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Histopathological Studies on Parotid Gland Tumors in Japanese Children

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Summary. Thirty-two cases of parotid gland tumors in Japanese children (under 16 years of age; 5.5% of total of 580 tumors) were examined and classified histopathologically. The results obtained were as follows.

1) Haemangiomas were found most frequently (59.4%) and could be divided into either cavernous haemangioma (31.3%) or capillary haemangioma (28.1%). The second highest frequent tumor was pleomorphic adenoma (28.1%).

2) Capillary haemangioma in infancy was called hypertrophic, juvenile, or congenital. Capillary haemangioma occurred within one year after birth. The tumor was found predominantly in females and on the right side.

3) Cavernous haemangioma was recognized in patients of a higher age than capillary haemangioma and was considered to arise from the extralobular connective tissues. In some cases it was difficult to discriminate the tumor from arterio-venous malformation.

4) Pleomorphic adenoma did not possess any histological characteristics different from those seen in adults.

5) Malignant tumors were relatively rare, and consisted of mucoepidermoid tumor, malignant lymphoma, and adenocarcinoma.

Some difference in the incidence of the tumors was noted between Japanese or European and American children but the reasons for this are unknown.

Key words: Parotid gland tumors in children – Congenital capillary hemangioma – Pleomorphic adenoma.

Introduction

A parotid gland swelling in children is due to either tumor or inflammatory disease. The latter has been noted with higher frequency in children than in

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adults and includes mumps, cytomegalic inclusion disease, cat-scratch fever, or various other inflammatory conditions (Seifert and Donath 1976; Krolls et al. 1972).

Parotid gland tumors are frequently seen in middle to old-age patients (Thackray and Lucas 1974) but rather uncommonly in children. From the clinicopathological aspects, it may be worthwhile to analyze the difference in both the incidence and histological characteristics of the tumors between children and adults. In addition, a comparison of incidence rates regarding sex, age and behavior in Japanese children, allowing a comparison with published material about children in other countries is important.

The content of this report focuses on the problems mentioned above and also attempts to clarify the composition of some tumors seen commonly in children.

Materials and Methods

In this study, 580 parotid gland tumors were examined, which have been collected in the Department of Otolaryngology, School of Medicine, Chiba University, and at the Asahi Hospital, Asahi, Chiba Prefecture, Japan. The tumors were classified by the WHO classification. In total 32 cases (5.5%) were noted in patients younger than 16 years of age, which were referred to as „children". In Japan, the following age divisions made up this classification:

1) new born (under one month), 2) infant (from one month to one year), 3) childhood (from one year to six years), and 4) school period (from seven to fifteen years).

Tissue specimens for light microscopy were fixed in 10% formalin. Ten step-serial blocks were taken from these tumors and embedded in paraffin. For malignant tumors, the portions in which the capsules were suspected of being either infiltrated or even destroyed by the carcinoma tissues were examined by step-serial sections. The sections were stained with Haematoxylin-Eosin (HE.), Elastica-van Gieson, Azan-Mallory, PAS-Alcian blue, and silver impregnation for reticulin fibers.

Results

In the present survey, haemangiomas were the most common type of parotid gland tumor in children (59.4%) as shown in Table 1 (WHO classification). The second most common type of tumor was pleomorphic adenoma (28.1%). Malignant tumors of the parotid gland in children were very rare, but when they occurred, they consisted of mucoepidermoid tumor, malignant lymphomas and adenocarcinoma.

1. Haemangioma

Haemangiomas which developed in the parotid gland in children could be divided into either the cavernous (31.3%) or capillary (28.1%) type. The former arose from the extralobular connective tissues surrounding each lobe of the parotid gland. In these tumors we recognized a cavernous dilatation of the vascular lumen lined by flattened endothelial cells, which frequently resulted

Table 1. Incidence of parotid gland tumors in children

	Sex				Laterality					Total	
	Male		Female		Left		Right		Unknown		
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	Cases	%
Pleomorphic adenoma	4	44.4	5	55.6	3	33.3	6	66.7	0	9	28.1
Mucoepidermoid Tumor	0	0.0	1	100.0	0	0.0	1	100.0	0	1	3.1
Adenocarcinoma	1	100.0	0	0.0	1	100.0	0	0.0	0	1	3.1
Angiomas											
cavernous haemangioma	6	60.0	4	40.0	5	50.0	5	50.0	0	10	31.3
capillary haemangioma	2	22.2	7	77.8	2	22.2	7	77.8	0	9	28.1
Lymphoma	2	100.0	0	0.0	0	0.0	0	0.0	2	2	6.3
Total	15	46.9	17	53.1	11	34.4	19	59.4	2	32	100.0

in compressive atrophy of the involved lobes (Fig. 1). The wall of cavernous haemangioma was composed basically of smooth muscle fibers and sparse elastic fibers, which showed the features of a vein (Fig. 2). Thus there were some difficulties in differential diagnosis from arterio-venous malformation.

