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Case report

Oesophageal squamous cell carcinoma with lymphoid stroma

A case report

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Summary. We treated a 70-year-old Japanese man with squamous cell carcinoma of the oesophagus with evidence of lymphoid stroma. The tumour consisted of a main lesion invading the muscular layer of the oesophagus, in association with wide areas of carcinoma in situ. The tumour stroma of the lesion was nondesmoplastic and was uniformly infiltrated mainly by abundant lymphocytes and plasma cells. Immunohistochemically, the lymphocytes consisted of a large number of T lymphocytes and a small number of B lymphocytes. S-100 protein positive cells were marked in the tumour cell nests and necrotic change of tumour cells was frequent. Abundant infiltration of lymphocytes and plasma cells was also wide-spread beneath the carcinoma in situ, together with the lymphoid follicles. Carcinoma with lymphoid stroma can occur not only in the breast, uterine cervix, nasopharynx and stomach but also in the oesophagus.

Key words: Oesophageal carcinoma – Squamous cell carcinoma – Lymphoid stroma – S-100 Protein positive cell

Introduction

The prognostic significance of lymphocytic infiltration in human cancers of various organs has been well documented (Black et al. 1971; Hiratsuka et al. 1984). In general, patients with tumours with abundant lymphocytic infiltration have a better prognosis than do those with no or only a sparse lymphocytic infiltration. There are particular special carcinomas included in the former group: Watanabe et al. (1976) described gastric carcinoma with lymphoid stroma, medullary carcinoma with lymphoid infiltration of the breast is a well known entity (Moore and Foote 1949), and Hasumi et al. (1974) obtained evidence for a medullary carcinoma with marked lymphoid infiltration of the uterine cervix. Some nasopharyngeal carcinomas have been reported to be accompanied by a dense stromal infiltration of lymphocytes (Micheau 1986).

Such a lesion in the oesophagus has not, apparently, been reported. We treated a patient with such a lesion and the results of immunohistochemical analysis of the infiltrating cells are described herein.

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Case report

A 70-year-old Japanese man was admitted with a 1-month history of anorexia, retrosternal discomfort and lumbago. The patient was referred to Kyushu University Hospital on July, 1987. Physical examination of the abdomen revealed a pulsatile mass 8 cm in diameter. Laboratory data were within normal limits except for slight anaemia.

CT scan and ultrasound revealed an infrarenal abdominal aortic aneurysm. In addition, an upper gastrointestinal roentgenogram disclosed two diverticula with an irregularity of the surrounding mucosa in the middle thoracic oesophagus. Endoscopy revealed two diverticula 25 cm from the front teeth, and an adjacent irregular, reddish lesion located distally. An wide unstained area, including the diverticula, was seen from 22 cm to 29 cm from the front teeth, following Lugol's solution applied during endoscopic examination, and squamous cell carcinoma was confirmed by biopsy.

The preoperative diagnosis was coincidental abdominal aortic aneurysm and oesophageal squamous cell carcinoma, and a two-stage operation was planned. As a first step aneurysmorraphy was done, then a subtotal oesophagectomy and dissection of the lymph nodes was performed and the oesophagus reconstructed. The postoperative course was uneventful and the patient was discharged one month later. He is well with no evidence of recurrence, at the time of writing.

Materials and methods

The resected oesophagus and part of the stomach were fixed in formalin. Microscopic sections of the whole resected oesophagus were made from step-sectioned blocks 5 mm in width and were stained with haematoxylin and eosin.

Selected paraffin blocks were recut and stained immunohistochemically for UCHL1, MX-Pan B, LeuM1, and S-100 protein. UCHL1 and MX-Pan B (L26) are specific and reliable markers for T lymphocytes and B lymphocytes, respectively, in formalin-fixed, paraffin-embedded sections (Linder et al. 1987; Cartun et al. 1987). LeuM1 is a marker for mature granulocytes and monocytes (Chan et al. 1988; Santamaria et al. 1988). Five-micron sections were incubated overnight at 4° C with each anti-serum, with a dilution of 1/200, 1/100, 1/50, and 1/250, respectively. UCHL1 and S-100 protein were obtained from DAKOPATTS (Copenhagen, Denmark). MX-Pan B which is identical with L26 was purchased from Kyowa (Tokyo, Japan). LeuM1 was purchased from Becton Dickinson (CA, USA). For localization each antiserum, the avidin-biotin-peroxidase complex (ABC) method of Hsu et al. (Hsu et al. 1981) was applied. Avidin-biotin reagents were purchased from Vector Laboratories, Inc. (Burlingame, CA).

