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Hamartoma of the parotid gland: a case report with immunohistochemical and electron microscopic study

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Summary. A case of a solid parotid tumour in a 16-year-old boy is presented. Histologically, the tumour demonstrated some peculiar findings. An acinar pattern was predominant although every component seen in the normal salivary gland was present, namely, serous and mucous gland acini, ducts, myoepithelial cells, adipose and lymphoid tissue. Large eosinophilic granules were abundant in the large acinar cell cytoplasm. Immunohistochemically, the tumour demonstrated the proteins which are present in the normal parotid gland, for example, amylase, lactoferrin and lysozyme. Electron microscopic features were quite similar to those of normal parotid tissue except for accumulation of a large number of cytoplasmic granules in the acinar cells. There has been no previous report of a tumour with the same features as seen in this case. Our pathological diagnosis is hamartoma, although the possibility of hyperplasia or neoplasia can not be excluded.

Key words: Hamartoma – Parotid gland – Immunohistochemistry

Introduction

Salivary gland masses, other than those due to mumps are rare in children and adolescents. Their frequency is less than 5% of the total tumour-like lesions of the salivary gland (Castro et al. 1972; Krolls et al. 1972; Schuller and McCabe 1977). They are classified as non-neoplastic (inflammation and hyperplasia), hamartomatous (vasoformative or non-vasoformative) and neoplastic (Wright et al. 1985). More than one half of neoplastic lesions are benign (Kauffman and Stout 1963). Almost all non-neoplastic disorders reported are composed of inflammatory lesions and vasoformative hamartomas, for example, haemangioma.

This report describes a case of 16-year-old boy with an adenolipoma-like hamartoma of the parotid gland, which has not hitherto been described in the literature.

Report of the case

A 16-year-old boy noted a nodule in the right infla-auricular area, which did not enlarge during the three months prior to

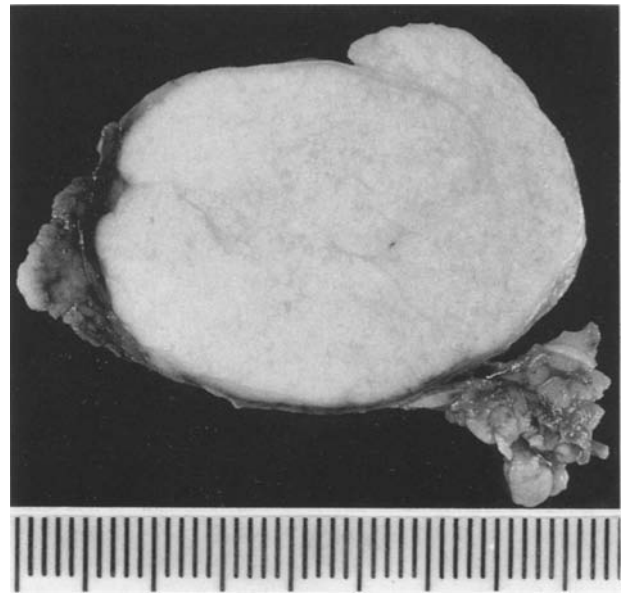

Fig. 1. Gross appearance of the tumour. It is solid, well encapsulated and lobulated by fibrous septa. The superficial lobe of the parotid gland is seen around the tumour

