

**SHORT COMMUNICATION****Case report**

# Ultrastructural study of primary lacrimal adenocarcinoma

H. GONG, H. HAYASHIDA, T. KITAOKA, T. AMEMIYA

Department of Ophthalmology, Nagasaki University School of Medicine, Nagasaki - Japan

**PURPOSE.** Primary adenocarcinoma of the lacrimal gland is a rare malignant tumor of the orbit. Up to now, there has been no presentation of its ultrastructural features. The histopathological findings and fine structures of one case of adenocarcinoma of the lacrimal gland are described in the present work.

**METHODS.** The patient was a 59-year-old Japanese man with proptosis that had persisted for one month. A tumor was extirpated, and the tissues were prepared for light and electron microscopic examination.

**RESULTS.** Electron microscopic examination demonstrated that the tumor cells had well-developed microvilli and lumens. These ultrastructure features are similar to those seen in adenocarcinomas at other sites.

**CONCLUSIONS.** These observations suggest that the accurate diagnosis of rare malignant adenocarcinoma depends not only on routine techniques such as light microscopy of hematoxylin-eosin and PAS-diastase stained slides, but also on electron microscopic findings. (*Eur J Ophthalmol* 2001; 11: 301-5)

**KEY WORDS.** Adenocarcinoma, Lacrimal gland, Electron microscope

Accepted: April 23, 2001

## INTRODUCTION

Adenocarcinoma of the lacrimal gland is a rare malignancy with a distinctive histologic pattern. It is commoner in males and has been reported to metastasize early, with a low survival rate (1, 2). The ultrastructure of the normal lacrimal gland and of some of its epithelial tumors has been well described (3-5) but the fine structure of adenocarcinoma of the lacrimal gland has not been clearly defined. This report presents the histopathologic features and ultrastructural findings of a case of adenocarcinoma of the lacrimal gland.

## PATIENT AND METHODS

### Case report

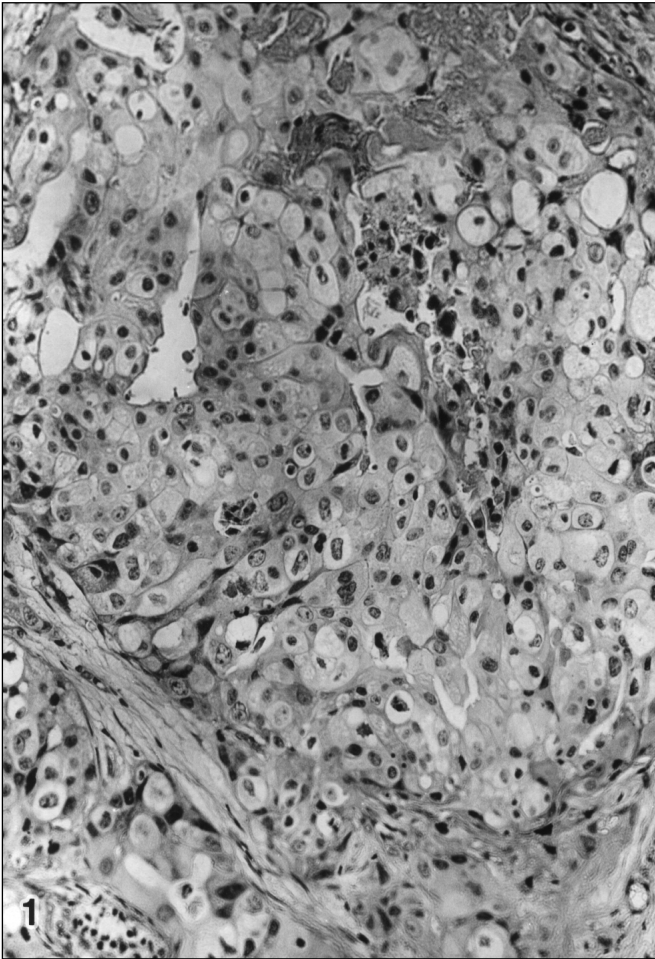
A 59-year-old Japanese man was referred to the Department of Ophthalmology because of a one-month history of a right upper lid mass. He had a history of

cerebrovascular accident nine years ago and his family history was non-contributory. Visual acuity was 0.4 on the right and 0.9 with + 1.0 D spherical lens on the left. Hertel exophthalmometer was 20 mm, OD and 16 mm, OS. The upper lid was slightly full but no discrete mass was palpated. The rest of the physical examination was unremarkable. Computed tomography (CT) of the orbit showed an isolated dense mass lateral to the right eye with bony destruction of the lacrimal gland fossa. CT scans detected no primary lesion other than the right lacrimal gland tumor.

