and nasal septum and was involving the left nasal bone and both upper lateral cartilages. The lower lateral cartilages were not involved. It extended into the frontal and ethmoid sinuses and into the right orbit through the lamina papyracea. The sphenoid sinuses were clear. The diseased tissue was resected, including the right lateral nasal wall, with a subdermal dissection preserving the nasal skin and lower lateral cartilages. The intracranial defect was repaired using fascia lata and bone harvested from the right iliac crest and the nasal cavity was packed with ribbon gauze impregnated with bismuth, iodoform and paraffin paste (BIPP).

Histological examination of the resected specimen showed invasive tumour composed of solid sheets and cribriform areas of small basophilic cells. There was prominent perineural infil-

tration. This was diagnosed as adenoid cystic carcinoma (ACC). After review of the initial biopsies it was felt that treatment should be planned along the lines for ACC, as this was the predominating malignant component.

Five days after surgery the patient became confused, suffering hypnogogic hallucinations. A cerebrospinal fluid (CSF) leak was discovered and a lumbar drain inserted. Ten days postoperatively the nasal packs were changed and examination showed good healing with no obvious CSF leak. The patient's mental state gradually improved and she was discharged home five weeks postoperatively. A further examination under anaesthetic of the nose was carried out two months later. At that time there was a small area of erosion of the nasal skin but excellent healing elsewhere in the cavity. Biopsies from the erosive area showed inflammatory tissue only and were thought to be secondary to pressure necrosis from the BIPP pack.

Six months postoperatively the patient underwent radiotherapy with minimal upset. The patient continued to be reviewed at monthly intervals and no signs of recurrence developed. Follow up MR scans were planned at yearly intervals. Twelve months postoperatively however the patient was admitted feeling generally unwell and became comatose shortly afterwards. CT scanning of the brain showed multiple ring enhancing lesions in the right frontal lobe suggestive of abscess formation (Figure 6). In addition, there were enhancing lesions with a broad base attached to the skull vault in the left frontal, left temporal, right frontal and right fronto-temporal regions, which were diagnosed as dural metastases. CT scanning of the paranasal sinuses showed contrast enhancement along the periphery of the maxillary antra that was felt likely to represent recurrence. CT scanning of the rest of the body demonstrated several small, low-density areas within the liver that were highly suspicious of metastases. She was diagnosed with massive tumour recurrence and no further treatment was carried out. She did not regain consciousness and died three days later. A postmortem was not requested.

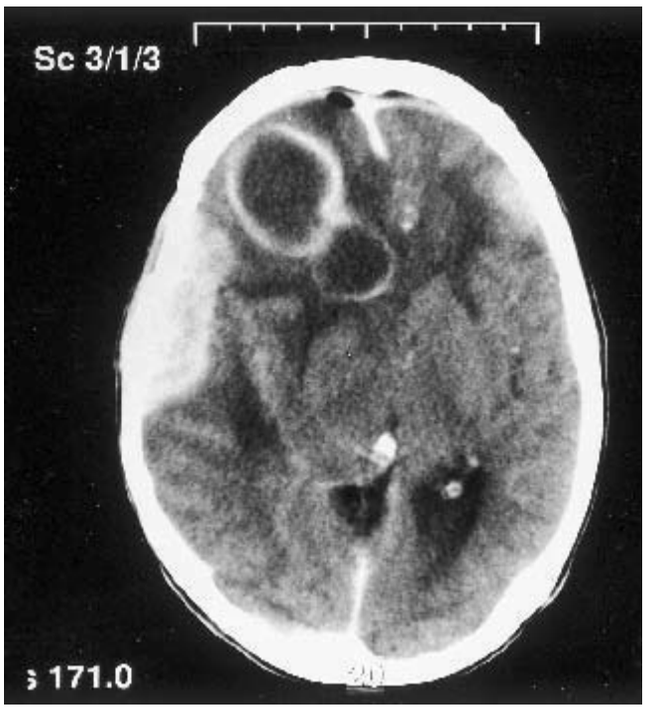

Figure 6. Axial CT scan with contrast showing ring enhancing lesions and broad-based enhancing lesions representing abscess formation and dural metastases respectively.

