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CASE REPORT

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Micropapillary carcinoma of the parotid gland arising in mucinous cystadenoma

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Abstract We describe a 45-year-old man who had a 2-year history of a slowly enlarging tumor in the left parotid gland. Histologically, the tumor was a mucinous cystadenoma with focal apocrine differentiation, which revealed a widespread invasive micropapillary adenocarcinoma component. A rim of lymphoid tissue surrounded the margins of the micropapillary carcinoma. The invasive micropapillary adenocarcinoma component was morphologically identical with the invasive micropapillary carcinoma of the mammary gland. The tumor is different from so-far recognized salivary gland tumor entities.

Keywords Salivary gland · Micropapillary carcinoma · Mucinous cystadenoma

Introduction

Some pseudoneoplastic lesions and neoplasms of the major salivary glands have a strong histopathologic resemblance to the tumors of the breast. Sclerosing polycystic adenosis (sclerosing polycystic sialadenopathy) resembles the changes seen in fibrocystic disease of the breast [4, 20], and epithelial–myoepithelial carcinoma of the salivary glands is morphologically identical to some adenomyoepitheliomas of the breast, including its occasional malignant behavior [5, 10, 13, 15, 16, 18]. Collagenous spherulosis [1, 9], salivary duct carcinoma [14], adenoid cystic carcinoma, and pleomorphic adenoma are other examples of this interesting phenomenon. We present here a unique carcinoma arising in the parotid gland, which resembles a recently described invasive micropapillary carcinoma of the breast [17]. We are not aware of such a tumor ever to have been observed in salivary glands.

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Materials and methods

The tissues of the tumor were fixed in 4% formaldehyde, embedded in paraffin, and routinely stained. The sections were then deparaffinized and predigested by pepsin (0.05% in HCl acid, for 20 min). For immunohistochemistry, the following primary antibodies were employed; cytokeratin (AE1-AE3, 1:500; Boehringer), (CAM5.2, 1:50; Becton-Dickinson), S-100 protein (polyclonal, 1:1000; Dako), smooth muscle actin (HHF-35, 1:500; Dako), synaptophysin (polyclonal, 1:1000; Dako), chromogranin (monoclonal, 1:100; Dako), and MIB1 antibody (1:100, Immunotech, Marseille, France).

Sections 4 µm thick were cut from the specimens and placed on slides coated with 3-aminopropyltriethoxy-silane (Sigma). For immunohistochemistry with the MIB1 antibody, sections were incubated twice in a microwave oven for 5 min at 700 W in citrate buffer (pH 6.0) prior to incubation with primary antibody. The binding of the primary antibodies was visualized using the supersensitive streptavidin–biotin–peroxidase complex (Biogenex). Appropriate positive controls were used with each primary antibody. The color was developed using diaminobenzidine supplemented with hydrogen peroxide. The sections were lightly counterstained with Mayer's hematoxylin.

Clinical history and pathological findings

A 45-year-old man had a 2-year history of a slowly enlarging mass in the left parotid gland. The tumor was surgically excised with the safe margins of the adjacent non-tumorous tissues. Two years after surgical excision, the patient is well and without signs of recurrence.

Grossly, the tumor was 4×3×3 cm in size, poorly circumscribed without signs of necrosis or hemorrhage. It had a soft consistency and was white to gray in color on cut section.

