

Case Report

Primary Oat-Cell Carcinoma of the Larynx

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Summary. A primary oat-cell carcinoma of the larynx in a 63-year-old man is reported. The oat-cell pattern appeared intermingled at one edge with a squamous carcinoma. The origin of this mixed tumour is considered together with the literature of extrapulmonary carcinomas having an oat-cell pattern.

Key words: Laryngeal oat-cell carcinoma — Extrapulmonary oat-cell carcinoma — Oat-cell carcinoma.

Extrabronchial tumours with the histological features of oat-cell carcinoma of lung are appearing with increasing frequency in the literature. Oesophageal oat-cell carcinomas have been reported by McKeowan (1952), Taniguchi et al. (1973), Turnbull et al. (1973), and Cook et al. (1976). Corrin et al. (1973) described a case in the pancreas with ectopic ACTH production and Tateishi et al. (1976) have reported at least three cases in the uterine cervix. Koss et al. (1972) described 14 cases in the minor salivary glands and other cases have been reported in the trachea (Sweeney et al., 1977) and prostate (Wenk et al., 1977). Only two cases of primary laryngeal oat-cell carcinoma have been reported to date, Olofsson and Van Nostrand (1972) and Benish et al. (1975), the latter with an E.M. study.

We present another case of a primary carcinoma of larynx with an oat-cell pattern and discuss the histogenesis of this tumour.

Case Report

A 63-year-old man, heavy smoker, presented with a 7 month history of odynophagia and dysphagia.

At laryngoscopy a polypoid lesion was revealed emerging from the right arytenoepiglottic fold with extension to ipsilateral arytenoid, piriform sinus and false cord. Right sided cervical

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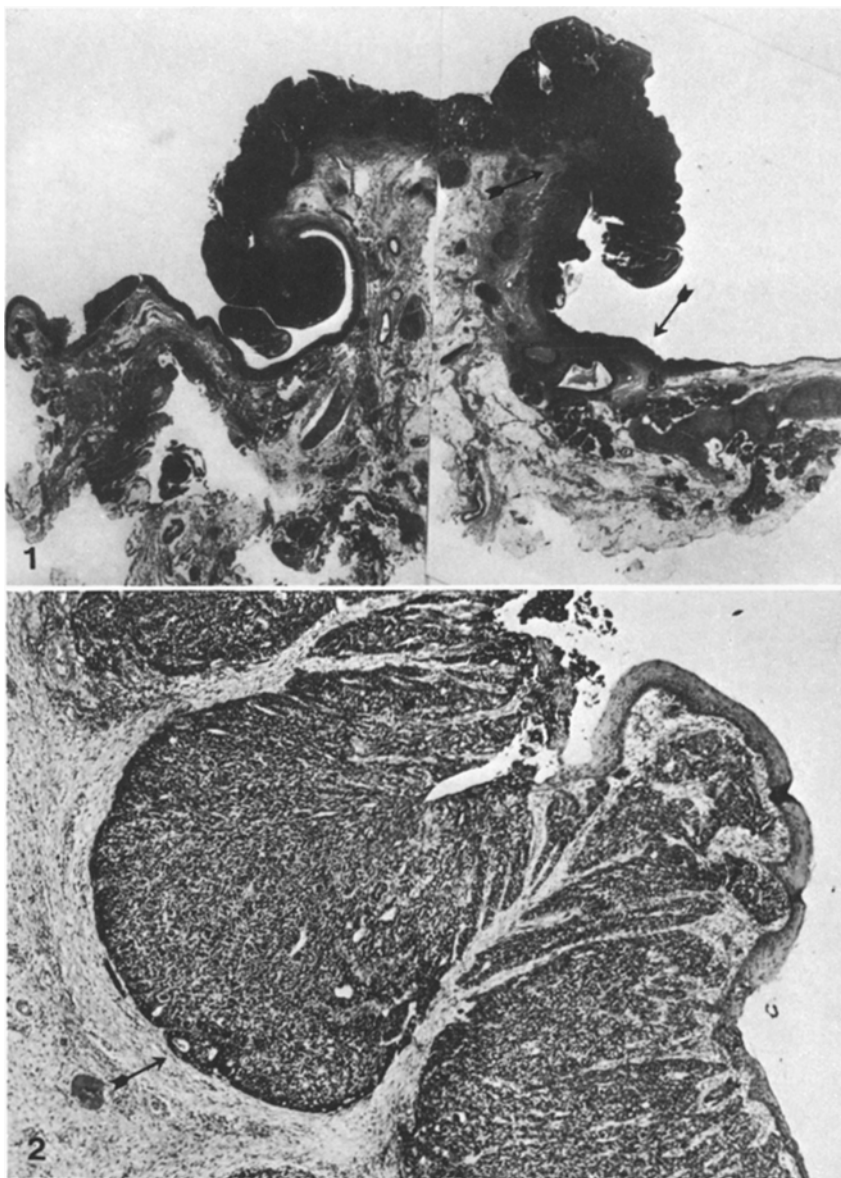