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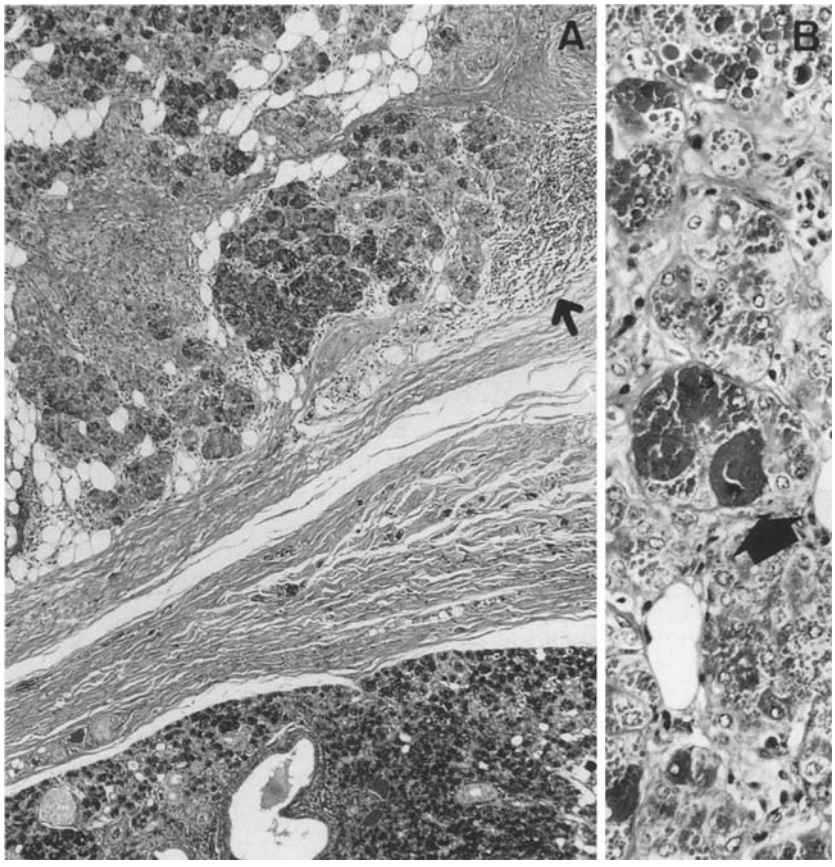

Fig. 2A. Low power view of the tumour (*upper*) and surrounding normal parotid gland (*lower*). Acini, ducts and adipose tissue are seen in the tumour. Lymphoid tissue is also present (*arrow*). ×40 (H&E); **B** Large eosinophilic granules are present in the serous acinar cells of the tumour. Some granules are large enough to obscure the nucleus (*arrow*). ×100 (H&E)

physician examination. He visited the National Cancer Center Hospital on June 3, 1986. On physical examination, the nodule was painless and measured approximately 3 cm in diameter. There was no symptom to suggest involvement of the facial nerve. The tumour was firm, smooth, well circumscribed but poorly mobile. Although Wolff-Parkinson-White cardiac syndrome had been diagnosed several years earlier, he had been asymptomatic and had received no treatment. Family history was not contributory. The tumour was excised by right superficial lobectomy of the parotid gland. There has been no recurrence during 3-months' follow-up.

Gross pathology and light microscopy. The tumour, measuring 4.0 × 3.2 × 3.0 cm, was located in the superficial lobe and was well circumscribed by a thin capsule. It was firm with a smooth surface. The cut surface was solid and bulged slightly. It was lobulated and mixed yellowish and milky white in color (Fig. 1).

Microscopically, the tumour is lobulated by thick fibrous septa. It consists of well differentiated organoid structures with serous and mucous acini, ducts, fat and lymphoid tissue. A serous acinar pattern dominates (Fig. 2). Adipose tissue occupies less than one half of the lesion. The average size of the acinar cells is about twice that of normal parotid gland. One striking feature of acinar cells within the tumour is the presence of abundant number of cytoplasmic eosinophilic granules of varying size. These granules are PAS-positive and diastase resistant. Generally, the granules are larger than normal zymogen granules and the cytoplasm of some cells is packed with eosinophilic hyaline droplets like Russell bodies (Fig. 2). The mucous acinar cells are infrequently observed. The majority of the ducts resemble those of the intercalated portion. They show not only tubular pattern but also arbor or nest like pattern with stratification of the ductal cells. Eosinophilic granules are often present in their cytoplasm. Extralobular secretory ducts are well organised.

Immunohistochemical studies were carried out using the avidin-biotin peroxidase complex (ABC) method (Hsu et al. 1981). The following primary antisera were used: rabbit antisera against human lactoferrin (LF), lysozyme (LZ) (both from Dakopatts A/S, Denmark) and salivary amylase (from Nordic Immunological Laboratories, Netherland). The site of the immunoreaction was visualized with 3,3′-diaminobenzidine tetrahydrochloride as the chromogen. The specificity of the reaction was verified by staining positive and negative control tissue sections and also by negative staining without the primary antiserum. The localization patterns of LF and LZ are almost identical in the tumour. There is intensively positive LF and LZ reactivity in every acinar cell and intercalated duct cells which have visible eosinophilic granules in their cytoplasm (Fig. 3). The localization of LF and LZ in the normal parotid acinar cells is similar to that of the tumour except that fewer acinar cells are positive and that ducts in normal gland are uniformly negative. Amylase is demonstrated in a few acinar cells in the tumour. However, the majority of acini and all ductal cells are negative. In the positive cells, the small eosinophilic granules are stained. In contrast, in the normal parotid gland, this enzyme is strongly positive in the granules of acinar cells but negative in ducts (Table 1).

