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Germinal center derived malignant lymphoma in cystadenolymphoma

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Summary. Two cases of malignant non-Hodgkin's lymphoma arising in an Albrecht-Arzt-tumour are reported. In the first case a centroblastic-centrocytic lymphoma in a palatinal cystadenolymphoma of a 64-year-old female is described. In the other case a centroblastic lymphoma developed in an Albrecht-Arzt-tumor of the submandibular region in an 82-year-old man. The occurence of a high-grade malignant lymphoma in cystadenolymphoma has not been reported in the literature so far.

Key words: Albrecht-Arzt tumour – Cystadenolymphoma – Germinal center cell lymphoma

Introduction

Albrecht-Arzt-tumour (cystadenolymphoma, Warthin's tumour) is a benign lesion of salivary glands composed of cystic or glandular spaces lined by columnar epithelium and a lympoid stroma harbouring germinal centers. Malignant change in this tumour appeares to be extremely rare. A few cases of carcinomas developing from the glandular component have been reported (Baker et al. 1980; Brown et al. 1984). Up to now only five cases of neoplastic transformation of the lympoid tissue in a Warthin's tumor have been reported in the literature, described as nodular lymphoma, poorly differentiated, lymphocytic type (Colby and Dorfman 1979), proliferation of small cleaved follicular center cells with scattered larger transformed lymphocytes (Miller et al. 1982; Hall et al. 1985), and two cases of malignant lymphoma, centroblastic-centrocytic type (Banik et al. 1985). We give an account of another case of low-grade and the first case of high-grade malignant lymphoma arising in a cystadenolymphoma.

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Methods

Tissue specimens were fixed in formalin and embedded in paraplast. Sections for light microscopy were stained with haematoxylin and eosin (HE), giemsa and Gomori silver impregnation. Immunohistochemical staining was performed on paraplast sections applying the three step peroxidase antiperoxidase (PAP) method according to Mepham et al. (1979) using the antisera to IgG, IgM, IgA, kappa, lambda, lysozyme, alpha$_1$-antichymotrypsin, alpha$_1$-antitrypsin and common leukocyte (all antisera DAKO, Copenhagen, DK). Peroxidase reactivity was demonstrated with 3'3-diaminobenzidine-tetra-hydrochloride (DAB; Walter, Kiel, FRG). The non-Hodgkin's lymphomas were classified according to the Kiel-classification (Lennert et al. 1975; Lennert 1978).

Case reports

Case 1. A 64-year-old female consulted her physician in August, 1982 because of a soft painful swelling at the junction of the hard and soft palates. Two months later a biopsy was taken from the now enlarged and easily bleeding, soft tumor. Microscopic examination revealed predominantly reactive lymphatic tissue with local infiltration by large atypical cells. These findings and the impression that the main tumour bulk was located in a deeper region than that of the first biopsy specimen, justified another biopsy. During collection of the second tissue specimen serous fluid escaped at incision. No further tumour foci were found during subsequent screening. Laboratory investigations revealed no pathological findings.

Pathology. The biopsy specimens obtained from the palate measured up to 1 cm in diameter. Histological examination reveals cystic lesions with highly eosinophilic contents lined by a double-layered epithelium. The inner layer is composed of tall, prismatic eosinophilic cells; the outer layer consists of cuboidal or flat epithelial cells. In the supporting stroma infiltrates consisting of small lymphocytes, occasional blasts, plasma cells, and macrophages are seen (Fig. 1a). Focally, however, follicular (Fig. 1b) and sometimes diffuse, aggregates of centrocytes admixed with some centroblasts (Fig. 1c) and a few multinucleated blasts, some of which show atypical mitosis, can be demonstrated. The usual composition of germinal centers has disappeared in this part of the tumour; starry sky macrophages are absent. No intracytoplasmic immunoglobulins can be detected in the lymphoid cells of the tumour by immunohistochemistry. The neoplastic lymphoid infiltrates are localized in the deep submucosal layer without infiltration of the mucosa. The histopathological diagnosis was cystadenolymphoma with low grade malignant lymphoma, centroblastic-centrocytic type, follicular without sclerosis.

Case 2. An 82-year-old man presented with loss of appetite and firm nodular swelling in the left submandibular region, which had grown rapidly over the preceding two weeks. The tumour was excised for histological diagnosis. X-ray examination revealed enlargement of the mediastinum. The remainder of the physical examination and all laboratory tests, including the haematological variables, were within normal limits.