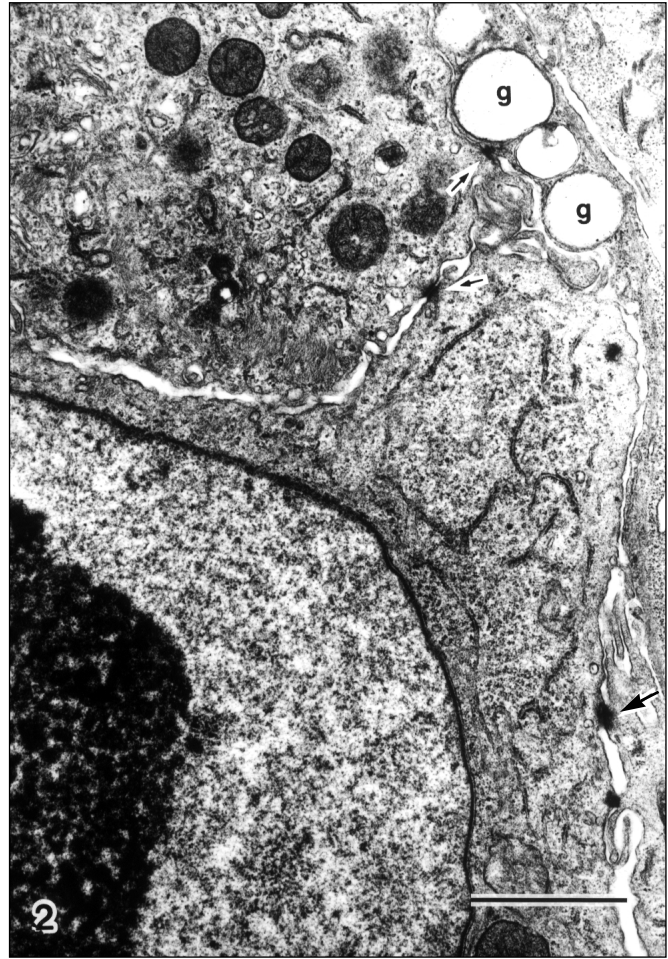
The tumor was completely removed with its capsule by a conjunctival approach under general anesthesia. The tumor subsequently recurred, and the patient died of an unknown cause one year after operation.

### Laboratory methods

Specimens were obtained in the operating room and immediately cut into two parts. One part, for light microscopic examination, was placed immediately



**Fig. 1** - Light microscopic appearance of an adenocarcinoma of the lacrimal gland. The lumens of acinous structures are seen. The nuclei are exceptionally large, and mitotic figures can be observed (Original magnification 200 x).



**Fig. 2** - Electron micrograph of an adenocarcinoma of the lacrimal gland. It contains large acinar-type granules (g) of various electron densities. Many ribosomes and considerable amounts of rough-surfaced endoplasmic reticulum are present in the cytoplasm. There are several desmosome-like connections (arrows) between the cells. The nucleus shows abundant chromatin (Bar = 2  $\mu$ m, original magnification 7000 x).

in 10% neutral formalin and embedded in paraffin. The sections were stained with hematoxylin eosin (H&E) and PAS. The other part, for electron microscopy, was cut into small pieces and fixed in 4% glutaraldehyde in 0.05 M cacodylate buffer for one hour, then post-fixed in 1% osmium tetroxide in veronal acetate buffer for one hour after an overnight washing with 0.05 M cacodylate buffer containing 0.44 M sucrose and embedded in Luveak 812. Ultrathin sections were cut with a Porter-Blum MT 2 microtome and examined with Hitachi H-300 and JEOL JEM-1210 electron microscopes.