On electron microscopy the acini of the tumour are composed of pyramidal acinar cells which are arranged around a central lumen. The acinar cells have a height of 20 μm to 30 μm compared with 15 μm to 20 μm in the normal parotid

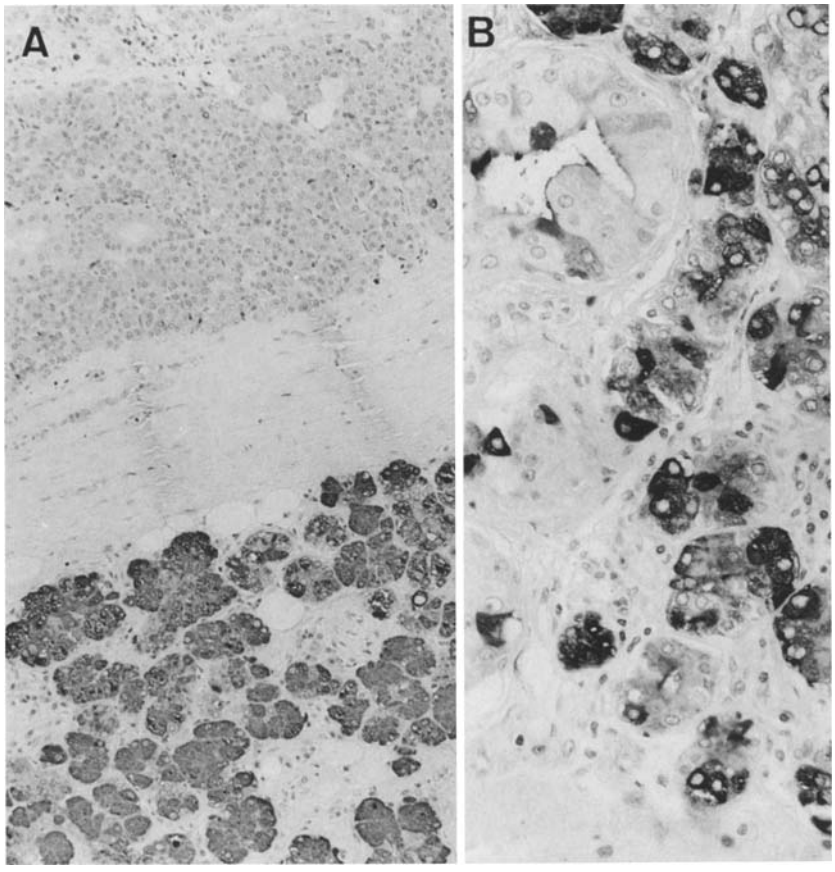

Fig. 3A. Immunohistochemical localization of lactoferrin in the tumour (*lower*) and in normal salivary gland (*upper*). In the former, lactoferrin is more intensely positive. ×40 (Immunoperoxidase staining); **B** Lysozyme distribution. Almost all acinar cells and some ductal cells are positively stained for lysozyme. ×100 (Immunoperoxidase staining)

gland. Opposing cell membranes are joined together by tight junctions near the lumen, by a series of desmosomes in the middle position and, more basally by interdigitation of the folded lateral cell surfaces. The nuclei are centrally located. Rough endoplasmic reticulum and mitochondria are located around the nucleus (Fig. 4). Most of the numerous granules in the acinar cells are larger than 5 μm and some are 8 μm in diameter, and thus much bigger than those of the normal parotid acinar cells (1 μm to 3 μm) (Riva and Riva-Testa 1973). In the tumour acinar cells, the granules sometimes fuse together. They often fill the entire cytoplasm and displace and disfigure the nuclei to stellate shape. Tumour acini are bordered by a single layer of myoepithelial cells as in the normal tissue. The ductal cells are relatively unspecified except that smaller-sized granules are often present in the cytoplasm (Fig. 4).