Capillary haemangioma, which has recently been referred to as benign infantile haemangioendothelioma (Nagao et al. 1980), most frequently occurred shortly after birth (in newborns) and usually showed progressive enlargement of the parotid gland without any symptoms such as pain or facial nerve paralysis. Macroscopically, each lobe of the parotid gland surrounded by fine fibers seemed to become hypertrophic (Fig. 3). Histologically, the tumor cells, with an oval or rounded nucleus, showed a uniform growth pattern in the intralobular connective tissues of the parotid gland. Acinic cells and intercalated ducts were widely replaced by tumor cells, leaving only scattered islets of these elements (Nagao et al. 1980). The tumor cells mostly presented solid proliferations, but scattered vascular channels containing a few red cells were noticed (Fig. 4 and 5).

As mentioned above, the haemangioma showed rapid growth clinically and displayed a pattern of invasive growth. It should be noted that this type of growth may sometimes provide an erroneous impression of malignancy.

The incidence of capillary haemangioma was frequent in females (77.8%) and on the right, as shown in Table 1. The age distribution is shown in Table 2. All patients were under the age of 12 months. 44.4% of the tumors measured above 5 cms in greatest diameter, as shown in Table 3.

In contrast, the occurrence of cavernous haemangioma seemed to be unrelaed to sex and laterality. Cavernous haemangioma was found frequently in patients of higher age (childhood or school period) than capillary haemangioma, and the tumor tended to be smaller in size (Table 3).

2. Pleomorphic Adenoma

Pleomorphic adenoma was of the next-highest frequency following haemangiomas (Table 1) (28.1%). The incidence was much lower than in adults.