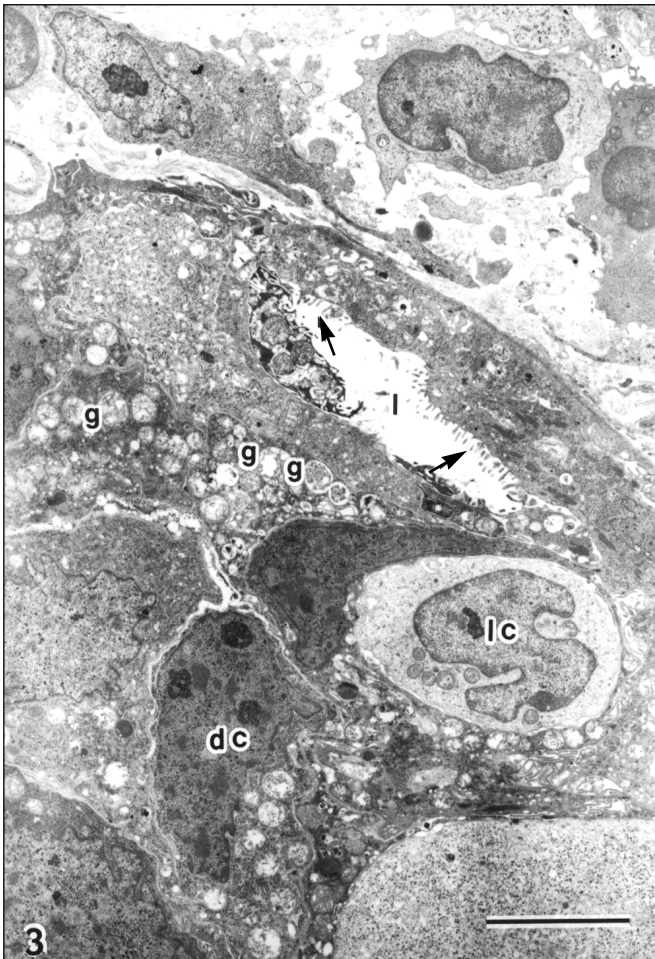
## RESULTS

### Gross findings

The tumor mass measured 26 x 21 mm and had a firm cut surface.

### Light microscopic findings

The tumor was surrounded by a membrane of connective tissue and infiltrated by inflammatory cells. There were a few lumen-like spaces containing alcian



**Fig. 3** - Electron micrograph of an adenocarcinoma of the lacrimal gland. The nest contains light cells (lc) and dark cells (dc). In the former cytoplasmic organelles are abundant, but in the latter cytoplasm is sparse. In a lumen structure (l), the apical parts of the cells have numerous microvilli (arrows), and there are mucus granules within the lumen. Numerous mucus granules of various sizes and density are also seen in the cytoplasm (g) (Bar = 6  $\mu$ m, original magnification 2000 x).



**Fig. 4** - A tumor cell nest consists of light and dark cells. A dark cell contains numerous multivesicular bodies (arrows). Light cells have many ribosomes, mitochondria and rough-surfaced endoplasmic reticulum (Bar = 3  $\mu$ m, original magnification 5000 x).

blue staining materials. Cytological examination showed neoplastic cells containing large hyperchromatic nuclei; some were arranged in an adenoid pattern near the normal lacrimal gland (Fig. 1).

### *Electron microscopic findings*

The tumor cells were of two types, dark and light, with various degrees of differentiation. In highly differentiated tumor cells, the cytoplasm contained many

organelles: mitochondria, rough-surfaced endoplasmic reticulum and ribosomes (Fig. 2). The nuclei were large and irregular. The nucleoli were large, and the chromatin of the nucleus was conspicuous. There were desmosome-like connections between the cells (Fig. 2). The tumor cells formed luminal structures (Fig. 3), with many microvilli on their edges, and the lumens had low electron-dense secretion granules (Fig. 3). Dark and light cells were seen (Figs. 3-4), and many multivesicular bodies (Fig. 4).

## DISCUSSION

The classification of epithelial neoplasms of the lacrimal gland is roughly comparable to that of the salivary gland (6), both these tumors having similar histopathologic features (7, 8). However, some of the neoplasms commonly found in salivary glands do not occur in lacrimal glands (8, 9).

The most common lacrimal gland epithelial neoplasm is pleomorphic adenoma (51%) (10). The remaining tumors are malignant, the most common being adenoid cystic carcinoma (30%). Adenocarcinoma is the basic malignant neoplasm of all glandular structures (2, 11, 12), showing tumor-forming histologic patterns with a mucus-producing tendency particularly in the differentiated forms. It can occur *de novo* in 7% of patients with lacrimal gland tumors (5, 9, 10, 13), and is more common in males than females. Metastasis occurs earlier and the survival rate is low compared to adenoid cystic carcinoma (10, 14).