Discussion

The characteristic findings of this parotid tumour were as follows: 1. Every component of normal salivary gland was present with a mature structure. 2. The tumour was well encapsulated. 3. Abundant eosinophilic granules were present in the cytoplasm of the serous acinar cells. On electron microscopy, they were not swollen mitochondria but granules which were several times larger than those of normal parotid acinar cells. Immunohistochemically, active secretory potential was suggested since LF and LZ were strongly positive and amylase was also present. 4. The size of acini was approximately twice that of acini of the normal gland. Our histopathological diagnosis is an adenolipomatous hamartoma. However, whether the tumour in this case is hamartomatous, hyperplastic or neoplastic is difficult to determine with certainty.

The name hamartoma is applied to tumor-like lesions which arise during the development of an organ or tissue (Gardner 1978). They may show a wide range of histological appearances since hamartomas may be composed of adult tissues which are normal component of the tissue or of primitive mesenchyme representing the embryonic remnants of precursors of the developing structure (Gardner 1978; Zarbo and McClatchey 1983). This case can be included in the former type of hamartoma. In the literature, we found four reports of non-vascular hamartoma of the salivary gland, but available descriptions were brief (Toraya et al. 1970; Krolls et al. 1972). These reports did not describe the kinds of tissue combinations observed in hamartomas.

Adenolipoma may be another reasonable name for this case. However, adenolipoma is generally considered to be a hamartoma although some have

