Virchows Archiv A Pathol Anat (1992) 420:371–374

Virchows Archiv A
Pathological Anatomy and Histopathology
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Case report

Salivary duct carcinoma: report of a case and review of the literature

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Received September 10, 1991 / Received after revision and accepted November 19, 1991

Summary. Salivary duct carcinoma is a rare primary tumour of the salivary glands arising most frequently in the parotid gland. It has a male preponderance and occurs most often in patients over the age of 50 years. Its distinctive histological features include dilated ducts containing cells arranged in cribriform, papillary or solid patterns often with central necrosis and reminiscent of intraduct carcinoma of the breast. These features are associated with an obvious invasive component. It is an aggressive neoplasm and may metastasize widely, causing death in a high proportion of cases.

Key words: Salivary gland – Salivary duct carcinoma

Introduction

Salivary duct carcinoma is a neoplasm which has characteristic histological features, first described by Kleinsasser et al. in 1968. Since that time approximately 60 cases have been reported. This paper presents a further case, and reviews the literature emphasizing the important points in the diagnosis of this distinctive tumour.

Case report

A 59-year-old man presented with a 6-month history of total right-sided facial weakness and a 2-month history of a swelling at the angle of his right mandible. A parotid sialogram and CT scan showed a lesion arising within the parotid gland. At operation, an infiltrating tumour was found extending from the angle of the mandible to the base of the skull. A total parotidectomy with clearance of the base of the skull and radical neck dissection was performed with grafting of the facial nerve branches to the orbicularis occuli muscle. The patient received post-operative radiotherapy and was free from recurrence 3 months post-operatively.

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Results

The excised parotid gland measured $7.5 \times 4.0 \times 3.5$ cm and there was an attached radical neck dissection. At the deep pole of the gland there was a hard, white mass 2.5 cm in maximum diameter which contained foci of necrosis and had an irregular, infiltrating margin which was, in places, invading adjacent muscle.

Tissue blocks were formalin-fixed, routinely processed to paraffin and sections stained with haematoxylin and eosin, diastase/periodic acid-Schiff (PAS) and elastic van Gieson. Immunocytochemical staining for cytokeratin (CAM 5.2, Becton Dickinson, Oxford, UK), epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), S-100 protein and vimentin (all Dako, High Wycombe, UK) was performed.

Electron microscopic examination of formalin-fixed tissue was undertaken.

Haematoxylin and eosin stained sections showed many distended ducts filled with cells arranged in cribriform, papillary and solid patterns (Fig. 1a). The resemblance to intraduct carcinoma of the breast was striking, with "Roman bridge" type formations in some areas (Azzopardi 1979). In many ducts there was central necrosis giving a comedo-carcinoma appearance. The cells themselves had finely granular, eosinophilic cytoplasm and fairly well defined cell boundaries. The nuclei were round to oval in shape, with many possessing a single, prominent nucleolus (Fig. 1b). There was an infiltrating component to the neoplasm, which in most areas was poorly differentiated, although scanty tubule formation was seen focally. The stroma around the invasive tumour was hyalinized (Fig. 1c). Mitotic figures were inconspicuous both in the circumscribed islands and in the invasive component, but peri-neural and vascular invasion were identified in some areas (Fig. 1d).