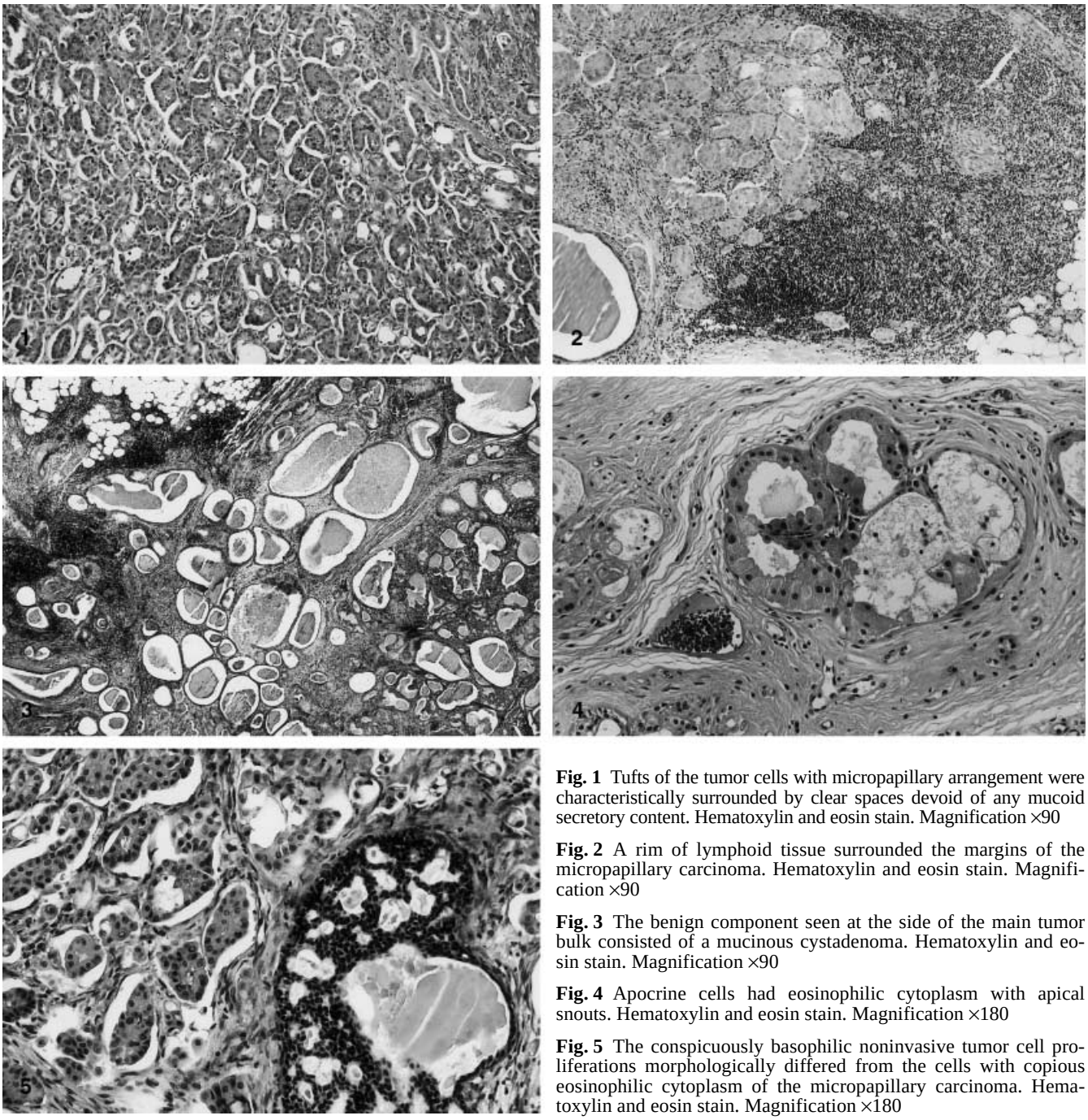

Fig. 1 Tufts of the tumor cells with micropapillary arrangement were characteristically surrounded by clear spaces devoid of any mucoid secretory content. Hematoxylin and eosin stain. Magnification ×90

Fig. 2 A rim of lymphoid tissue surrounded the margins of the micropapillary carcinoma. Hematoxylin and eosin stain. Magnification ×90

Fig. 3 The benign component seen at the side of the main tumor bulk consisted of a mucinous cystadenoma. Hematoxylin and eosin stain. Magnification ×90

Fig. 4 Apocrine cells had eosinophilic cytoplasm with apical snouts. Hematoxylin and eosin stain. Magnification ×180

Fig. 5 The conspicuously basophilic noninvasive tumor cell proliferations morphologically differed from the cells with copious eosinophilic cytoplasm of the micropapillary carcinoma. Hematoxylin and eosin stain. Magnification ×180

Microscopically, the greatest bulk of the tumor consisted of an invasive carcinoma arranged in micropapillae separated by either a small amount of fibrocollagenous stroma or by delicate strands of intervening fibrovascular tissue. Tufts of the tumor cells with micropapillary arrangement were characteristically surrounded by clear spaces devoid of any mucoid secretory content (Fig. 1). There were numerous psammoma bodies in the stroma. The tumor cells contained conspicuously eosinophilic cytoplasm, which stained negatively with periodic acid–Schiff base (PAS) and mucicarmine, and vesicular, slightly pleomorphic nuclei. The number of mitoses was low (2 per 10 HPF). Myoepithelial cells were absent in the invasive micropapillary carcinoma component. A rim of lymphoid tissue surrounded the margins of the micropapillary carcinoma (Fig. 2). The other part of the tumor was represented by a benign component seen at the side of the main tumor bulk consisting of a mucinous cystadenoma (Fig. 3), which revealed a PAS- and mucicarmine-positive cytoplasm and secretion. The mucinous cells of the cystadenoma component revealed transitions to eosinophilic secretory cells with apical snouts typical of apocrine differentiation (Fig. 4). The cystadenoma revealed focally micropapillary intraductal formations. The