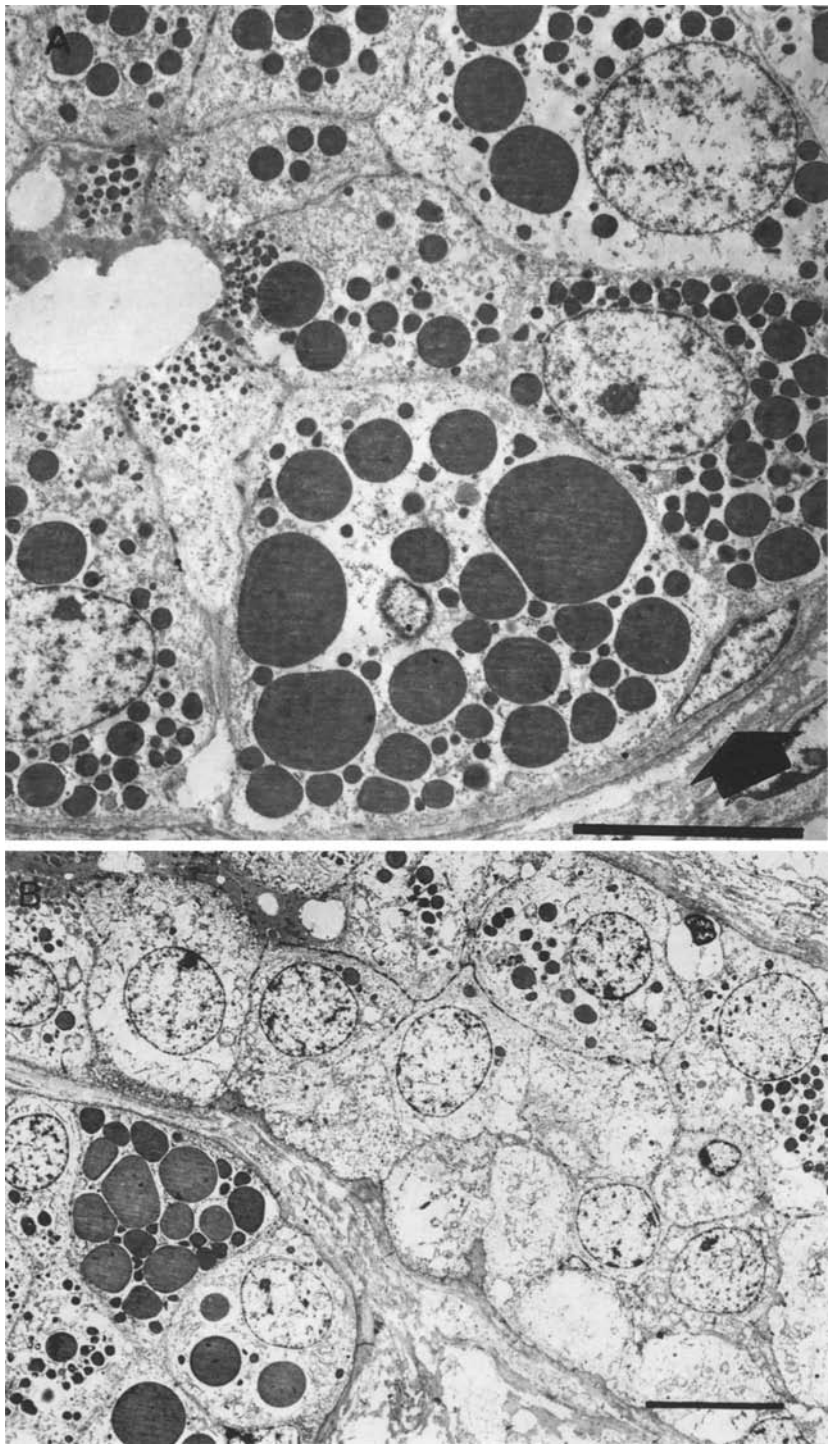

Fig. 4. Electron micrograph of (**A**) an acinus and (**B**) a duct in the tumour. (**A**) Large granules measuring larger than 5 μm are common. A single myoepithelial cell is also seen (*arrow*). ×1500 (**B**) Tubular structure resembling the intercalated duct. Poligonal ductal cells show stratification. ×900 Bar: 0,9 μm

pointed out its partial neoplastic character (Nagao et al. 1985). No report of adenolipoma arising in the parotid gland was encountered. In the entire head and neck area, reports of hamartomas are extremely rare (Legolvan et al. 1977; Patterson et al. 1981; Zarbo and McClatchey 1983). Among those hamartomas, adipose tissue is commonly, but not always, present in their mesenchymal components.

There is no report of focal adenomatoid hyperplasia occurring in the parotid gland. All the previous cases were not encapsulated and found in

Table 1. Distribution and staining intensity of lysozyme, lactoferrin and amylase in tumour and normal parotid tissue: Results of immunohistochemical study

	Lysozyme	Lactoferrin	Amylase
Normal parotid			
Acinus	+	+	+++
Duct	−	−	−
Tumor			
Acinus	+++	+++	+
Duct	+	+	−

Grading: +++ diffuse marked staining; + partial staining; − no staining

the minor oral salivary glands, especially in the palate (Arafat et al. 1981; Brannon et al. 1985). All reported cases showed hyperplasia of the mucous gland acini, and the ages of the patients were from 24 to 55.

Remarkable eosinophilic staining of the cytoplasm is also reported to occur in oncocytic hyperplasias and similar conditions (Becker et al. 1982; Vigliani and Genetta 1982). In the present case, oncocytic transformation was not seen. Eosinophilic staining of the cytoplasm was due to the presence of granules which contain abundant protein and not due to swollen mitochondria. Clinically, oncocytic lesions usually appear in the elderly.

A true neoplasm was the least likely possibility; in well differentiated acinic cell carcinoma, the cytoplasm is basophilic in haematoxylin-eosin stain and the myoepithelial cells are not found in the acinar and intercalated duct portion (Eversole 1971). The reported histology of other known neoplasms are distinct from that of this case.

We studied immunohistochemical staining patterns of amylase, LF and LZ in order to determine whether the tumour cells produced the proteins which are seen in normal acinar cells. We showed that this tumour produced the same proteins although their pattern of localization was somewhat different from the normal gland (Caselitz et al. 1981; Korsrud and Brandtzaeg 1982). The large eosinophilic granules appeared to contain secretory proteins. It is uncertain how the large granules were formed. Secretion of the proteins might be impeded because of congenital or secondary malformation of the duct system. Alternatively those proteins might overproduced or the tumour cells may engage in altered or incomplete synthesis of some product such that transport and secretion events are interrupted. The large size of the acini and abundant production of proteins were the reasons that we could not completely exclude the possibility of focal hyperplasia or neoplasia of the gland. The true nature of the tumour remains to be elucidated and further investigation of similar cases is necessary.

This tumour did not seem to proliferate rapidly; it showed no enlargement during the three months after the patient had palpated it for the first time. Perhaps it had grown very slowly without producing symptoms.

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