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Oat Cell Carcinoma of the Oesophagus

Case Description and Review of the Literature

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Summary. The small oat cell type of carcinoma is only rarely seen in extrapulmonary sites. To date, nineteen cases have been described in the oesophagus, almost all by Japanese authors. In this report we review the relevant literature and add one more case of pure type to the total.

The histopathological, histochemical and ultrastructural findings and the similarity of this tumour to the oat cell bronchial carcinoma, lead one to propose that it originates in the cells of the APUD series, which have been demonstrated in the normal oesophageal epithelium. Thus it represents on endocrine carcinoma of the oesophagus.

Key words: Oesophagus – Oat cell carcinoma – APUD – Argyrophilia

Introduction

The small cell carcinoma of oat cell type, is only rarely seen in extrapulmonary sites such as the oesophagus, where an origin from argyrophil cells has been suggested (Tateishi et al. 1974, 1976, Imai et al. 1978). Since the first description by McKeown in 1952, a total of fifteen cases have been published, almost all by Japanese authors (Table 1). The rarety of this tumour is demonstrated by Turnbull et al. (1973), which only found one case of this peculiar tumour reviewing 1,918 cases of primary malignant tumours other than squamous carcinomas of the oesophagus.

In this report we describe histochemical and ultrastructural studies of a case, which we believe to be the first example of this tumour to be reported from Spain.

Case Description

Male, 62 years old, an alcoholic, with a previous history of duodenal ulcer, who presented because of piercing pain, progressive dysphagia and febrile attacks for three months. Biochemical analysis

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Table 1. Published cases of pure oat cell carcinoma of the oesophagus[a]

No. of cases	Author	Age/sex	Site	Secretory granules		Amyloid	Ectopic hormone production
				Argyrophilia	E.M.		
1	McKeown et al. (1952)	68/M	Lower third	–	No		N.R.
2[b]	Taniguchi et al. (1973)	57/F	Lower third	+	No	Yes	ACTH
		62/M	Lower third	+	Yes	Yes	ACTH
1	Turnbull et al. (1973)	55/F	Lower third	–	–		N.R.
1[b]	Watanabe et al. (1974)	50/F	Middle third	+	Yes		N.R.
3[b]	Matsusaka et al. (1976)	67/M	Lower third	+	No		N.R.
		62/M	Middle third	+	No		N.R.
		70/M	Middle third	+	No		N.R.
4[b]	Tateishi et al. (1976)[c]	58/F	Middle third	+	No		ACTH
		58/M	Middle third	+	Yes	Yes	calcitonin
		71/M	Lower third	+	Yes		N.R.
		56/M	Lower third	+	No		N.R.
1[b]	Imai et al. (1978)	62/M	Middle third	+	Yes		N.R.
1	Kelsen et al. (1980)	76/F	Middle third	–	–		N.R.
1	Reid et al. (1980)	60/F	Lower third	+	Yes		
1	Present case	62/M	Middle third	–	Yes	No	

N.R. = Not referred

[a] We exclude those cases that have areas of squamous or of glandular differentiation

[b] Japanese cases

[c] In this report are included those cases described previously by Taniguchi et al. (1973); moreover, two of the cases mentioned are studied later in the cytological review of small cell carcinoma by Horai et al. (1978)

revealed hypoproteinaemia, elevated BSR and hyperuricaemia. There was no evidence of hormonal dysfunction.

Radiological examination revealed the presence of a large tumour at the level of the middle third of the oesophagus (Fig. 1A), without any evidence of tumour in the lungs. During excision, metastases were found in paraoesophageal and mediastinal lymph nodes. The patient died suddenly, one week later. Permission for autopsy was not obtained.