stroma in the cystadenomatous part was dense and fibrous. In other parts of the tumor, we found a low-grade in situ intraductal component, which focally almost completely filled the ducts and was composed of small cells with basophilic cytoplasm. These conspicuously basophilic tumor cells of the noninvasive carcinomatous component morphologically differed from the cells with copious eosinophilic cytoplasm of the micropapillary carcinoma (Fig. 5). The interface between the tumor components was sharp. We found no lymphatic invasion in our case.

Immunohistochemically, all the cells of the tumor stained positively with antibodies to both cytokeratins and S-100 protein. Actin stained only the thin external myoepithelial layer of the ducts of the cystadenomatous component. The staining with antibodies to synaptophysin and chromogranin gave negative results. The MIB1 antibody stained very rare nuclei of tumor cells in the cystadenomatous part. More frequent MIB1-positive nuclei were observed in the micropapillary carcinomatous component of the tumor; however, the MIB1 index (percentage of tumor cell nuclei positively stained with the MIB1 against Ki-67 antigen) was rather low even within the invasive micropapillary component and represented 8%.

Discussion

Some pseudoneoplastic lesions and neoplasms of the major salivary glands can have a strong histopathologic resemblance to certain tumors of the breast. Our case seems to be remarkably similar to the nine cases of invasive micropapillary carcinoma of the breast recently described by Siriaunkgul and Tavassoli [17]. The tumor was composed of tufts of tumor cells lying within clear spaces lined by attenuated spindle cells, suggestive of massive lymphatic invasion. Myoepithelial cells were absent in the micropapillae. Five of nine cases of micropapillary carcinoma of the breast contained psammoma bodies [17]. Very similar histological features of the micropapillary carcinoma of the breast were present in the invasive micropapillary carcinoma component of our patient. The difference was, however, seen in the intraductal noninvasive component. Whereas intraductal carcinoma of the micropapillary carcinoma of the breast was composed purely of micropapillary or mixed micropapillary and cribriform patterns [17], a mucinous cystadenoma with solid low-grade intraductal in situ proliferation composed of basophilic cells was revealed in our case.

Invasive micropapillary carcinoma is a recently described variant of ductal breast cancer with a poor prognosis [11, 21]. Micropapillary growth pattern is, however, not unique to the breast. Micropapillary urinary bladder carcinoma was recently characterized, and even focal micropapillary pattern was associated with more aggressive behavior [7]. As we are not aware of any reported case of micropapillary carcinoma in the salivary glands, and in our case the follow-up period is short, we are unable to comment on the biological behavior. However, it seems reasonable to expect that micropapillary invasive carcinoma of the parotid gland is a low-grade malignancy as the MIB1 proliferative index was only 8%.

The apocrine differentiation is regularly present in the so-called sclerosing polycystic adenosis of major salivary glands (sclerosing polycystic sialadenopathy) which was recently described by two groups of authors [4, 20]. Focal apocrine metaplasia was recently described in a case of salivary duct carcinoma arising in basal cell adenoma [16], and we have also demonstrated a presence of focal apocrine differentiation in a case of benign oncocytic myoepithelioma [19]. In the present case, there was focal apocrine differentiation seen at the side of mucinous differentiation in the cystadenomatous component. This dual mucinous and apocrine differentiation is rarely seen in cutaneous tumors. In fact, in cutaneous tumors, some authors consider mucinous differentiation as indirect proof of apocrine differentiation of the skin adnexal neoplasms [12].

The differential diagnosis of the invasive micropapillary carcinoma of the parotid gland is relatively easy, because hardly any tumor of the salivary glands bears any resemblance to it. Mucinous cystadenocarcinoma of the salivary glands may look similar to the cystadenomatous parts of our case; however, the micropapillary invasive growth is not seen in mucinous cystadenocarcinomas [6]. Salivary duct carcinoma is a high-grade carcinoma of the salivary glands whose name was derived from the similar looking breast carcinoma [2, 8, 14]. It is composed of ductal cells with formation of structures resembling distended salivary ducts entirely differing from the micropapillary formations seen in our case The recently described low-grade salivary duct carcinoma has intraductal proliferations similar looking to the in situ component in our case; the micropapillary invasive growth was, however, also absent [3].

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