Lacrimal adenocarcinomas show lumen formation (2, 5), whereas a pseudoluminal pattern with tubular-like matrix material is more usual in adenoid cystic carcinoma (3, 5, 15). The mucin content of adenocarcinoma can be demonstrated with mucicarmine and alcian blue stains; these features are absent in the undifferentiated type (16). The undifferentiated type of adenocarcinoma does not show these features. The proliferating cells of an adenocarcinoma are pleomorphic, mitotically active, irregularly layered in the tubular structures, and arranged in sheets or cords in extraluminal areas (2).

The diagnosis of adenocarcinoma, in general, depends on four routine techniques: light microscopy of H&E stained tissues, mucicarmine staining, PAS staining, and electron microscopy (16), but the frequency of their use varies and their diagnostic sensitivity may vary (17-19). Since adenocarcinomas of the lacrimal gland are very malignant, accurate diagnosis is important from both the therapeutic and the prognostic standpoint (1, 2, 5).

In the present study we did not find typical lumens with PAS-stained mucoid material, which were noted in light microscopic examinations. Only gaping lumens between tumor cells were seen typical of adenocarcinoma of the lung. Under electron microscopy the three most common epithelial tumors of the lacrimal gland (benign mixed tumor, malignant mixed tumor,

and adenoid cystic carcinoma) have significant ultrastructural differences (3). In benign mixed tumor, the inner cuboidal or columnar cells lining the tubular structures have characteristics similar to those of a normal lacrimal gland. Malignant mixed tumors have abnormal features: large indented nuclei, scanty cytoplasm, lipid inclusions, and abundant deposits of glycogen. In adenoid cystic carcinoma, the tumor cells contain ductal-type granules, which may resemble basal ductal cells with bundles, and the cystoid spaces of the tumor are composed of peripheral multilaminar basement membrane material and central thin fibrils.

Our study highlights the typical fine structural alterations in the tumor cells. There was an increase in mitochondria, free ribosomes and rough-surfaced endoplasmic reticulum. The Golgi apparatus reflected increased mucus production in the tumor cells. In most tumor cells, there was a marked increase of multivesicular bodies, suggesting heightened metabolic activity. Variations in the morphology of mucus granules and surface microvilli are also seen in other adenocarcinomas (11-12, 20-21). The most important ultrastructural features of our case were lumens with secretion granules and microvilli on the apical portion of the tumor cells. These findings are diagnostic of adenocarcinoma (16, 22). The nuclear changes are common in human malignancies.

Adenocarcinoma of a lacrimal gland arising *de novo* is rarely malignant and must be differentiated from adenoid cystic carcinoma in the lacrimal gland. There are of five types of adenoid cystic carcinoma: basaloid (solid), cribriform (Swiss cheese), sclerosing, comedocarcinoma (basaloid units with central necrosis) and tubular (manifesting true duct formation). In the present case light and electron microscopic examination revealed no basaloid masses, duct formation, necrosis in the tumor or cribriform pattern. There were also no pleomorphic adenoma-like findings such as hyalinized connective tissues, myxoid changes, or focal squamous metaplasia.

In pleomorphic adenomas the inner cells lining the tubules are usually similar to the duct cells of normal lacrimal glands (23), and the outermost cells have many tonofilaments. In this patient the pattern was rather simple, with none of the features of adenoid cystic carcinoma or pleomorphic adenoma. The inner cells lining the tubules had many secreting granules, rough endoplasmic reticulum, ribosomes, microvilli, and desmo-

some-like intercellular attachments despite the presence of many dark cells. To our knowledge, there have been no previous reports on the ultrastructural features and fine structures of this tumor.