Pathology. The nodular tumour mass removed at surgery measured approximately 3 cm in diameter and histologically shows cystic spaces formed by multiple papillary epithelial projections typical of cystadenolymphoma as described in the first case. Besides clusters of small lymphoid cells under the basement membrane, infiltration of the stroma by medium-sized to large cells is seen (Fig. 2a). Tumour cells with abundant, pale or slightly basophilic cytoplasm show large, round, occasionally irregular shaped nuclei with medium-sized nucleoli, often apposed to the nuclear membrane. Prominent, centrally located nucleoli are also detected in some cells (Fig. 2b). Immunohistochemistry of these cells reveals distinct positivity for common leukocyte antigen. Neither immunoglobulins (IgG, IgM, IgA, kappa, lambda) nor histiocytic markers (lysozyme, alpha$_1$-antitrypsin, alpha$_1$-chymotrypsin) can be detected. The histopathological diagnosis was a high-grade malignant lymphoma, centroblastic type, developing in an Albrecht-Arzt-tumour.

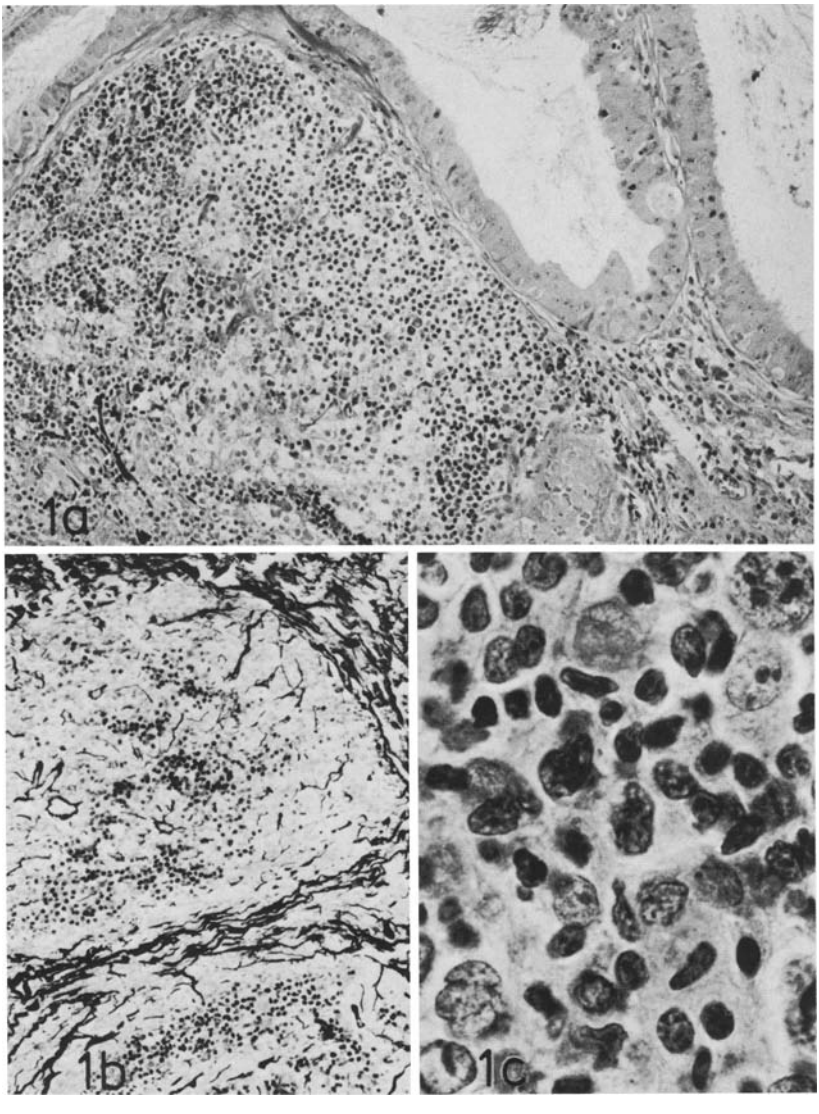

Fig. 1a. Warthin's tumour in the palate showing papillary infoldings of the epithelium, cyst formation, and surrounding lymphoid stroma (Giemsa; ×140). **b** An other area of the biopsy with a nodular infiltration pattern (Gomori; ×140). **c** The tumour is composed of centrocytes and a few large centroblasts (Giemsa; ×350)

Discussion

Cystadenolymphoma is regarded as a benign tumour that constitutes about 5 to 10 per cent of all parotid gland neoplasms and is a rare finding in submandibular or minor salivary glands of elderly patients (Thackray and Lucas 1974). In order to account for the coexistence of a neoplastic epithelial element and non-neoplastic lymphoid tissue, the heterotopic theory is fa-