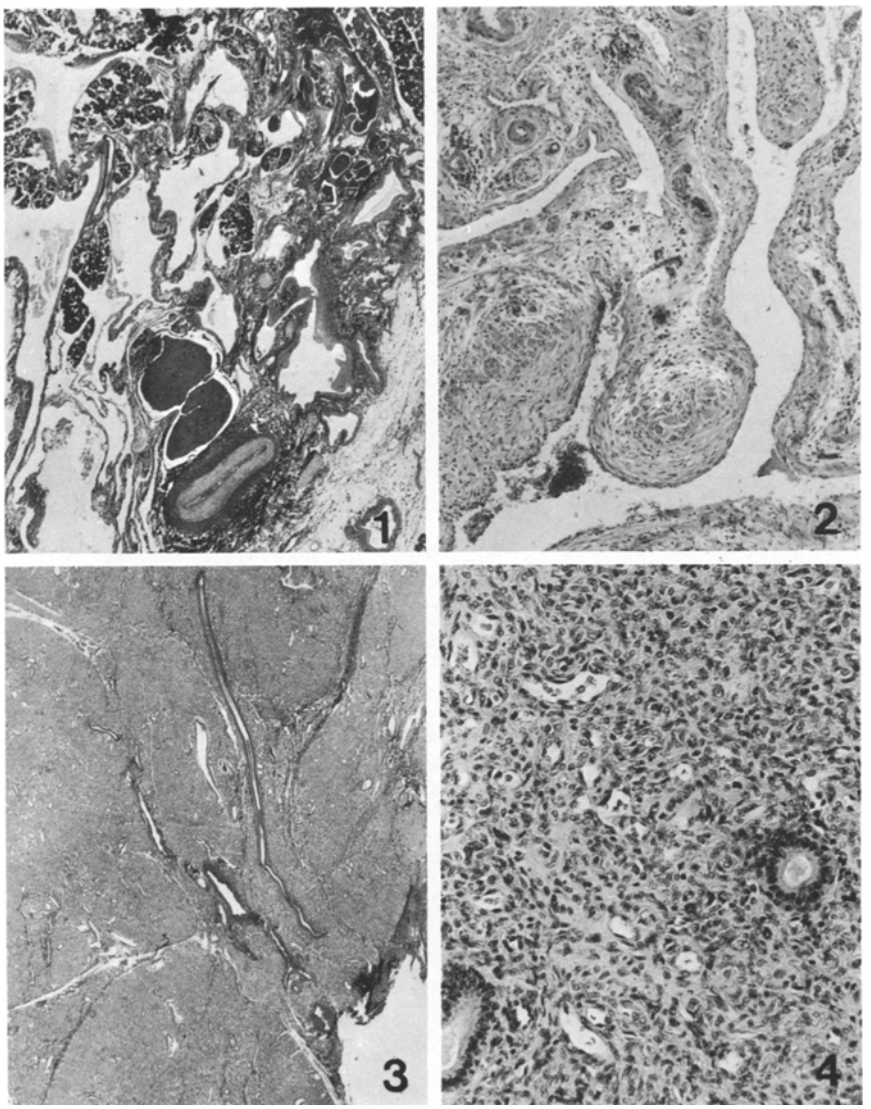

Fig. 1. Cavernous haemangioma. Some acinic lobuli are present which are atrophic and compressed by dilated vascular channels. HE. ×3

Fig. 2. Cavernous haemangioma. Vascular lumens lined by flattened endothelial cells show cavernous dilatation. In the wall of vascular channels sparse connective tissue and smooth muscle are seen. HE. ×100

Fig. 3. Capillary haemangioma. Each lobule is surrounded by fine fibers and shows hypertrophy. Lobular structures are maintained and the parotid gland appears to be enlarged as a whole. HE. ×3

Fig. 4. A high power view of Fig. 1. Tumor cells which are oval or round in shape show a solid proliferation. Note scattered vascular channels. Acinic cells have been replaced by tumor cells. Striated duct remains embedded in tumor tissues. HE. ×100

