

Oncocytic hyperplasia in the human minor salivary glands: a post-mortem study

Yasunori Takeda

Department of Oral Pathology, School of Dentistry, Iwate Medical University, 19-1 Uchimaru Morioka, Iwate 020 Japan

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Abstract. Oncocytic hyperplasia in the human labial salivary glands was sought in a series of 217 post-mortem subjects. Oncocytic change occurred in 183 subjects and hyperplasia was found in 19 of those (the overall incidence being 8.8%), ranging in age from the third decade to the ninth. The sex distribution showed a significantly greater rate in males (16 of 139 males, 11.5%; 3 of 78 females, 3.8%). Oncocytic hyperplasia occurred in the duct system, and not in the acinar regions; it was frequently seen in the interlobular and intralobular ducts. Oncocytic hyperplasia was classified into four types; focal hyperplasia of the duct wall resulting in partial thickening of the duct wall; marked hyperplasia resulting in thickening of the duct wall, extending over half of the circumference; marked hyperplasia extending to the whole duct wall and intralobular adeno-tubular hyperplasia with or without cystic dilatation. About half of the subjects with oncocytic hyperplasia showed a few hyperplastic foci in one gland. The changes increased in severity in older subjects.

Key words: Oncocyte – Hyperplasia – Oncocytosis – Aging – Minor salivary glands

Introduction

Oncocytes are the epithelial cells characterized by an abundant, granular, and eosinophilic cytoplasm, and a centrally situated pyknotic nucleus. These cells were first observed in the human salivary glands, but similar cells have since been observed in numerous other organs. Ultrastructural and histochemical studies suggest the oncocytes represent a metaplastic change accompanied by a mitochondriopathy, although the biological significance of oncocytes is unknown.

Oncocytic transformation of duct and acinar epithelial cells may occur singly or in small clusters in normal human salivary glands, and appears to increase in frequency with aging. Pathologically, there are three main

groups of oncocytic salivary gland lesions, which most commonly occur in the parotid gland: oncocytic hyperplasia (multifocal oncocytic adenomatous hyperplasia and diffuse oncocytosis), oncocytoma (benign and malignant), and other tumours with a more or less prominent oncocytic component (Thackray and Lucas 1974; Seifert and Donath 1976; Seifert and Sobin 1991). In addition, frequency and histopathology of oncocytic hyperplasia in the major salivary glands in post-mortem subjects, especially in the parotid gland, have been studied in detail (Hamperl 1931; Steinhardt 1933; Skorpil 1940; Meza-Chávez 1949; Bauer and Bauer 1953). However, there are few studies on histopathology of oncocytic hyperplasia in the human minor salivary glands. The aim of the present study, using a post-mortem series, was to investigate whether oncocytic hyperplasia is seen in the human minor salivary glands.

Materials and methods

Several minor salivary glands of the lower lip were taken from each of 217 autopsy subjects not affected by tumours of the head and neck, tumours of haematopoietic and lymphoreticular systems, or local infectious diseases, and who had had no administration of steroid drug within the previous 2 months. The causes of death for 217 subjects included malignant neoplasms, cirrhosis, hepatitis,

Table 1. Age and sex distribution of autopsy subjects

Age range (year)	Male	Female	Total
–10	6	2	8
11–20	5	3	8
21–30	10	7	17
31–40	13	8	21
41–50	9	11	20
51–60	19	16	35
61–70	45	9	54
71–80	27	14	41
81–	5	8	13
Total	139	78	217