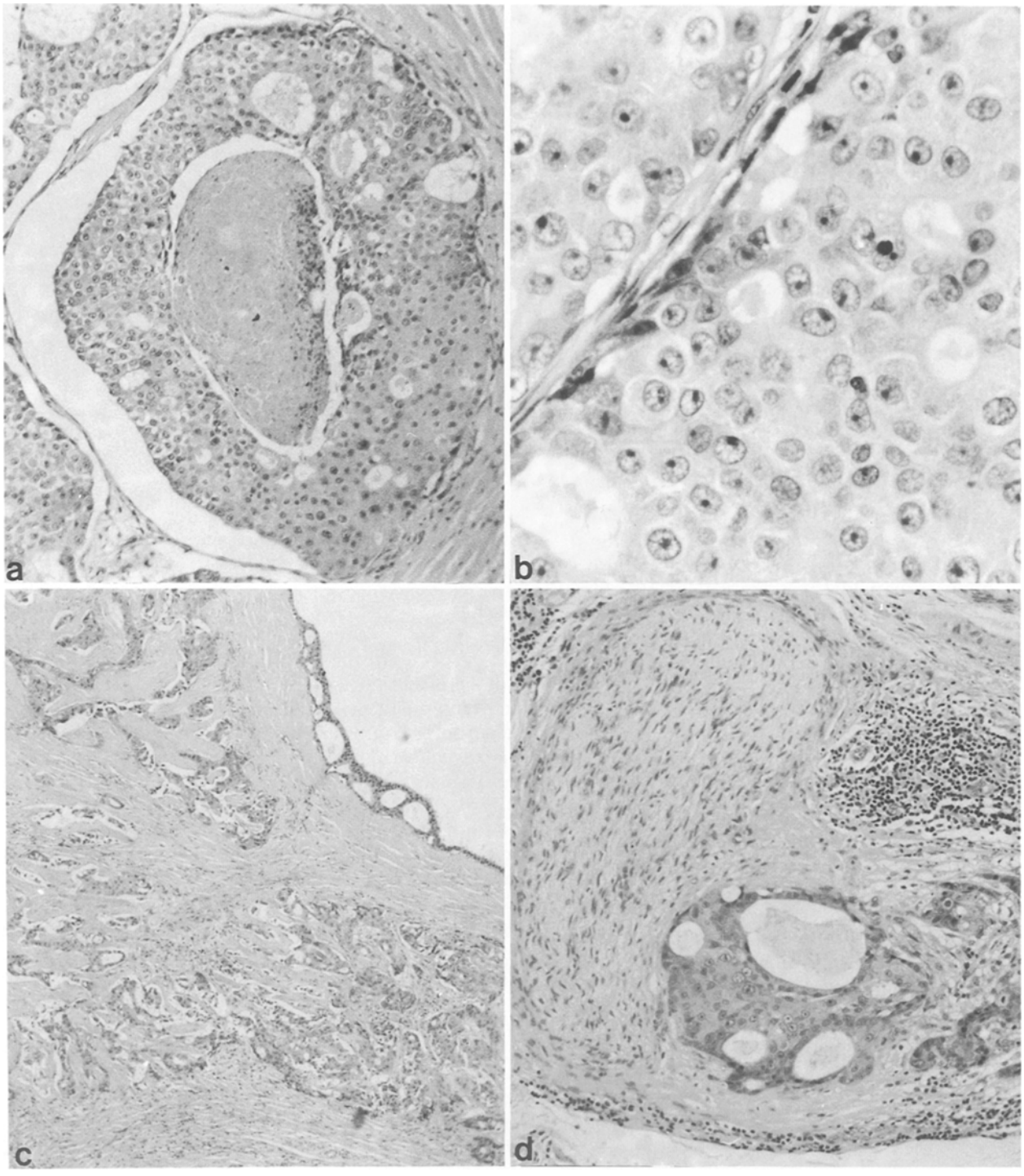

Fig. 1. **a** Intraduct carcinoma with characteristic comedo-necrosis. ×100. **b** High-power view to illustrate cellular detail. Note lumina, copious cytoplasm and prominent nucleoli. ×400. **c** Invasive component with surrounding hyaline stroma. Part of a cystically dilated duct is present top right with "Roman bridge" formations of intraduct carcinoma lining it. ×100. **d** Peri-neural invasion by tumour with associated chronic inflammatory cell infiltrate. ×250

Focal positive staining for mucin was identified with the diastase/PAS method.

Within the radical neck dissection, metastatic carcinoma was identified in only one lymph node.

The tumour cells were positive for CAM 5.2, EMA and CEA. No myoepithelial cells were demonstrated within the tumour by S-100 staining, a method which has been used previously (Kahn et al. 1985). No specific features were seen with electron microscopy.

Discussion

Salivary duct carcinoma is a rare tumour of the salivary glands, not well recognized, and which was not specifi-

Table 1. Clinical findings in patients with salivary duct carcinoma

Authors	Year	No. of cases and gender	Age range (years)	Site[a]	Outcome
Kleinsasser et al.	1968	2 M	56 and 64	Parotid	2 dead of disease 18 months
Fayemi and Toker	1974	4 M	53–72	Parotid	1 dead of disease 2.5 years
Chen et al.	1981	3 M 2 F	59–70	Parotid	4 dead of disease 5 months to 3 years
Garland et al.	1984	4 M	56–83	Parotid	1 dead of disease 4.25 years
Gal et al.	1985	1 M	57	Parotid	No follow up
Hui et al.	1986	12 M 3 F	27–83	10 Parotid 5 Submandibular	8 dead of disease 14 months to 6 years 3 alive with disease 1–2 years
Afzelius et al.	1987	7 M 5 F	49–82	Parotid	7 dead of disease 6 months to 4 years 1 alive with disease 3 years
Zohar et al.	1988	4 M	47–61	2 Parotid 1 Sublingual 1 Minor gland of lip	1 dead of disease 2 years 1 alive with disease 6 years
Lopez et al.	1990	1 M	56	Parotid	1 dead of disease 8 months
Brandwein et al.	1990	10 M 2 F	51–60	11 Parotid 1 Submandibular	5 dead of disease 1–10 years 3 alive with disease 1–4 years
Butterworth (Present case)	1990	1 M	59	Parotid	No evidence of disease at 3 months

[a] Also 3 cases described in minor salivary glands of buccal vestibule (62 years, F; Pesce et al. 1986), tongue (60 years, F; Chen 1983), and larynx (54 years, M; Ferlito et al. 1981). No follow-up information is available

cally mentioned in a recent extensive review of salivary gland neoplasms (Eveson and Cawson 1985).