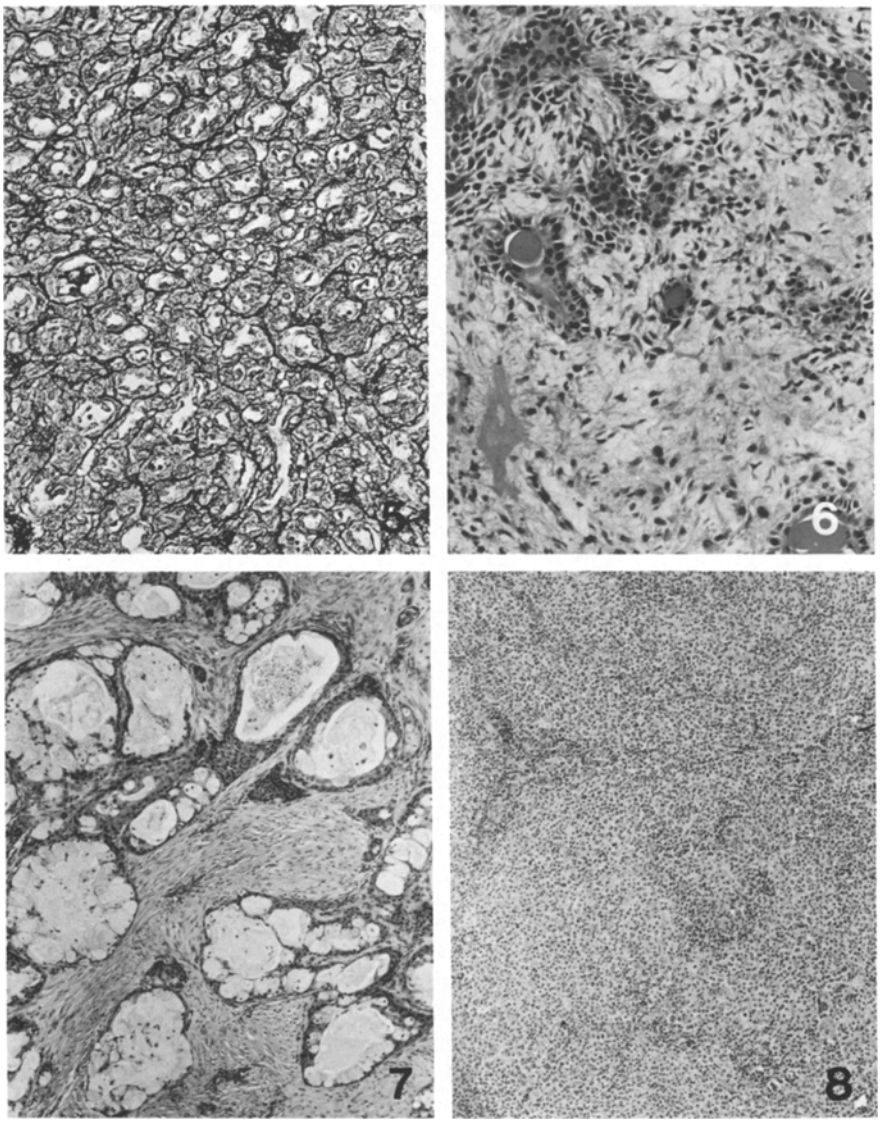

Fig. 5. Capillary haemangioma. Distinctive basement membranes are seen, separating tumor cells to form a vascular unit. Silver stain. ×100

Fig. 6. Pleomorphic adenoma. The tumor cells arising from myoepithelial cells show a partially glandular structure. The formation of cartilage is seen in part of the tumor tissue. HE. ×100

Fig. 7. Mucoepidermoid tumor. Columnar epithelial cells producing mucin show glandular formation. Squamous epithelium in the basal area proliferates so as to push the columnar epithelial cells toward the lumen. HE. ×40

Fig. 8. Malignant lymphoma (follicular type). The proliferating tumor cells show follicular structures. HE. ×100

Table 2. Incidence of parotid gland tumors in children related to patient's age

	0–12 mos.		1–6 yrs.		7–15 yrs.		Total
	Cases	%	Cases	%	Cases	%	cases
Pleomorphic adenoma	0	0.0	0	0.0	9	100.0	9
Mucoepidermoid tumor	0	0.0	0	0.0	1	100.0	1
Adenocarcinoma	0	0.0	0	0.0	1	100.0	1
Angiomas							
cavernous haemangioma	1	10.0	5	50.0	4	40.0	10
capillary haemangioma	9	100.0	0	0.0	0	0.0	9
Lymphoma	0	0.0	1	50.0	1	50.0	2
Total	10	31.3	6	18.7	16	50.0	32

Table 3. Incidence of parotid gland tumors in children related to tumor size

	0–1.9 cm		2.0–4.9 cm		Over 5 cm		Unknown	Total
	Cases	%	Cases	%	Cases	%	cases	cases
Pleomorphic adenoma	0	0.0	9	100.0	0	0.0	0	9
Mucoepidermoid tumor	0	0.0	0	0.0	1	100.0	0	1
Adenocarcinoma	0	0.0	1	100.0	0	0.0	0	1
Angiomas								
cavernous haemangioma	3	30.0	7	70.0	0	0.0	0	10
capillary haemangioma	0	0.0	5	55.6	4	44.4	0	9
Lymphoma	0	0.0	0	0.0	1	50.0	1	2
Total	3	9.4	22	68.8	6	18.8	1	32

Clinically, pleomorphic adenoma did not usually express itself by pain but the tumors in the depth of the parotid gland were often associated with facial nerve palsy. However, most patients did not come to hospital until they were aware of a parotid swelling rather than just the palsy.

Macroscopically, the surface of the tumors, encapsulated by fibrous tissues, was observed to be regular. Histologically, the tumors consisted of cartilagenous or osteoid tissues, myxomatous areas, and epithelial elements. Basically, the tumor cells showing active growth were epithelial cells producing a glandular lumen, which was surrounded by myoepithelial cells (Fig. 6). Not infrequently, the cells showed squamous epithelial metaplasia. Mucinous materials were often seen to remain in the glandular lumen.