Fig. 1. The polypoid lesion is superficially infiltrated by the oat-cell carcinoma. At one edge there is a small area containing a squamous cell carcinoma (?). An in-situ squamous carcinoma is present at one side of the lesion (✓). (H & E $\times 4$)

Fig. 2. Squamous epithelium superficially covers the oat-cell carcinoma. The arrow indicates a tubular structure. (H & E $\times 50$)

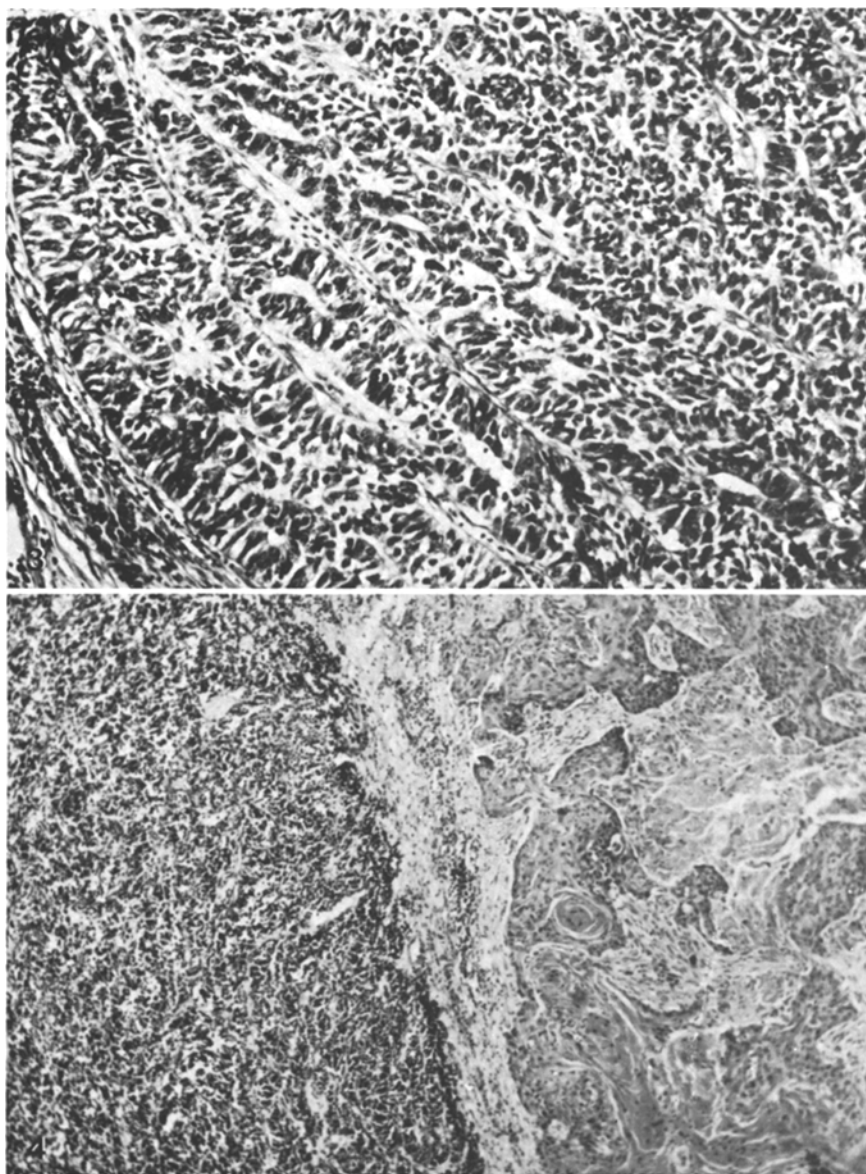


Fig. 3. The oat-cell carcinoma showing the typical ribbons and rosettes of hyperchromatic cells invading the subepithelial tissues of the polyp. (H & E $\times 100$)

Fig. 4. Typical squamous-cell carcinoma present at the edge of the tumour. (H & E $\times 100$)

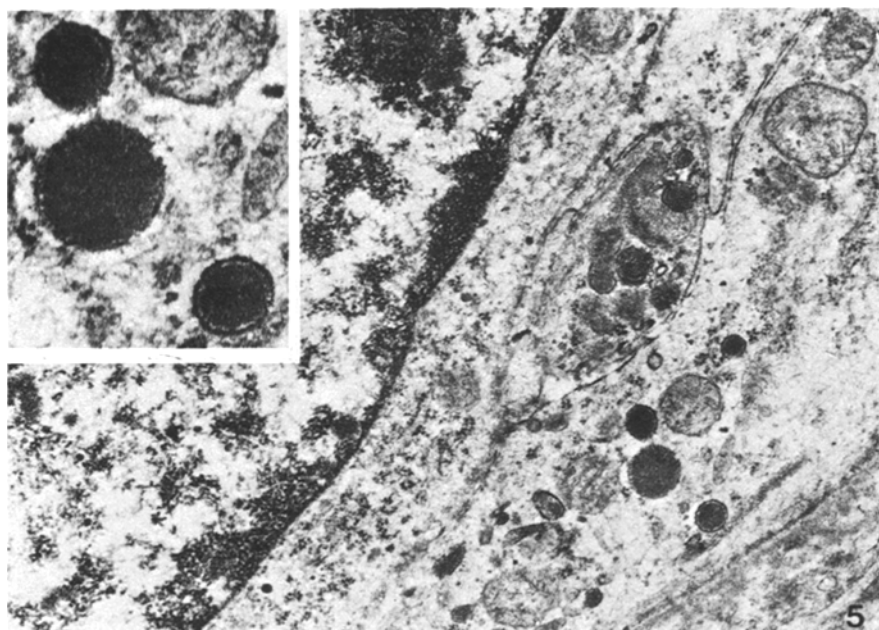


Fig. 5. Electron micrograph of oat-cell containing dense-core bodies with clear halo. (Uranyl acetate and Lead citrate $\times 24,500$; insert $\times 65,600$)

lymph-nodes were enlarged. Neither mediastinal nor pulmonary involvement were observed at X-ray examination. A right hemilaryngectomy with right sided cervical lymph node dissection was performed.

The patient was well for eight months but he showed signs of bilateral cervical involvement at the last contact, ten months after surgical excision. Since then no further follow-up has been possible.

Pathology

The surgical specimen consisted of the epiglottis, right arytenoepiglottic fold and pyriform sinus.

A polypoid lesion with a thin stalk and large apex was attached to the arytenoepiglottic fold. It measured 1.6 cm across the apex and the stalk was 0.8 cm in length.

The nodal dissection contained 14 lymph-nodes, two of which showed macroscopic evidence of metastatic deposits.

Histology

The polypoid lesion was covered by centrally ulcerated squamous epithelium. Deep to this a neoplastic proliferation with the pattern of an oat-cell carcinoma (Azzopardi, 1959), was present (Figs. 1 and 2).