Pathology

Macroscopic. The tissue removed surgically consisted of the lower two thirds of the oesophagus and the upper third of the stomach (Fig. 1B). There was a fungating tumour 10 cm diameter with a wide base at the level of the middle

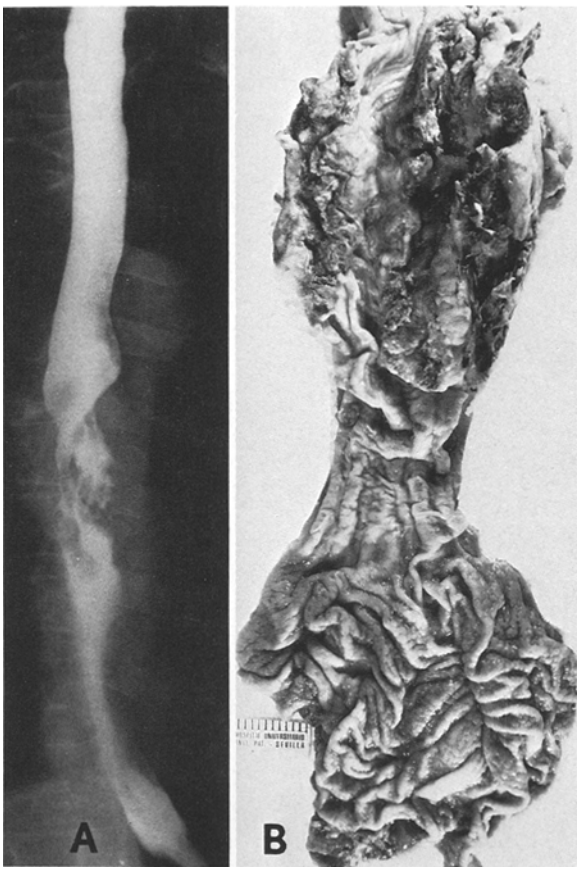

Fig. 1A, B. Carcinoma of the oesophagus, which appears radiologically as a filling defect in the middle third (**A**). In the surgically removed piece (**B**), comprising oesophagus and stomach, it is seen that the tumour has a fungoid appearance and also partially occupies the lower third of the oesophagus

third, infiltrating the whole of the oesophageal wall. At 1 cm from the edge of the gastric resection there was an ulcer, 0.8 cm in diameter, with clear base and reddish elevated edges.

Light Microscopy. Fifteen blocks were made from the tumour and an average of thirty serial sections from each block were examined. In addition to routine stains, all sections were also stained by the Masson-Fontana and Grimelius techniques in order to demonstrate argent-affinity and argyrophilia respectively. As a control we used sections corresponding to the cardio-oesophageal junction. The immunoperoxidase technique (PAP) was used to demonstrate calcitonin and ACTH in the tissue (Elias and Johnsen 1979).

The tumour is composed of indifferentiated cells, without contact with the epithelium (Fig. 2) and infiltrates all the layers of the oesophageal wall. The neoplastic cells show scanty cytoplasm, hyperchromatic round or ovoid nuclei,

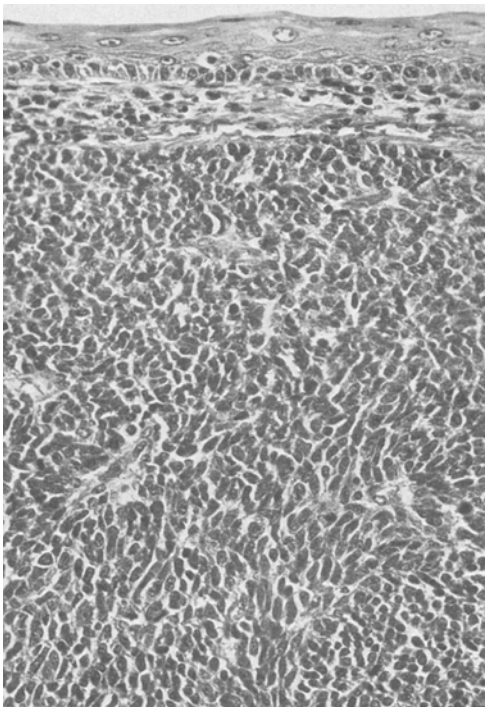

Fig. 2. Undifferentiated tumour with the appearance of pulmonary oat cell tumour, which has no contact with the oesophageal squamous epithelium. H.E. ×250