3. Mucoepidermoid Tumor

Clinically, the tumor was usually associated with pain in the area of the parotid gland and/or facial nerve palsy. Macroscopically, it was mostly encapsulated by fibrous tissues, but always showed partial destruction of the capsule when

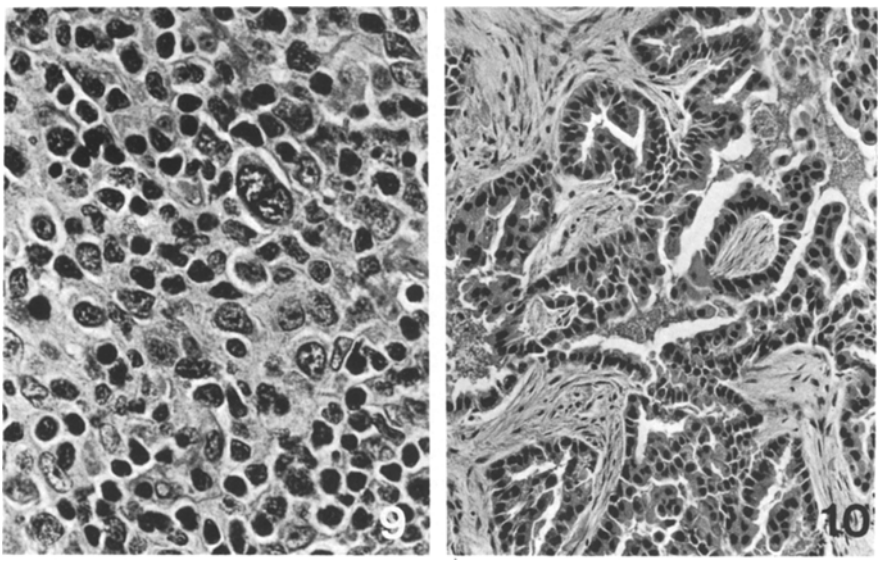

Fig. 9. A high power view of Fig. 8. Mixed histiocytic and lymphocytic lymphoma. HE. ×400

Fig. 10. Adenocarcinoma. Adenocarcinoma showing a papillary proliferation. The epithelial cells exhibit some double layer structures. HE. ×100

examined in detail. On the cut surface, multiple small cysts were seen. This tumor was cloudy gray-white in color due to the mucin produced.

Histologically, mucin was seen to remain in the lumen of the cysts, as determined by positive mucicarmin staining. The cells lining the cystic wall consisted of columnar goblet cells and squamous epithelium with intermediate cells. Squamous epithelium was seen at the periphery of the cysts and proliferated so as to push the columnar epithelium toward the lumen of the cysts from the basal area (Fig. 7). In some cases, intermediate cells, formed intercellular bridges, between the goblet cells and basal cells.

Either capsular involvement or infiltration into the perineural space was always found somewhere in the tumor tissues, indicating apparent malignancy. It was to be noted that there were some cases which were difficult to discriminate from epidermoid carcinoma when squamous epithelium was predominant. In these cases, we should diagnose mucoepidermoid tumor when the sparse goblet cells which exist in the squamous epithelium shows positive mucicarmin staining. The differential diagnosis was important because the prognosis of this tumor usually was better than that of epidermoid carcinoma.

4. Malignant Lymphoma

There were some difficult problems in the diagnosis of malignant lymphoma arising from the parotid gland, because it was often invaded by malignant lymphomas from the lymph nodes. The two tumors reported by us were pre-

sumed to have arisen from the parotid gland for the reasons that the tumors were clinically localized in the parotid gland, they were of a nodular type histologically, and there were no lymph nodes involved. Macroscopically, the tumors were elastic, soft and gray-white and, histologically, they were nodular lymphomas of mixed histiocytic and lymphocytic type (Figs. 8 and 9).

5. Adenocarcinoma

Macroscopically, this was a gray-white tumor without any capsular formation.

Histologically the tumor showed papillary and/or tubular proliferations (Fig. 10). Differential diagnosis from acinic cell carcinoma or mucoepidermoid tumor is important. Acinic cell carcinoma has secretory granules in the basophilic cytoplasm, and shows tubular patterns but not definite papillary proliferation. In mucoepidermoid tumor, there is always coexistant portions in which the tumor differentiats to squamous epithelium. Our case was diagnosed as adenocarcinoma by these criteria.

