The Journal of Laryngology and Otology
September 1997, Vol. **111**, pp. 883–885

Cystadenoma of the parotid gland with unusual prominent lymphoid stroma

STEFAN PAHL, WERNER PÜSCHEL, PHILIPPE FEDERSPIL*

Abstract
A rare variant of the cystadenoma of salivary gland origin is presented, which occurred in the parotid of a 36-year-old, otherwise healthy female patient. The tumour showed a dense follicle-containing lymphoid stroma, resembling papillary cystadenoma lymphomatosum (Warthin's tumour). In contrast to that, the epithelial lining gave a more irregular impression and oncocytic metaplasia were completely absent. Light microscopic and immunohistochemical features of the tumour are described and compared with those of classical cystadenoma and papillary cystadenoma lymphomatosum (Warthin's tumour). Other relevant multicystic epithelial parotid lesions, which are commonly associated with a prominent lymphoid component are discussed.

Key words: Cystadenoma lymphomatosum, papillary; Parotid neoplasms

Introduction

Several non-neoplastic and neoplastic multicystic epithelial intraparotid lesions are often associated with follicular lymphoid tissue, a fact that may pose significant diagnostic difficulties (Auclair, 1994). Differential diagnostic considerations must include benign lymphoepithelial cysts, branchial cysts, parenchymal neoplasms with tumour-associated lymphoid proliferation, neoplasms that arise within an intraparotid lymph node and metastatic disease. The following report describes a cystadenoma of intraparotid origin with a prominent lymphoid stroma. This feature is very atypical in cystadenoma and may particularly be confused with papillary cystadenoma lymphomatosum (Warthin's tumour).

Case report

A 36-year-old woman with no contributory medical and family history, complained of a non-tender swelling in her right parotid region for one year. Over the last six months, she noticed a more rapid growth. A complete ENT examination found a non-tender tumour without fixation or skin change in the right parotid gland measuring 3 cm in greatest diameter. Facial nerve function was normal. On December 14, 1995 the tumour was removed by a partial parotidectomy under facial nerve monitoring in the Department of Otorhinolaryngology, University of Homburg, Germany. It was found to be localized in the lower pole of the lateral portion of the parotid gland. The post-operative course was complicated by a completely reversible facial nerve paresis for four months. On follow-up examination nine months post-operatively, there was no evidence of recurrence clinically nor on ultrasound study.

Pathology

Gross examination of the resected superficial lobe of the parotid gland revealed a well-circumscribed, tan, mucus-filled and multicystic lesion of 3 cm in greatest dimension. Haematoxylin-eosin stained sections showed a double-layered epithelial lining of the cystic spaces. The apical epithelial layer was composed of tall, cylindrical cells, which built up irregularly stratified pseudopapillary projections into the lumen. The cytoplasm was amphophilic, and oncocytic metaplasia were completely absent. Squamous cells, sebaceous cells, mucous cells or ciliated columnar cells could not be found within the lining epithelium. The basal layer was composed of cytoplasm-rich polygonal cells with vesicular nuclei, situated on a thick basal lamina. Nucleoli were bland and an increased mitotic rate could not be encountered. Lymphoid stroma was dense and showed numerous lymphoid follicles with

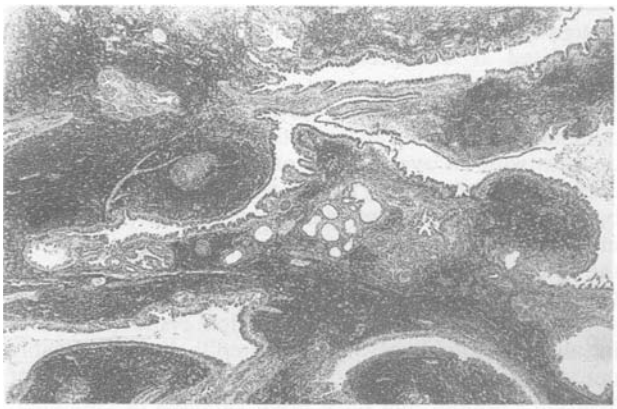

FIG. 1
Low power view showing an adenomatous multicystic lesion with a dense follicle-containing lymphoid stroma (H & E; × 40)

From the Departments of Pathology and Otorhinolaryngology*, University of Homburg, 66421 Homburg/Saar, Germany.
Accepted for publication: 30 June 1997.