The tumour was composed of trabeculae of small cells with scanty angular cytoplasm and hyperchromatic nuclei, without obvious nucleoli. These cells were often arranged in ribbons and rosettes (Fig.3) which sometimes merged insensibly into tubular structures. In the lumina of tubules, PAS positive material was demonstrated despite diastase pre-treatment. Areas of necrosis were absent and no Feulgen positive deposits were noted in vessel walls. Mitosis were numerous. The Bodian and Grimelius silver impregnations for argyrophilic cells were considered negative.

The neoplastic cells tended to infiltrate the superficial squamous epithelium which appeared ulcerated. The infiltration was limited to the base of the peduncle. At one margin of the latter a small focus of infiltrating squamous carcinoma was seen intermingled with the oat-cell pattern

(Fig. 4). The squamous epithelium at one edge of the polyp showed typical changes of in-situ malignancy. The mucous glands appeared unchanged.

Two lymph nodes showed deposits consistent with an oat-cell carcinoma.

Electron-Microscopy

Several formalin-fixed blocks were processed for electron microscopy (E.M.). After post-fixation in 1% phosphate buffered osmium tetroxide, dehydration, and embedding in Araldite-Epon, sections were stained with alcoholic uranyl acetate and Reynold's lead citrate and examined with a Siemens 101 electron microscope.

Dense-core bodies with a clear halo and limiting membrane identical to those observed in a case of oat-cell carcinoma of oesophagus by us (Cook et al., 1976) and to those described by Benish et al. (1975) in a previous case of oat-cell carcinoma of larynx, were present in about 10% of the cells, ranging in size from 105 to 250 nm. When present they were sparsely distributed with a maximum of five neurosecretory granules in a single cell (Fig. 5).

Discussion

The tumour we have described showed the histological patterns of ribbons, rosettes and tubules, the typical cytology and electron-dense neurosecretory granules which characterise oat-cell carcinoma (Azzopardi, 1959; Hattori et al., 1972). The clinical history, the polypoid nature of the lesion, the presence of an in-situ carcinoma at the edge and the lack of evidence of lung involvement are probative features for a primary origin of the tumour. We think that this case and those described by Olofsson and Van Nostrand (1972) and Benish et al. (1975) support the belief that oat-cell carcinoma may occur as a primary laryngeal carcinoma.

The origin of such carcinomas from argyrophilic cells (as suggested by Hattori et al. for the pulmonary forms) is questionable, since no argyrophilic endocrine cells have been demonstrated in the human larynx although endocrine-like non argyrophilic cells have been found in the larynx of rat by Ewen et al. (1972) and enterochromaffin-like cells in the proximal tracheal epithelium of mouse have been reported by Ericson et al. (1972). However the possibility that argyrophilic cells are occasionally present in the human larynx cannot be excluded and this view is supported by the observation of the primary carcinoid described by Goldman et al. (1969). Both the lung and larynx arise from a medial diverticulum of the foregut which suggests that a comparable cell population may be present.

An alternative origin for the present tumour might be from a basal undifferentiated cell of the squamous epithelium. The laryngeal lesion consisted of a tumour having an oat-cell pattern with a small component of squamous carcinoma. Although it is not possible to exclude the presence of two colliding carcinomas of different origins these two different neoplastic proliferations seem to have a single origin. This has been frequently observed, McKeowan's second case and both cases of oat-cell carcinoma of oesophagus reported by us showed a squamous-cell carcinoma intermingled with the oat-cell pattern. This feature had also been described in one case of the series by

Azzopardi (1959) in the lung, and by Koss et al. (1972) in one case in the minor salivary gland series. Furthermore two cases reported by Tateishi et al. (1975) in the uterine cervix showed areas of squamous 'metaplasia' which occurred only in the center of neoplastic cell nests. These findings suggest that the association between oat-cell pattern and squamous carcinoma is more than coincidental. It is possible that both components have been derived from the same cell with subsequent divergent differentiation along two distinct lines as postulated by Azzopardi and Pollock (1963) and Azzopardi and Evans (1971) for adeno-carcinomas of stomach and prostate. If the divergent differentiation theory is true we would expect future reports of coincidental oat-cell and squamous carcinoma perhaps showing transitions between the two tumours (see Cook et al., 1976).