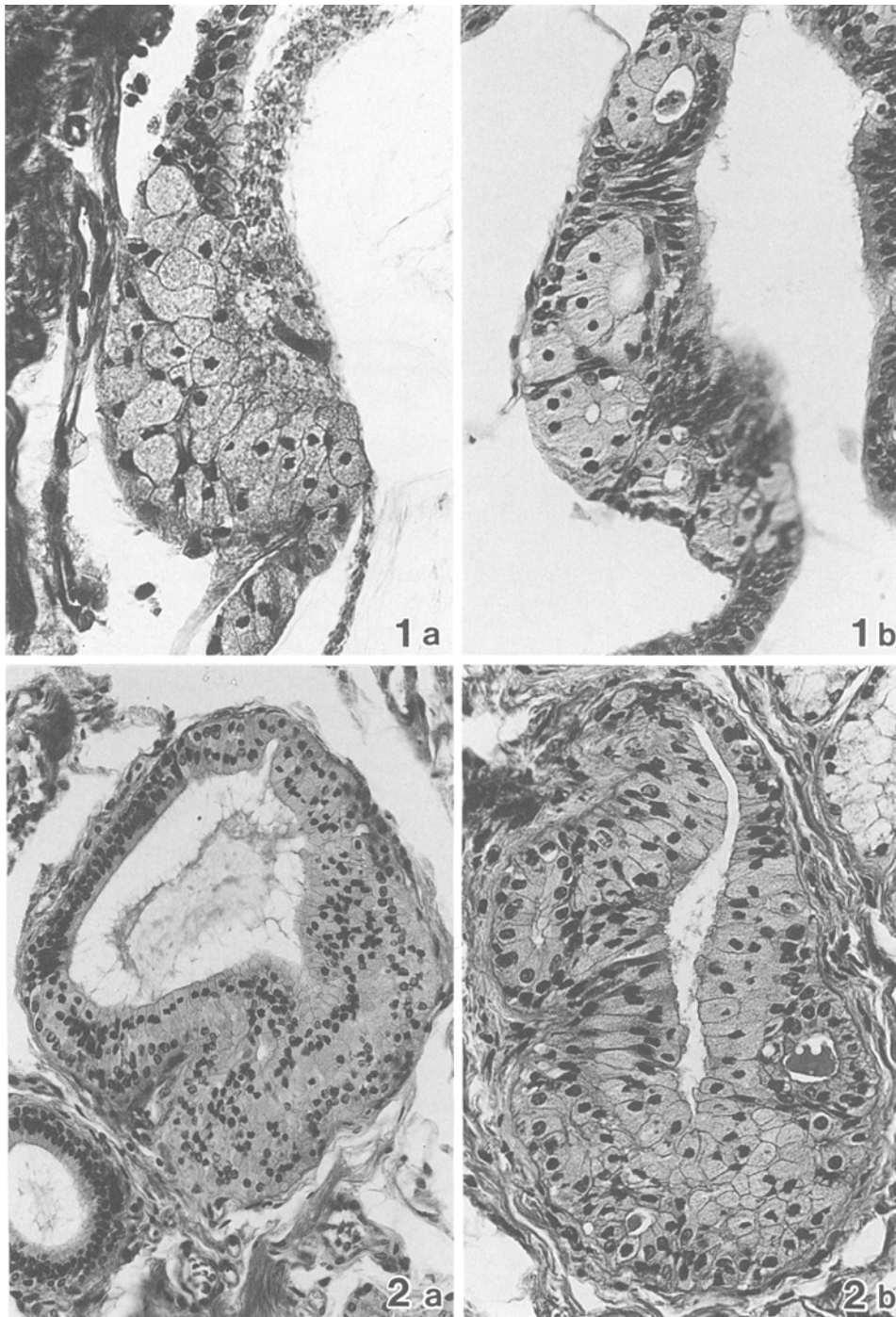


Fig. 1. Focal oncocytic hyperplasia of the duct wall in the interlobular area, resulting in partial thickening of the duct wall. **a** Solitary nodule of oncocytic hyperplasia. **b** Oncocytic hyperplasia showing a multitubular structure. $\times 400$

Fig. 2a, b. Oncocytic hyperplasia of the duct wall in the interlobular area, resulting in marked thickening of the duct wall, extending over half part of the circumference of the duct wall. Tubular structures are scattered in the thickened duct wall. **a** $\times 200$; **b** $\times 350$

renal failure, cardiovascular diseases, injury, bleeding into the gastrointestinal tract, metabolic disturbance, and senility. Table 1 shows the age and sex distribution of 217 autopsy subjects. The materials were fixed in 10% neutral-buffered formalin, embedded in paraffin, and serial sections of 5 μ m thickness were stained with haematoxylin and eosin and prepared for microscopic examination.

The glands in each subject were examined histologically and scanned for the presence of oncocytic change with or without hyperplasia.

Results

Oncocytic change with or without hyperplasia was found in 183 of 217 subjects, the overall incidence being 84.3% (Table 2). The frequency increased with each advancing decade, though oncocytic change was found in 50 to 60% of subjects under the fourth decade. The frequency was slightly higher in females than in males, but the difference was not statistically significant. Oncocytic change was frequent in the duct system; it had a tendency to be most frequent in the interlobular ducts (72.3%), less in the

Table 2. Incidence of oncocytic changes with or without hyperplasia in labial salivary glands in each decade of age

Age range (year)	Number of examined subjects	Oncocytic change ^a (per cent positive ^b)	Oncocytic hyperplasia (per cent positive ^b)
-10	8	5 (62.5)	0
11-20	8	5 (62.5)	0
21-30	17	9 (52.9)	1 (5.9)
31-40	21	13 (61.9)	1 (4.8)
41-50	20	18 (90.0)	1 (5.0)
51-60	35	31 (88.6)	2 (5.7)
61-70	54	50 (92.6)	8 (14.8)
71-80	41	39 (95.1)	5 (12.2)
81-	13	13 (100.0)	1 (7.8)
Total (per cent positive)		183/217 (84.3)	19/217 (8.8)

^a including oncocytic hyperplasia

^b positive subjects/examined subjects in each decade

intralobular ducts (62.8%), and still less in the main excretory ducts (46.7%). Oncocytic change in the acinar cells was seen in only 11.5% of subjects with oncocytic change. There was no correlation between oncocytic change and degenerative changes of the salivary gland parenchyma, lymphoid cell infiltration, or significant disease at death.