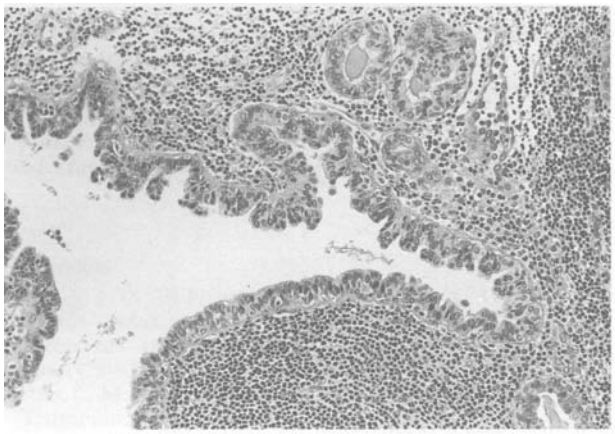

FIG. 2
The epithelial lining is composed of double-layered cells without oncocytic metaplasia (H & E; × 400)

germinal centres. Distribution of T-lymphocytes and B-lymphocytes corresponded to that of a lymph node. Moreover, a marginal sinus near the fibrous capsule could be noted, thus suggesting the origin of the lesion within an intraparotid lymph node. However a vas afferens or efferens could not clearly be identified on step sections. The surrounding salivary gland parenchyma was without abnormalities and infiltrative growth could not be observed.

Immunohistochemical investigations revealed a strong immunoreactivity of the apical cells with antibodies against pancytokeratins AE 1/3, KL 1 and epithelial membrane antigen, whereas the basal polygonal layer of cells was clearly positive for smooth muscle actin. Both cell layers were variably positive for polyclonal S-100 protein. Immunohistochemical expression of Epstein-Barr virus-associated latent membrane protein was negative, as was thyroglobulin, thus excluding metastatic thyroid cancer.

Discussion

Cystadenoma of salivary gland origin is a rare, benign epithelial neoplasm, characterized by an adenomatous papillary cystic proliferation. Its terminology has been inconsistent and a frequently used synonym is papillary cystadenoma. Analogous tumours occur at other organ sites as well. Cystadenocarcinoma is thought to be the malignant counterpart of cystadenoma and should be considered if enhanced cytological atypias or frank infiltrative growth are present.

Epidemiological features include a slight female predominance (2:1) and an age peak in the sixth to eighth decades with an average age of 57 years at the time of diagnosis. The frequency of occurrence is 4.1 per cent of all benign epithelial salivary gland tumours. It is relatively more frequent among benign tumours in the minor than in the major glands (7.0 versus 3.1 per cent respectively) (Ellis and Auclair, 1996).

Morphological hallmarks are multiple cystic spaces with intraluminal infoldings. The lining epithelium is variably one to two layers thick, more irregular than that of Warthin's tumour and most often cuboidal or columnar, but mucous and oncocytic cells are sometimes present focally and can even predominate occasionally. Squamous epithelium may be present focally but rarely predominates. The nuclei of all cell types are uniformly bland and mitotic figures are extremely rare. A dense lymphoid stroma with germinal centres is generally not a feature of cystadenoma (Auclair *et al.*, 1991). If present, it may be misinterpreted as atypical Warthin's tumour (Debain *et al.*, 1980) or other non-neoplastic and neoplastic salivary gland lesions with a prominent lymphoid component (Auclair, 1994).

In contrast to cystadenoma the epithelial component of Warthin's tumour is very characteristic and uniform. It is composed of a double layer of finely granular, oncocytic columnar and cuboidal cells. Nuclei of apical cells are regularly oriented toward the lumen of cystic spaces. There may be variations in the form of squamous cell metaplasia or sebaceous metaplasia (Seifert *et al.*, 1980; Eveson and Cawson, 1986).

The very rare malignant counterpart is the so-called 'carcinoma ex Warthin's tumour'. Up to now eight such cases have been reported in the literature. The most frequent types, according to one study, have been adenocarcinomas, followed by squamous cell carcinoma and undifferentiated carcinoma (Podlesak *et al.*, 1992). Most of them have occurred in older males, who have been exposed to prior irradiation.

Immunohistochemical findings in papillary cystadenoma lymphomatosum (Warthin's tumour) are different from those of cystadenoma. In Warthin's tumour expression of S-100 protein is negative in both cell layers as is smooth muscle actin reactivity of basal cuboidal cells (Segami *et al.*, 1989). In contrast to that, immunohistochemical characteristics of cystadenoma correspond roughly to those of excretory duct epithelium. Differential diagnosis of non-neoplastic parotid lesions with associated lymphoid tissue must also include benign lymphoepithelial cysts. This has been described extensively in the literature in HIV-positive patients (Camilleri and Lloyd, 1990; Mandel and Reich, 1992; Shaha *et al.*, 1993). The epithelial lining is most often stratified squamous.