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References

- Azzopardi, J.G.: Oat-cell carcinoma of the bronchus. *J. Pathol. Bacteriol.* **78**, 513-519 (1959)
- Azzopardi, J.G., Pollock, D.J.: Argentaffin and argyrophil cells in gastric carcinoma. *J. Pathol. Bacteriol.* **86**, 443-451 (1963)
- Azzopardi, J.G., Evans, D.J.: Argentaffin cells in prostatic carcinoma: differentiation from lipofuscin and melanin in prostatic epithelium. *J. Pathol.* **104**, 247-251 (1971)
- Benisch, B.M., Tawfik, B., Breitenbach, E.E.: Primary oat-cell carcinoma of the larynx: an ultra-structural study. *Cancer* **36**, 145-148 (1975)
- Cook, M.G., Eusebi, V., Betts, C.M.: Oat-cell carcinoma of the oesophagus: a recently recognized entity. *J. Clin. Pathol.* **29**, 1069-1073 (1976)
- Corrin, B., Gilby, E.D., Jones, N.F., Patrick, J.: Oat-cell carcinoma of the pancreas with ectopic ACTH secretion. *Cancer* **31**, 1523-1527 (1973)
- Ericson, L.E., Hakanson, R., Larson, B., Owman, C., Sundler, F.: Fluorescence and electron microscopy of amine-storing enterochromaffin-like cells in tracheal epithelium of mouse. *Z. Zellforsch.* **124**, 532-537 (1972)
- Ewen, S.W.B., Bussolati, G., Pearce, A.G.E.: Uptake of L-dopa and L-5-hydroxytryptophan by endocrine-like cells in the rat larynx. *Histochem. J.* **4**, 103-110 (1972)
- Goldman, N.C., Hood, I., Singleton, G.T.: Carcinoid of the larynx. *Arch. Otolaryngol.* **90**, 90-93 (1969)
- Hattori, S., Matsuda, M., Tateishi, R., Nishihara, H., Horai, T.: Oat-cell carcinoma of the lung. *Cancer* **30**, 1014-1024 (1972)
- Koss, L.G., Spiro, R.H., Hajdu, S.: Small cell (oat-cell) carcinoma of minor salivary gland origin. *Cancer* **30**, 737-741 (1972)
- McKeown, F.: Oat-cell carcinoma of the oesophagus. *J. Pathol. Bacteriol.* **64**, 889-891 (1952)
- Olofsson, J., van Nostrand, A.W.P.: Anaplastic small cell carcinoma of larynx. *Ann. Otol. Rhinol. Laryngol.* **81**, 284-287 (1972)
- Sweeney, E.C., Hughes, F.: Primary carcinoma of the trachea. *Histopathology* **1**, 289-299 (1977)
- Taniguchi, K., Tateishi, R., Horai, T.: ACTH-producing oat-cell carcinoma of the oesophagus. Report of two cases. *Saishin-Igaku* **28**, 1834-1838 (1973)
- Tateishi, R., Wada, A., Hayakawa, K., Hongo, J., Ishii, S., Terakawa, N.: Argyrophil cell carcinomas (Apudomas) of the uterine cervix. *Virchows Arch. A Path. Anat. and Histol.* **366**, 257-274 (1975)
- Turnbull, A.D., Rosen, P., Goodner, J.T., Beattie, E.J.: Primary malignant tumours of the oesophagus other than typical epidermoid carcinoma. *Ann. Thorac. Surg.* **15**, 463-473 (1973)
- Wenk, R.E., Bhagavan, B.S., Levy, R., Miller, D., Weisburger, W.: Ectopic ACTH, prostatic oat-cell carcinoma, and marked hypernatremia. *Cancer* **40**, 773-778 (1977)