It was first described by Kleinsasser et al. in 1968, but 3 of these cases are now recognized as low-grade neoplasms of epithelial/myoepithelial type (Afzelius et al. 1987; Chen and Hafez 1981; Evans and Cruickshank 1970; Garland et al. 1984), as is the tumour described by Thackray and Lucas (1974).

Of these tumours, 80% occur in the parotid gland and 50 of the 64 cases so far reported have occurred in males, most in patients over the age of 50 years (Afzelius et al. 1987; Brandwein et al. 1990; Chen 1983; Chen and Hafez 1981; Fayemi and Toker 1974; Ferlito et al. 1981; Gal et al. 1985; Garland et al. 1984; Hui et al. 1986; Kleinsasser et al. 1968; Lopez et al. 1990; Luna et al. 1987; Pesce et al. 1986).

Patients usually present with a mass and often with facial nerve involvement. Even with aggressive therapy, the prognosis is poor with a 60–70% mortality (Afzelius et al. 1987; Brandwein et al. 1990; Chen and Hafez 1981; Garland et al. 1984; Hui et al. 1986; Zohar et al. 1988).

Table 1 summarizes the clinical features of this tumour in published series.

Local invasion, lymphatic spread and distant metastases (most commonly to the lungs, bones, brain and liver) have all been described. Local recurrence after surgery may also be a problem (Chen and Hafez 1981; Garland et al. 1984; Hui et al. 1986). Younger age at diagnosis (Afzelius et al. 1987), a primary tumour larger than 3.0 cm (Hui et al. 1986) and submandibular gland tumours (Hui et al. 1986) all worsen the prognosis.

Several authors have noted the similarity of this lesion to ductal carcinoma of the breast (Afzelius et al. 1987; Garland et al. 1984; Hui et al. 1986; Kleinsasser et al. 1968).

Thus diagnostic features of importance are the presence of circumscribed, intraductal islands of cells typically showing central comedo-necrosis, but which may also have a papillary, cribriform or solid architecture. The "Roman bridge" formation in our case also emphasizes the similarity to mammary duct carcinoma (Azzopardi 1979). In a few cases, serial sectioning has revealed a transition from normal ductal epithelium to that of the intraduct tumour (Hui et al. 1986). In most cases, the cells in these areas have been fairly uniform with eosinophilic, rather granular cytoplasm (apocrine-like) and round nuclei with one or more nucleoli. The mitotic rate is variable (Chen and Hafez 1981; Hui et al. 1986; Zohar et al. 1988). In addition all cases have had an invasive component which is often poorly differentiated, sometimes with extreme cellular pleomorphism, but it may maintain a papillary or tubulo-acinar architecture. Hyalinization of the stroma around the invasive foci is also a feature (Garland et al. 1984). Myoepithelial cells are not present in this tumour.

Electron microscopy has revealed the presence of peculiar intra-cytoplasmic cocoon-shaped bodies in which tubule and membrane material is found, arranged in paired linear parallel densities 8 nm in width (Innes et al. 1982), possibly derived from lysosomes or degenerating mitochondria.

The differential diagnosis of salivary duct carcinoma includes mucoepidermoid carcinoma, terminal duct carcinoma (polymorphous low-grade adenocarcinoma) and epithelial/myoepithelial carcinoma (Afzelius et al. 1987; Garland et al. 1984). The first of these may be quite difficult to distinguish from salivary duct carcinoma, but

well-formed cribriform or papillary patterns are rare, and the presence of a squamous element is very helpful as this is not seen in salivary duct carcinoma. Terminal duct carcinoma is composed of small tubules with no necrosis, and no tendency to form papillary patterns. Epithelial/myoepithelial carcinomas may have ductal epithelial nests, but necrosis is rare and myoepithelial cells can be demonstrated around the nests albeit in varying numbers (Corio et al. 1982).

Metastatic carcinoma (e.g. from the breast or lung) presenting in the salivary glands is rare, but it may resemble salivary duct carcinoma. Ultimately, distinction relies on clinical investigation.

According to Batsakis (Batsakis 1980; Batsakis et al. 1989), those salivary gland tumours in which myoepithelial cells are an integral component arise from the intercalated duct of the salivary unit and are low-grade neoplasms. However, those tumours arising from the excretory duct (salivary duct carcinoma, mucoepidermoid carcinoma, squamous carcinoma) do not contain myoepithelial cells, are high-grade tumours and hence behave aggressively.