Reprints requests to:  
Huaqing Gong, MD, PhD  
Department of Ophthalmology,  
Nagasaki University School of Medicine,  
Nagasaki 852-8501, Japan  
hgong@net.nagasaki-u.ac.jp

---

## REFERENCES

1. Zimmerman LE, Sanders TE, Ackernan LV. Epithelial tumors of the lacrimal gland: Prognostic and therapeutic significance of histologic types. *Int Ophthalmol Clin* 1962; 2: 337-67.
2. Henderson JW. Primary epithelial neoplasms. *Orbital tumors*. 3rd ed. Raven Press Ltd: New York, 1994; 323-42.
3. Iwamoto T, Jakobiec FA. A comparative ultrastructural study of the normal lacrimal gland and its epithelial tumors. *Hum Pathol* 1982; 13: 236-62.
4. Konrad EA, Thiel HJ. Adenocarcinoma of the lacrimal gland with sebaceous differentiation: A clinical study using light and electron microscopy. *Graefes Arch Clin Exp Ophthalmol* 1983; 221: 81-5.
5. Wright JE, Rose GE, Garner A. Primary malignant neoplasms of the lacrimal gland. *Br J Ophthalmol* 1992; 76: 401-7.
6. Foote-Jr FW, Frazell EL. Tumors of the major salivary glands. *Cancer* 1953; 6: 1065-123.
7. Godtfredsen E. Pathology of mucous and salivary gland tumors in the lacrimal gland and the relation to extra-orbital mucous and salivary gland tumors. *Br J Ophthalmol* 1948; 32: 171-9.
8. Forrest AW. Pathologic criteria for effective management of epithelial lacrimal gland tumors. *Am J Ophthalmol* 1971; 71: 178-92.
9. Zimmerman LE. New concepts regarding certain orbital and lacrimal gland tumors. *Ocular and adnexal tumors*. St Louis: CV Mosby, 1964; 395-428.
10. Font RL, Gamel JW. Epithelial tumors of the lacrimal gland: an analysis of 265 cases. *Ocular and adnexal tumors*. Birmingham: Aesculapius Publishing, 1978; 787-805.
11. Koga A, Momii S, Eguchi M, Makino T. Ultrastructure of well-differentiated adenocarcinoma of the gallbladder. *Ultrastruct Pathol* 1991; 15: 41-8.
12. Kudo R, Sagae S, Hayakawa O, Ito E, Horimoto E, Hashimoto M. Morphology of adenocarcinoma *in situ* and microinvasive adenocarcinoma of the uterine cervix: A cytologic and ultrastructural study. *Acta Cytol* 1991; 35: 109-16.
13. Ni C, Kuo PK, Dryja TP. Histopathological classification of 272 primary epithelial tumors of the lacrimal gland. *Chin Med J* 1992; 105: 481-5.
14. Evans HL, Batsakis JS. Polymorphous low-grade adenocarcinoma of minor salivary glands: A study of 14 cases of a distinctive neoplasm. *Cancer* 1984; 53: 935-42.
15. Vangveeravong S, Katz SE, Rootman J, White V. Tumors arising in the palpebral lobe of the lacrimal gland. *Ophthalmology* 1996; 103: 1606-18.
16. McGregor DH, Dixon AY, McGregor DK. Adenocarcinoma of the lung: A comparative diagnostic study using light and electron microscopy. *Hum Pathol* 1988; 19: 910-3.
17. Churg A. The fine structure of large cell undifferentiated carcinoma of the lung: Evidence for its relation to squamous cell carcinoma and adenocarcinoma. *Hum Pathol* 1978; 9: 143-56.
18. Auerbach O, Frasen JM, Parks VR, Carter HW. A comparison of World Health Organization (VVHO) classification of lung tumors by light and electron microscopy. *Cancer* 1982; 50: 2079-88.
19. Nash G. The diagnosis of lung cancer in the 80's: Will routine light microscopy suffice? *Hum Pathol* 1983; 4: 1021-3.
20. Goldman H, Ming SC. Fine structure of intestinal metaplasia and adenocarcinoma of the human stomach. *Lab Invest* 1968; 18: 203-10.
21. Elema JD, Keuning HM. The use of electron microscopy for the diagnosis of cancer in bronchial biopsies. *Hum Pathol* 1988; 19: 304-8.
22. Kaneko C, Niimi H, Shinzato M, Shamoto M. Comparative studies of the same adenocarcinoma cells, macrophages, and mesothelial cells by light microscopy, scanning electron microscopy, and transmission electron microscopy. *Diagn Cytopathol* 1994; 11: 333-42.
23. Erlandson RA, Corden-Cardo C, Higin TJ. Histogenesis of benign pleomorphic adenoma (mixed tumor) of the major salivary glands. An ultrastructural and immunohistochemical study. *Am J Surg Pathol* 1984; 8: 803-20.