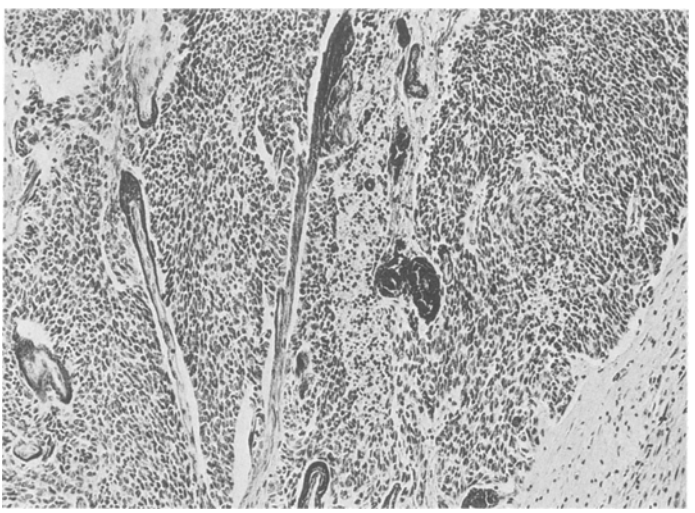

Fig. 3. Panoramic view, which shows the monomorphic pattern of the tumour, with wide areas of necrosis and numerous vessels with haematoxylinophilic deposits in their walls. H.E. ×100

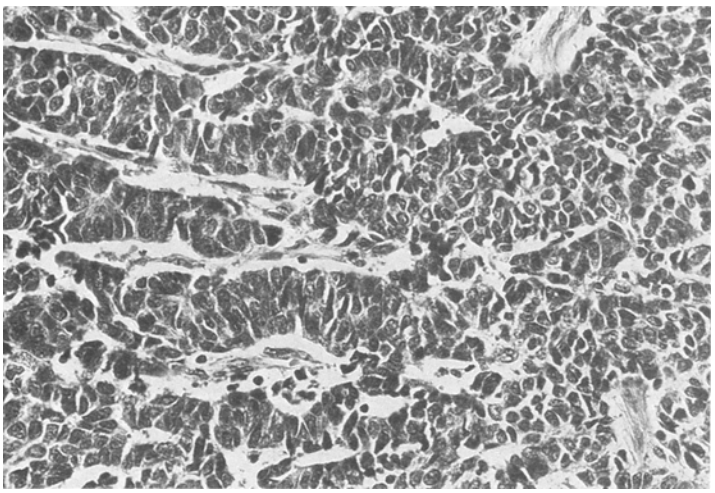

Fig. 4. Area of transition from solid to trabecular pattern. H.E. ×250

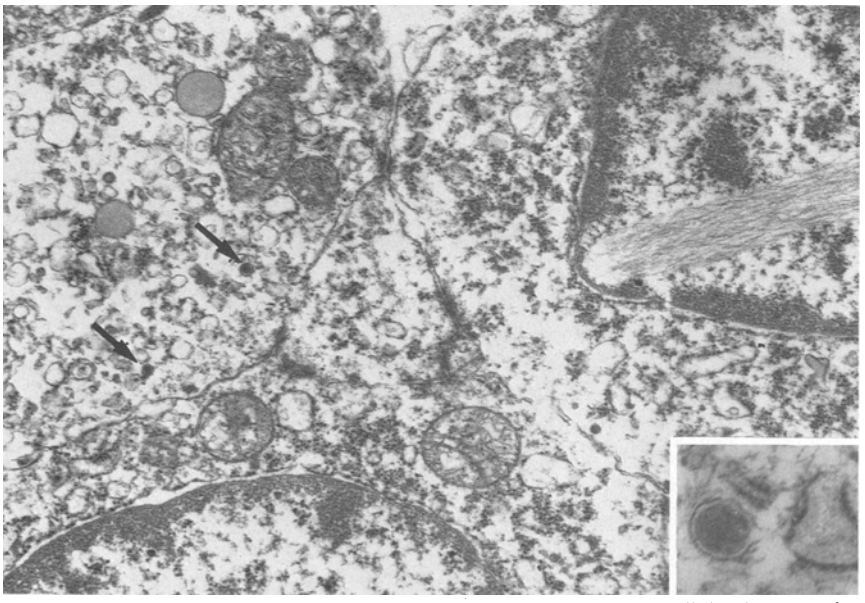

Fig. 5. Electronmicrophotograph showing the existence of abundant intercellular desmosomic unions, a filamentous intranuclear inclusion, as well as some secretory granules (arrows) of about 100 nm diameter, with limiting membrane (inset). ×10,000

scarcely perceptible nucleoli and a high mitotic index. The techniques for demonstration of glycogen, mucoid material and cytoplasmic argent affinity gave negative results. There are wide areas of necrosis in which the walls of the vessels showed haematoxylinophilic deposits (Fig. 3). In some deep regions the tumour adopted a trabecular pattern (Fig. 4). Occasionally, a scanty amount of hyaline

material was seen between polygonal cells, which did not give the reaction of amyloid.