Oncocytic hyperplasia was found in 19 of 217 subjects (the overall incidence being 8.8%) and of 183 subjects with oncocytic change (the incidence being 10.4%), ranging age from the third decade to over the ninth (Table 2). The sex distribution showed a significantly greater rate in the males (16 of 139 males, 11.5%; 3 of 78 females, 3.8%). Oncocytic hyperplasia occurred in the duct system, and not in the acinar regions; it had a tendency to be frequent in the interlobular and intralobular ducts.

Oncocytic hyperplasia could be histologically classi-

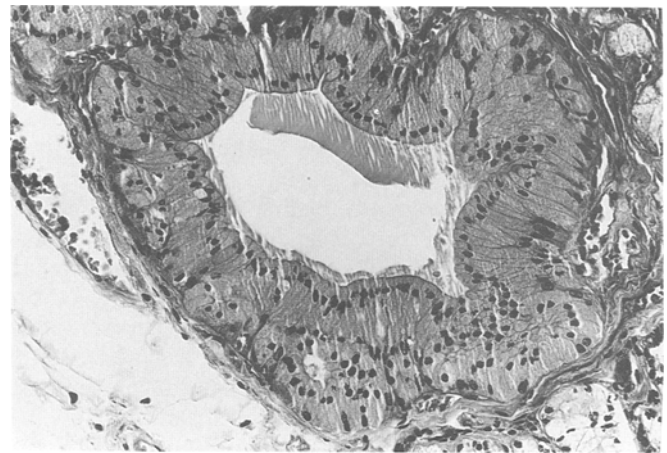


Fig. 3. Oncocytic hyperplasia of the whole duct wall in the interlobular area. $\times 180$

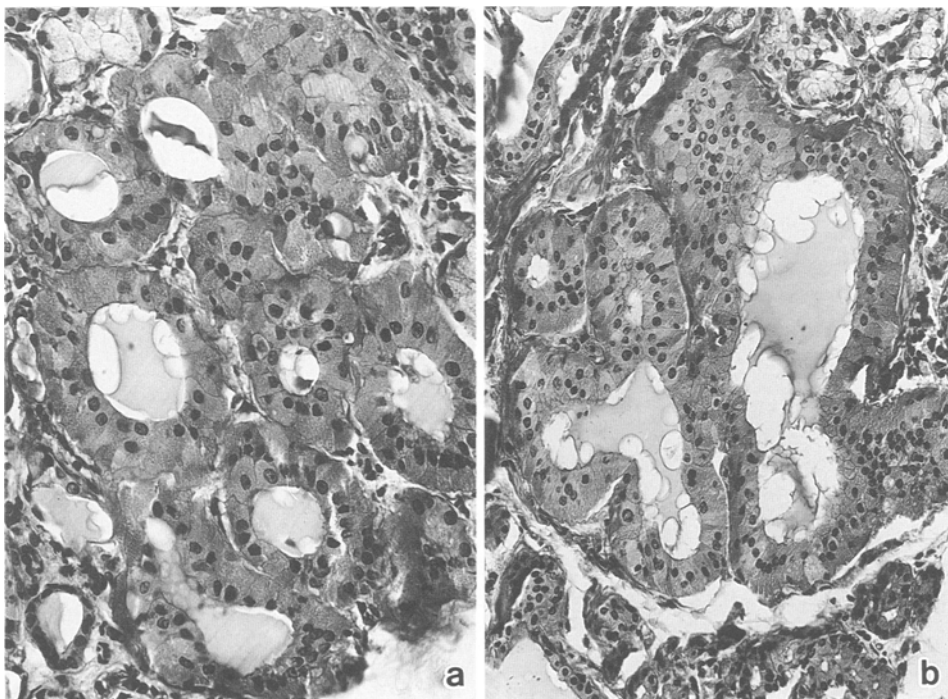


Fig. 4a, b. Oncocytic hyperplasia showing adeno-tubular structure with or without cystic dilatation of the lumina in the intralobular area. Each adeno-tubular structure is composed of single- or double-layered oncocytic epithelium. **a** $\times 350$; **b** $\times 250$

Table 3. Histological types of oncocytic hiperplasia. Each open circle correspondes to one focus of oncocytic hiperplasia. About half subjects have more than a few foci in one gland