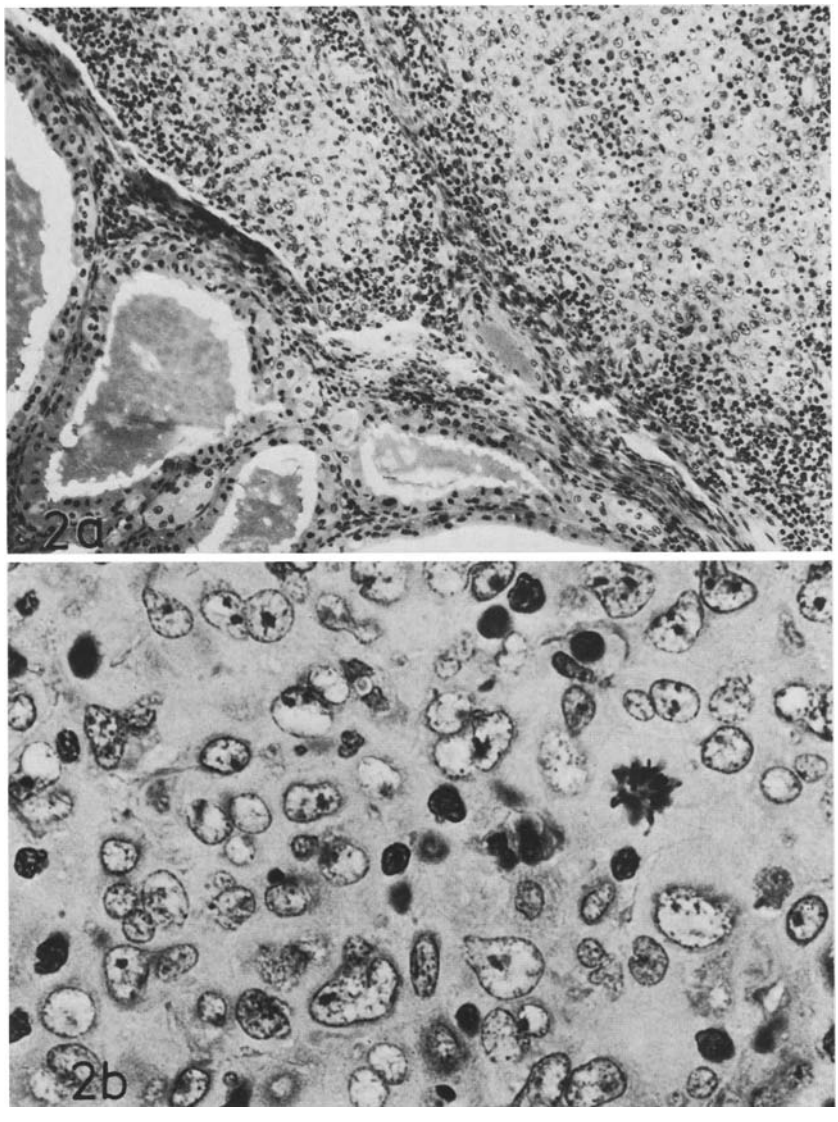

Fig. 2a Cystic lesion in a Warthin's tumour form the submandibular region with double layered epithelium and proteinaceous granular material in the lumen. Lymphoid stroma is infiltrated by clusters of large pale cells (arrow) (Giemsa; ×140). **b** Tumour cells with round or lobulated nuclei and medium-sized or prominent nucleoli, characteristic of centroblastic lymphoma (Giemsa; ×880)

voured, suggesting that the tumour arises from ductal inclusions entrapped during embryonic development in lymph nodes adjacent to or within salivary glands (Albrecht and Arzt 1910; Thompson and Bryant 1950). As expected from the immunological findings in normal or reactive lymph nodes, lymphoid cells of Albrecht-Arzt-tumour were found to be composed of T-lym-

phocytes and polyclonal B-lymphocytes (Diamond and Brylan 1979). The results of immunohistopathological studies on the frequency distribution and density of plasma cells also conflict with an autoimmune pathogenesis for Warthin's tumour (Foulsham et al. 1984).

The malignant lymphoid component observed in cystadenolymphoma by Colby and Dorfman (1979), Miller et al. (1982), Hall et al. (1985) and Banik et al. (1985), as well as our two cases were germinal center derived lymphomas. In five cases malignant lymphoma centroblastic-centrocytic type was diagnosed, in one patient a centroblastic lymphoma developed in an Albrecht-Arzt-tumour. Centroblastic-centrocytic lymphoma also was the preferential diagnosis in a study of Schmid et al. (1982) on primary malignant lymphomas localized in salivary glands, exclusive of cases with immunesialadenitis as underlying disease. In contrast, malignant non-Hodgkin lymphomas are not an uncommon finding in patients with primary immunesialadenitis with or without other symptoms of Sjögren's syndrome and have mostly been classified as immunocytic or immunoblastic type (Lennert et al. 1979).

Malignant lymphomas in an Albrecht-Arzt-tumour are an extremely rare finding. It can be assumed that there are no microenvironmental factors in cystadenolymphoma which facilitate the developement of germinal center cell lymphomas. An adenolymphmatous component of a fully developed malignant lymphoma easily can be missed because of the often small biopsies taken from salivary gland tumours.

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