Presence and distribution of CA 19-9 in human salivary glands and salivary gland tumors

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Introduction

Monoclonal antibody NS 19-9 has been developed by Koprowski *et al.*¹⁾ in 1979 using colo-rectal carcinoma cell line (SW 1116) as an immunogen. The antigen CA 19-9, expressed sialyl Lewis^x,²⁾ has been detected in sera of various gastrointestinal cancer patients. The presence of CA 19-9 in colorectal, pancreatic and gastric adenocarcinomas has been demonstrated by immunohistochemical method^{3,4)}. The antigen has also been detected in normal tissues such as epithelium of bile ducts, bronchial glands, large ducts of salivary gland and prostate^{3,4)}.

In this study we examined the distribution pattern of CA 19-9 in normal salivary glands and salivary gland tumors.

Materials and Methods

Normal salivary gland specimens included 12 major salivary glands (5 parotid, 3 submandibular and 4 sublingual glands) and 21 minor salivary glands (12 palatal, 5 labial, 2 buccal, 1 lingual and 1 molar glands), as shown in Table 1. Salivary gland tumors used in this study were as follows: 12 cases of pleomorphic adenomas, 6 cases of adenoid cystic carcinomas and one case of papillary cystadenoma lymphomatosum. Table 2 shows more details of these salivary gland

tumors. All of these materials were fixed with 10% neutralized-buffered formalin and embedded in paraffin. For localization of CA 19-9, an avidin-biotin-peroxidase complex method⁵⁾ was applied to each deparaffinized section. Monoclonal antibody NS 19-9 was kindly provided by Toray-Fuji Bionics Inc. The antibody diluted 1 : 500 was used as a primary antibody. To increase antigenicity, the sections were incubated in 0.1% pronase for 15 min at 37°C as pretreatment.

Results and Discussion

In major salivary glands positive reaction products for CA 19-9 were demonstrated in the cytoplasm and apical portions of some ductal cells. Atkinson *et al.*³⁾ and Arends *et al.* have reported CA 19-9 was demonstrated in epithelium of the large ducts of normal salivary glands by an immunohistochemical method. A positive reaction was also seen in some mucous cells of sublingual glands. On the other hand reactivity for CA 19-9 in minor salivary glands, especially in palatal, labial and lingual glands, was higher than that in major salivary glands (Table 1). Positive reactions were localized in not the only cytoplasm of mucous and ductal cells but also in the luminal borders and contents of the intercalated, striated and excretory ducts (Fig. 1). McDicken and Scott⁷⁾ have reported that

Table 1 Reactivity for CA 19-9 in normal salivary glands

Site	Number	CA 19-9-grade					
		duct			acinus		
		0	1	2	0	1	2
<i>Major salivary glands</i>							
Parotid glands	5	2	3	0	5	0	0
Submandibular glands	3	2	1	0	3	0	0
Sublingual glands	4	2	2	0	2	2	0
<i>Minor salivary glands</i>							
Palatal glands	12	4	3	5	4	3	5
Labial glands	5	0	2	3	0	2	3
Lingual glands	1	0	0	1	0	0	1
Buccal glands	2	0	2	0	0	2	0
Molar glands	1	0	1	0	0	1	0

grade 0: staining was absent.

grade 1: positive staining was seen in a few ducts or acini only.

grade 2: positive staining was seen in many ducts or acini.

only occasional positive staining for carcino-embryonic antigen (CEA) was seen in the acini cells and non-neoplastic duct cells of minor salivary glands. On the other hand Caselitz *et al.*⁶⁾ have described that the presence of CEA was demonstrated at the border of the acinar cells and duct cells in inflamed parotid glands.

CA 19-9 was detected in 8 out of 12 pleomorphic adenomas, 5 out of 6 adenoid cystic carcinomas and one papillary cystadenoma

Fig. 1 Palatal gland.

Positive reaction products for CA 19-9 are seen in cytoplasm of many mucous cells, apical portion of duct cells and luminal contents. Counterstained with hematoxylin.

lymphomatosum by the ABC method (Table 2). Positive reaction products were localized in the cytoplasm and luminal membrane of the ductal cells in pleomorphic adenomas (Fig. 2). They were also seen in the duct lumens. In only two cases keratinized cells of squamous metaplasia stained positively. In adenoid cystic carcinomas positive stained material was seen in mucoid materials of cystic spaces and duct-like structures (Fig. 3). The distribution of CA 19-9 in pleomorphic adenomas and adenoid cystic carcinomas was consistent with that of CEA previously described⁷⁾. Compressed and flattened epithelium and cyst contents of papillary cystadenoma

Table 2 Reactivity for CA 19-9 in salivary gland tumors of different histological types

Tumor type	Number	Site	CA 19-9-grade		
			0	1	2
Pleomorphic adenoma	12		4	3	5
	2	Parotid gland	1	1	0
	10	Palatal gland	3	2	5
Adenoid cystic carcinoma	6		1	2	3
	3	Sublingual gland	0	2	1
	3	Palatal gland	1	0	2
Adenolymphoma	1	Parotid gland	0	1	0

grade 0: staining was absent.

grade 1: positive staining was seen in a few neoplastic ducts or mucus only.

grade 2: positive staining was seen in many neoplastic ducts or mucus.

Fig. 2 Pleomorphic adenoma.
Positive reaction products for CA 19-9 are found in luminal borders and contents of neoplastic ducts. Counterstained with hematoxylin.

Fig. 3 Adenoid cystic carcinoma.
Positive reaction products are seen in cystic spaces and mucus of duct-like structures. Counterstained with hematoxylin.

lymphomatosum stained positively.

In preliminary experiments, CA 19-9 was detected in normal human saliva by enzyme immunoassay (EIA) using the ABC method.

These findings suggest that CA 19-9 is a new marker for normal as well as pathological conditions of salivary glands.

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