In conclusion, salivary duct carcinoma has a distinctive histopathological appearance and behaves clinically in an aggressive fashion. Radical surgery followed by radiation therapy is necessary in an attempt to control the disease, but despite this, the prognosis remains poor. For this reason, it is important to recognize this neoplasm as a separate entity.

Acknowledgements. The authors would like to thank Mr. M. Rothera for permission to publish details of this case, and also the technical staff of the Department of Histopathology, Hope Hospital.

References

Afzelius LE, Cameron WR, Svensson C (1987) Salivary duct carcinoma – a clinicopathologic study of 12 cases. Head Neck Surg 9:151–156

Azzopardi JG (1979) Problems in breast pathology. Major problems in pathology vol 11. Saunders, Philadelphia, pp 131–133

Batsakis JG (1980) Salivary gland neoplasia: an outcome of modified morphogenesis and cyto-differentiation. Oral Surg 49:229–232

Batsakis JG, Regezi JA, Luna MA, El Naggar A (1989) Histogenesis of salivary gland neoplasms: a postulate with prognostic implications. J Laryngol Otol 103:939–944

Brandwein MS, Jagirdar J, Patil J, Biller H, Kaneko M (1990) Salivary duct carcinoma (cribriform salivary carcinoma of excretory ducts). A clinicopathologic and immunohistochemical study of twelve cases. Cancer 65:2307–2314

Chen KTK (1983) Intraduct carcinoma of the minor salivary gland. J Laryngol Otol 97:189–191

Chen KTK, Hafez GR (1981) Infiltrating salivary duct carcinoma. A clinicopathological study of five cases. Arch Otolaryngol 107:37–39

Corio RL, Sciubba JJ, Brannon RB, Batsakis JG (1982) Epithelial-myoepithelial carcinoma of intercalated duct origin; a clinicopathologic and ultrastructural assessment of sixteen cases. Oral Surg 53:280–287

Evans RW, Cruickshank AH (1970) Epithelial tumours of the salivary glands. Major problems in pathology, vol 1. Saunders, Philadelphia, pp 265–275

Eveson JW, Cawson RA (1985) Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. J Pathol 146:51–58

Fayemi AO, Toker C (1974) Salivary duct carcinoma. Arch Otolaryngol 99:366–368

Ferlito A, Gale N, Hvala H (1981) Laryngeal salivary duct carcinoma. A light and electron microscopic study. J Laryngol Otol 95:731–738

Gal R, Strauss M, Zohar Y, Kessler E (1985) Salivary duct carcinoma of the parotid gland. Cytologic and histopathologic study. Acta Cytol 29:454–456

Garland TA, Innes DJ, Fechner RE (1984) Salivary duct carcinoma: an analysis of four cases with review of the literature. Am J Clin Pathol 81:436–441

Hui KK, Batsakis JG, Luna MM, Mackay B, Byers RM (1986) Salivary duct adenocarcinoma: a high grade malignancy. J Laryngol Otol 100:105–114

Innes DJ, Garland TA, Fechner RE (1982) Structures in salivary gland intraductal adenocarcinoma. Ultrastruct Pathol 3:193–197

Kahn HG, Baumal R, Marks A, Dardick I, Nostrand AWP van (1985) Myoepithelial cells in salivary gland tumours. An immunohistochemical study. Arch Pathol Lab Med 109:190–195

Kleinsasser O, Klein HJ, Hubner G (1968) Speichelgangcarcinome: Ein den Milchgangcarcinomen der Brustdrüse analoge Gruppe von Speicheldrüsentumoren. Arch Klin Exp Ohren-Nasen-Kehlkopfheilkd 192; 100–115

Lopez JI, Nevado M, Eizaguirre B (1990) Salivary duct adenocarcinoma (letter). J Clin Pathol 43:608

Luna MA, Batsakis JG, Ordonez NG, Mackay B, Tortoledo ME (1987) Salivary gland adenocarcinomas. Clinicopathologic analysis of three distinctive types. Semin Diagn Pathol 4:117–135

Pesce C, Colacino R, Buffa P (1986) Duct carcinoma of the minor salivary glands. A case report. J Laryngol Otol 100:611–613

Thackray AC, Lucas RB (1974) Tumors of the major salivary glands. Atlas of tumor pathology, 2nd series, fascicle 10. Armed Forces Institute of Pathology, Washington, D.C., pp 102

Zohar Y, Shem-Tov Y, Gal R (1988) Salivary duct carcinoma in major and minor salivary glands. A clinicopathological analysis of four cases. J Craniomaxillofac Surg 16:320–323