A very similar non-neoplastic lesion on histological grounds, but with different presumed histogenesis is the branchial cyst within the parotid (Bhaskar and Bernier, 1959; Fujibayshi and Itoh, 1981). Histologically a brancial cyst is most often univacuolar, lined by a stratified squamous epithelium, a pseudostratified columnar epithelium or a combination of both. Beneath the lining epithelium varying amounts of lymphoid tissue are found. The fact that a number of cysts within the parotid are lined by a pseudostratified ciliated columnar epithelium is said to confirm their origin from the endoderm of the branchial pouch.

A neoplastic lesion with an epithelial lining similar to that of cystadenoma is sialadenoma papilliferum. However, this rare benign tumour generally involves mucosal surfaces or salivary duct epithelium.

The case presented shows that absence of both epithelial oncocytic metaplasia and lymphoid stroma can not be the sole histological feature distinguishing cystadenoma from Warthin's tumour. Moreover, the pronounced irregular epithelial lining, characteristic of cystadenoma, and immunohistochemical findings must be considered in doubtful cases. On the other hand, the more troublesome, irregular epithelium of cystadenoma should not tempt one to diagnose 'carcinoma ex Warthin's tumour' or low grade cystadenocarcinoma in cases where frank infiltrative growth can not clearly be demonstrated.

References

Auclair, P. L., Ellis, G. L., Gnepp, D. R. (1991) Other benign epithelial neoplasms. In *Surgical Pathology of the Salivary Glands.* (Ellis, G. L., Auclair, P. L., Gnepp, D. R., eds.) W. B. Saunders, Philadelphia, pp 252–268.

Auclair, P. L. (1994) Tumor associated lymphoid proliferation in the parotid gland. A potential diagnostic pitfall. *Oral Surgery, Oral Medicine and Oral Pathology* **77:** 19–26.

Bhaskar, S. N., Bernier, J. L. (1959) Histogenesis of branchial cysts; a report of 468 cases. *American Journal of Pathology* **35:** 407–423.
Camilleri, A. C., Lloyd, R. E. (1990) Lymphoepithelial cyst of the parotid. *British Journal of Oral and Maxillofacial Surgery* **28;** 329–332.
Debain, J.-J., Peytral, C., Josset, P. (1980) Une forme inhabituelle de cystadenolymphome papillaire de la parotide. A propos d'un cas. *Annales de Oto-Laryngologie* (Paris) **12:** 1047–1055.
Ellis, G. L., Auclair, P. L. (1996) *Tumors of the Salivary Glands. Atlas of Tumor Pathology*, 3rd Series, Fascicle 17. Washington, D.C.: Armed Forces Institute of Pathology, pp 115–120.
Eveson, J. W., Cawson, R. A. (1986) Warthin's tumor (cystadenolymphoma) of salivary glands. A clinicopathologic investigation of 278 cases. *Oral Surgery, Oral Medicine and Oral Pathology* **61:** 256–262.
Fujibayashi, T., Itoh, H. (1981) Lymphoepithelial (so-called branchial) cyst within the parotid gland. Report of a case and review of the literature. *International Journal of Oral Surgery* **10:** 283–292.
Mandel, L., Reich, R. (1992) HIV parotid gland lymphoepithelial cysts. Review and case reports. *Oral Surgery, Oral Medicine and Oral Pathology* **74:** 273–278.
Podlesak, T., Doleckova, V., Sibl, O. (1992) Malignancy of a cystadenolymphoma of the parotid gland. *European Archives of Otorhinolaryngology* **249:** 233–235.
Segami, N., Fukuda, M., Manabe, T. (1989) Immunohistological study of the epithelial components of Warthin's tumor. *International Journal of Oral and Maxillofacial Surgery* **18:** 133–137.
Seifert, G., Bull, H. G., Donath, K. (1980) Histological subclassification of the cystadenolymphoma of the parotid gland. Analysis of 275 cases. *Virchows Arch A: Pathologische Anatomie und Histologie* **388:** 13–38.
Shaha, A. R., DiMaio, T., Webber, C., Thelmo, W., Jaffe, B. M. (1993) Benign lymphoepithelial lesions of the parotid. *American Journal of Surgery* **166:** 403–406.

Address for correspondence:
Dr Stefan Pahl,
Institut für Pathologie,
Universität Homburg,
66421 Homburg/Saar,
Germany.

Fax: 496841/163880.