DISCUSSION

Carcinoma ex pleomorphic adenoma (CePA) is a generally high-grade malignant neoplasm within which a remnant or scar of pleomorphic adenoma can be identified (Eveson and Renehan, 2002). In a review of 60 series of salivary gland neoplasms, involving approximately 15 000 cases, Gnepp (1993) found that 3.6 percent were CePA. Eighty-two percent involved the major salivary glands while only 18 percent were in the minor glands. No intranasal lesions were reported. The National Institutes of Health issued a report in 1981 tabulating malignant tumours in a population of approximately 100 000 000 and found a total of 85 cases of CePA of which only one was intranasal (no clinicopathological data was given).

Pleomorphic adenoma within the nasal cavity is rare, with only approximately 150 cases reported, and of these 80 - 90 percent occur on the nasal septum (Jassar et al. 1999). If the incidence of intranasal CePA developing within pleomorphic adenoma follows its counterpart in other sites, it is not surprising that there are only two other reported cases of intranasal CePA in the literature (Cho et al., 1995). They were described as adenocarcinomatous and undifferentiated carcinomatous change in pleomorphic adenomas of the nasal septum. These are the commonest patterns of differentiation within a CePA. Salivary gland neoplasms are recognised within CePA at other sites but are unusual (Gnepp, 1993; Tortoledo et al. 1984). Multiple differentiation patterns within a single tumour are even more unusual but, again, they have been recognised to occur (Farman et al., 1985). Torteledo et al. (1984) observed that there is no prototypical CePA because this is a heterogenous group of tumours with multiple potential differentiation patterns. In their study of 40 malignant mixed tumours they found histological subtype to be one of the most important prognostic indicators, with a five-year survival rate variation from 0 – 96% depending on grade of tumour. This series did not include any adenoid cystic, acinic cell or mucoepidermoid carcinomas so it is unclear where they lie in this spectrum.

In our case, adenoid cystic carcinoma (ACC) was the predominant pattern of differentiation. Although less common within CePA, this is the most frequent salivary type malignancy within the sinonasal tract (Manning and Batsakis, 1991). ACC occurs primarily within the paranasal sinuses. Its occurrence in

the nasal cavity is well recognised but it is rare on the septum. Indeed Howard and Lund (1985) reported only 1 of 20 cases of intranasal ACC seen during a 22-year period had originated from the nasal septum. ACC is a slow growing tumour but locally aggressive with a propensity for perineural spread, so is particularly likely to recur locally or have intracranial extension. The most important prognostic factors in ACC are histological grading, clinical staging and the quality of surgical margins. Histologically ACC has several subtypes, often coexisting. As the cellularity increases from tubular to solid the prognosis is said to worsen (Goepfert et al., 1983). Yamamoto et al. (1992) thought that the tumour tended towards the solid pattern with the passage of time leading to increased proliferation rates and likelihood of metastasis.

There is a spectrum of presentation of CePA from discreet masses within a predominantly benign mixed tumour with capsular containment to extensively infiltrating tumours with minimal residual benign component. The diagnostic difficulties arising from this latter presentation have been previously noted (Foote and Frazell, 1953) and are highlighted by our case. The benign component was barely recognisable in the initial biopsies, with no sign within the main block following definitive resection. The extent of infiltration and subsequent capsular invasion has also been found to be associated with prognosis (Tortoledo et al., 1984; Gnepp, 1993). This means it may be especially important to identify any histological remnant of benign, mixed tumour in a specimen, as this represents an aggressive, invasive carcinomatous component of a CePA, rather than a potentially more indolent primary carcinoma, which may presage a poorer prognosis.

In our case the tumour demonstrated intracranial extension and osseous destruction radiologically. The absence of a capsule and perineural invasion are also features associated with a poor prognosis. Despite treatment the patient developed widespread metastases within twelve months. Such aggressive biological behaviour is more in keeping with a diagnosis of CePA than adenoid cystic carcinoma.

This case demonstrates the importance of considering CePA in the differential diagnosis of minor salivary gland malignancies of the nasal septum. The prognosis of CePA is considerably worse than a de novo ACC which is much more likely to be slow growing. Diagnosis of CePA depends on careful sampling of the tumour after resection to locate any co-existing benign adenomatous component.

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