Age range (year)	Number of subjects with oncocytic hiperplasia	Histological types of oncocytic hiperplasia ^a			
		I	II	III	IV
21-30	1	○	○		
31-40	1	○			○
41-50	1	○	○	○	
51-60	2	○	○		○
61-70	8	○○○	○○○○○	○○○○○	○○○○○
71-80	5	○	○○○	○○	○○
81-	1				○

^a I, focal hiperplasia of duct wall; II, hiperplasia extending to more than half of the circumference of the duct; III, hiperplasia of the whole duct wall; IV, intralobular, mutiple adeno-tubular hiperplasia

fied into the following types; focal hiperplasia of the duct wall resulting in partial thickening of the duct wall to over three or four times the thickness of the normal duct wall (Fig. 1a, b); hiperplasia of the duct wall resulting in marked thickening of the duct wall, extending over half of the circumference of the duct (Fig. 2a, b); hiperplasia of the whole duct wall (Fig. 3) and adeno-tubular hiperplasia with or without cystic dilatation (Fig. 4a, b). About half of the subjects with oncocytic hiperplasia had a few hiperplastic foci in one gland. Focal oncocytic hiperplasia in the duct wall was found in the interlobular duct, and showed a solitary nodular structure (Fig. 1a) or multitubular structure (Fig. 1b). Oncocytic hiperplasia extending to over half the circumference was found in the interlobular duct, and there was marked thickening of the duct wall which was tortuous. The innermost cells were high columnar and tubular structures were scattered in the thickened duct wall (Figs. 2a, b, 3). Adeno-tubular oncocytic hiperplasia was found in the intralobular area, and each adeno-tubular structure was composed of single- or double-layered oncocytic epithelium (Fig. 4a, b). No clear cells were found in any hiperplastic foci.

Histological types of oncocytic hiperplasia in each decade are shown in Table 3. The change had a tendency to increase in severity in older subjects.

Discussion

Oncocytic salivary gland lesions (oncocytic hiperplasia, oncocytoma, tumours with a more or less prominent oncocytic component) arise almost exclusively in the parotid glands of individuals over the sixth decade of age. These oncocytic lesions originate from ductal or acinar epithelial cells which have undergone oncocytic change. Several pathological studies of the human parotid glands have demonstrated that oncocytic changes occur sporadically, or in small groups, with or without a hiperplastic tendency among ductal and acinar cells and occur more frequently with advancing age; they are rare before the

fifth decade (Meza-Chávez 1949; Bauer and Bauer 1953; Batsakis 1979). Oncocytic change and oncocytic hiperplasia were more frequent in the present series than in normal parotid glands taken at autopsy (Steinhardt 1933; Meza-Chávez 1949; Bauer and Bauer 1953), and histopathological findings of oncocytic hiperplasia in the minor salivary glands were similar to those in the parotid glands (Steinhardt 1933; Meza-Chávez 1949; Bauer and Bauer 1953). There have been very few reports of oncocytic lesions occurring in the minor salivary glands (Briggs and Evans 1967; Cohen and Batsakis 1968; Batsakis 1979).

Oncocytic change with hiperplasia is occasionally widespread and much of the gland may be affected. This condition is called oncocytosis and does not usually give rise to signs or symptoms other than enlargement of the gland. It is well-known that oncocytosis occurs almost exclusively in the parotid gland (Schwartz and Feldman 1969; Thackray and Lucas 1974; Becker et al. 1982; Sørensen et al. 1986; Palmer et al. 1990). In the present study of the minor salivary glands, various degrees of oncocytic hiperplasia of both interlobular and intralobular salivary gland epithelia were found, and about half of the subjects with oncocytic hiperplasia had a few hiperplastic foci in each gland. When compared with the reported cases of parotid oncocytosis, the extent of oncocytic hiperplasia found in the present study is too slight to term oncocytosis, although it is not clear how much of the salivary gland must be occupied by oncocytic hiperplasia for a pathological change to be called oncocytosis. In addition, the term "oncocytosis" is applied not only to diffuse or multinodular extensive hiperplasia of oncocytes but also to oncocytic change in normal salivary glands or salivary gland tumours by some investigators (Change and Harawi 1992).

Oncocytic change may not represent a pathological condition, and may be one of the structural components of the normal salivary glands in adult life. Oncocytic change with or without hiperplasia was seen in 50 to 60% of subjects of first to fourth decades and in 90 to 100% of subjects over the fifth decade in the present study. The adult normal parathyroid gland is composed of chief cells, oncocytes, and transitional cells. Oncocytes start appearing at puberty, first singly, then in small groups, and increase in number with advancing age, when, after the age of 60 years, they may form various-sized islands or nodules (Ghandur-Mnaymneh et al. 1986). Perhaps a similar pattern is normal for the salivary glands.

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