Discussion

According to other investigators (Thackray and Lucas 1974; Castro et al. 1972), parotid gland tumors in children are relatively rare when the age of children is defined as under 16 years. Krolls et al. (1972) reported that the incidence of salivary gland tumors in American children was 4.3%. According to Becker et al. (1978), 3.7% of a total 16000 cases of salivary gland tumors were found in German children. In the present report, the incidence of parotid gland tumors in Japanese children was 5.5%. In general, the incidence of these tumors is less than that in adults. The most common parotid gland tumor in adults has been shown to be pleomorphic adenoma, which accounts for about 70% of all tumors (Seifert and Donath 1976; Thackray and Lucas 1974; Foote and Frazell 1953; Ackerman and Rosai 1974). In comparison, for benign tumors in children, haemangiomas were the most frequent (Seifert 1965), and pleomorphic adenoma, Ranula and lymphoepithelial tumor followed in descending order, while for malignant tumors, mucoepidermoid tumor and undifferentiated carcinoma were most frequent (Castro et al. 1972). Krolls et al. (1972) reported that in American children, pleomorphic adenoma was most common and haemangioma was second, and that the two accounted for 90% of benign tumors in children. In Japanese children, however, the same tendency reported by Seifert (1965) was noticed, with haemangiomas being the most common tumor. From the viewpoint of geographical pathology, it is of considerable interest that there exists a definite difference in the types of parotid gland tumors which occur in different areas. Our results are similar to those for a European population but not for those in Americans, for reasons which are unknown.

Haemangiomas, which occurred at the highest frequency in children, could be divided into either cavernous or capillary types. The former had the clear characteristics of vein and hamartomatous lesions, resembling arterio-venous

fistulas rather than true tumors (Thackray and Lucas 1974). Histologically, the lesions were presumed to arise from the vessels in the extralobular connective tissues of the parotid gland.

In capillary haemangioma, which is also referred to as hypertrophic haemangioma (Wawro et al. 1955; Hoehn et al. 1970), juvenile haemangioma (Bhaskar et al. 1963), or congenital capillary haemangioma (Edwards et al. 1954; Campbell et al. 1956), benign infantile haemangioendothelioma (Nagao, et al. 1980), swelling in the area of the parotid gland was observed in newborns. Most tumors grew rapidly and then were removed surgically within one year (Wawro, et al. 1955; Goldman, et al. 1969). The proliferation of tumor cells occurred in the intralobular area of the parotid gland, replacing acinic cells. This finding, along with some cellular atypism (Nagao et al. 1980) may led to an erroneous diagnosis of malignant haemangioendothelioma. However, in the benign lesions there was neither the destruction of tumor capsule nor mitoses, proving that the tumors were benign in nature.

Pleomorphic adenoma is the most common parotid gland tumor in adults and occurs frequently in females in middle age (Seifert and Donath 1976; Thackray and Lucas 1974; Foote and Frazelle 1953). This tumor is the second most common to haemangiomas as reported by other investigators (Seifert 1965; Castro et al. 1972). Galich et al. (1969) noted that pleomorphic adenoma in children was more common in females; the same was true in adults. In the present study, however, it showed no preference regarding sex.

Carcinoma in pleomorphic adenoma was found to be common in older patients (Evans and Cruickschank 1970) but less so in younger ones. Castro et al. (1972) and Howard et al. (1950) recognized a few cases of the tumor in the elementary school period. Vawter and Tefft (1966) also reported two rare carcinoma cases. In the present study, we found no case of malignant transformation of pleomorphic adenoma.

Adenocarcinoma is very rare in children. The tumor was found in one of 33 cases (Castro et al. 1972), and 3 of 35 cases (Krolls et al. 1972). According to Seifert (1965), and Krolls et al. (1972), mucoepidermoid tumor was the most common malignant salivary gland tumor in children.

It is often difficult to diagnose primary malignant lymphoma of the parotid gland, since a lymphoma which suffers a leukaemic change may partially invade the parotid gland (Nime et al. 1976). The following criteria for the diagnosis may be helpful when: 1) other lymph nodes have not been involved by tumor cells clinically; 2) Follicular lymphoma in the parotid gland does not suffer a leukaemic change; 3) there are reasonable grounds for presuming that the tumor has arisen from benign lymphoepithelial lesion. We observed only two cases of malignant lymphoma but benign lymphoepithelial lesion was more commonly encountered (4 cases). The differential diagnosis of these conditions may not be difficult. It should be noted, however, that malignant lymphoma could arise from immune sialadenitis (e.g., Sjögren's syndrome) subsequent its malignant transformation (Heckmayr et al. 1976).

Neurofibroma and lymphangioma have been shown to develop in the parotid gland of children (Seifert 1965). These rather common tumors were not encountered in our series.

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