Immunoperoxidase staining failed to demonstrate the presence of calcitonin or ACTH in the tumour tissue. In spite of painstaking search, no glandular structures nor evidence of squamous differentiation was observed.

Finally, the presence of ulcerated metastasis in the stomach was confirmed microscopically, and tumour was present in para-oesophageal and mediastinal lymphatic nodes.

Electron Microscopy. Ultrastructural study carried out after the initial formalin fixation revealed isolated secretory granules, 100 to 150 nm in diameter (Fig. 5). The presence of desmosomal junctions (not associated with bundles of tonofilaments) was noted, between polygonal or slightly fusiform cells. The nuclei are ovoid and at times show laminar filamentous inclusions. A large number of free ribosomes may be seen in the cytoplasm, as well as well-developed rough endoplasmic reticulum, abundant mitochondria (rounded and of various sizes) and poorly prominent Golgi areas.

Discussion

Undifferentiated tumours whose appearance is similar to that of the pulmonary oat cell carcinoma (Azzopardi 1959) have been described in the larynx (Oloffsson and van Nostrand 1972; Benisch et al. 1975), trachea (Sweeney and Hughes 1977), salivary gland (Koss et al. 1972), thymus (Rosai et al. 1976), pancreas (Corrin et al. 1973) and uterine cervix (Albores-Saavedra 1979; Tateishi et al. 1975). In the oesophagus they have referred to under different names: anaplastic carcinoma (Matsusaka et al. 1976), oat cell pattern oesophageal carcinoma (McKeown 1952; Rosen et al. 1975; Cook et al. 1976; Imai et al. 1978; Reid et al. 1980), small cell carcinoma (Horai et al. 1978; Kelsen et al. 1980), argyrophil cell carcinoma (apudoma) (Tateishi et al. 1976). Up to the present, we know of reports of nineteen cases of which fifteen are pure forms (Table 1); of these, only four (and the one described here) were in western countries. Four cases showed a variable degree of squamous or glandular differentiation (McKeown 1952; Rosen et al. 1975; Cook et al. 1976; Chong et al. 1979).

The question of the histogenesis of these tumours still remains to be elucidated. The fact that squamous areas with evident cellular anaplasia (McKeown 1952; Rosen et al. 1975; Cook et al. 1976) have been found in the centre of the tumour, and that stretches of carcinoma "in situ" in the mucosa adjacent to the tumour occur (Rosen et al. 1975) raises the possibility that both cellular components (squamous cells and cells with oat grain morphology) have the same precursor cell (Cook et al. 1976) or that it is a matter of an anaplastic form of squamous carcinoma (Rosen et al. 1975). In our case, we did not find areas of squamous differentiation; even when ultrastructurally there was a great number of desmosomal unions, there was no evidence of bundles of tonofilaments nor of keratohyaline masses.

The presence of secretory granules, as well as the existence of amyloid material in some cases suggests that this pure form of oat cell carcinoma repre-

sents a malignant transformation in the argyrophil cells, which have been described in the normal oesophagus (Tateishi et al. 1974). This hypothesis is based on the close relationship to the oat cell carcinoma of the bronchus (Fisher et al 1978), from the point of view of histology (haematoxylinic material in the vessel walls, areas of trabecular pattern, wide zones of necrosis, high mitotic index), of cytology (small polygonal cells, sometimes slightly fusiform), of histochemistry (absence of argent-affinity and occasionally negative argyrophilia) and the presence of scanty-secretory granules at electron microscopy. In our case, the search for argent-affinity and argyrophilia were both negative, but we found sparse neurosecretory granules in the ultrastructural study.

There is no explanation for the presence of foci of squamous or mucoid differentiation, though some authors suggest that the Kulchitsky cell cannot always be the sole cellular progenitor of carcinoid tumours (Black and Haffner 1968). In any case thus would justify, on the one hand, the existence of pure forms of oat cell carcinoma in the oesophagus, and on the other, combinations with squamous cell carcinoma (such as sometimes occurs in the pulmonary oat cell carcinoma) or with adenocarcinoma (Chong et al. 1979).

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