Results

The gross specimen consisted of a subtotally resected oesophagus, measuring 12 cm longitudinally and 4.5 cm in diameter, part of the stomach, and 6 perioesophageal and perigastric lymph nodes. Two diverticula were present in association with a distally spreading irregular area. In the fixed specimen, there was a rectangular area unstained by Lugol's iodine measuring 6×5 cm which covered the diverticula (Fig. 1). Macroscopicically, the tumour was the flat type. The distance of the lower margin from the oesophago-gastric junction was 5 cm, and there was no tumour invasion in the fundus. One of the perigastric lymph nodes was swollen and appeared to be involved by tumour.

On light microscopy the main lesion showed a poorly differentiated squamous cell carcinoma invading mostly the submucosal layer and partly the proper muscular layer (Fig. 2a). The tumour cell nests were separated by intervention of a broad infiltration of lymphocytes, plasma cells, neutrophils, eosinophils, and macrophages. Tumour cells often showed necrotic or regressive change accompanied with lymphoid cell infiltration, within the cell nests (Fig. 2b). Formation of lymphoid follicles, with or without germinal centers, was seen not only in next to the preinvasive zone but also in the stroma of the invasive area (Fig. 3).

The adjacent area unstained by Lugol's solution revealed squamous cell carcinoma in situ. The diverticula were false (pulsion diverticula), representing herniations of the mucosal layer through weakened areas of defects in the muscularis propia. The mucosa covering the diverticulum also replaced by squamous cell carcinoma in situ. The characteristic finding was abundant infiltration of lymphocytes and plasma cells with lymphoid follicles, beneath the basal layer of the intra-epithelial carcinoma of the oesophagus (Fig. 4). These abundant round cell infiltrations were absent in the surrounding non-carcinomatous tissue. There were no regressive changes within or next to the preinvasive zone.

Lymph vessel permeation was seen in the main lesion. One perioesophageal and one perigastric lymph node contained carcinoma. The regional lymph nodes showed a reactive follicular hyperplasia, irrespective of the presence or absence of metastatic foci therein.

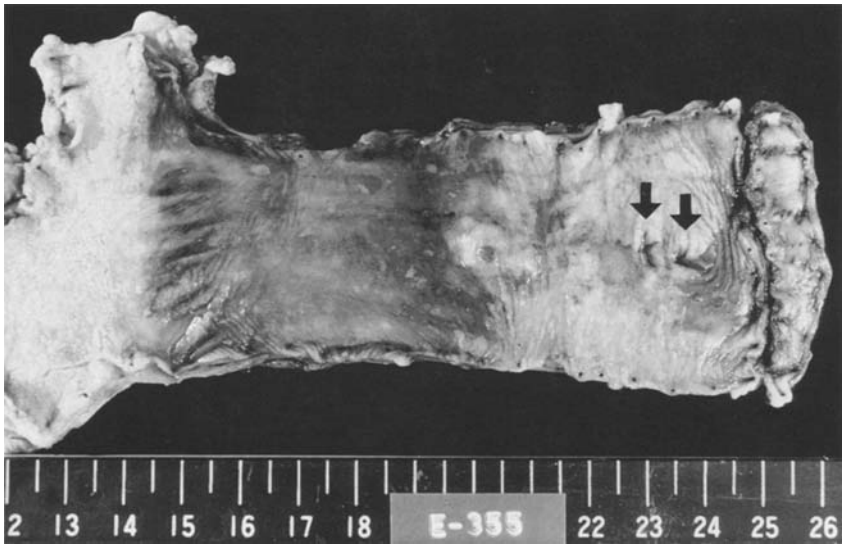


Fig. 1. Gross appearance of the resected oesophagus and partial stomach, with application of Lugol's solution. The right unstained area shows a squamous cell carcinoma of the oesophagus, the left unstained area the stomach. Note the two diverticula in the areas of oesophageal carcinoma (*arrows*)

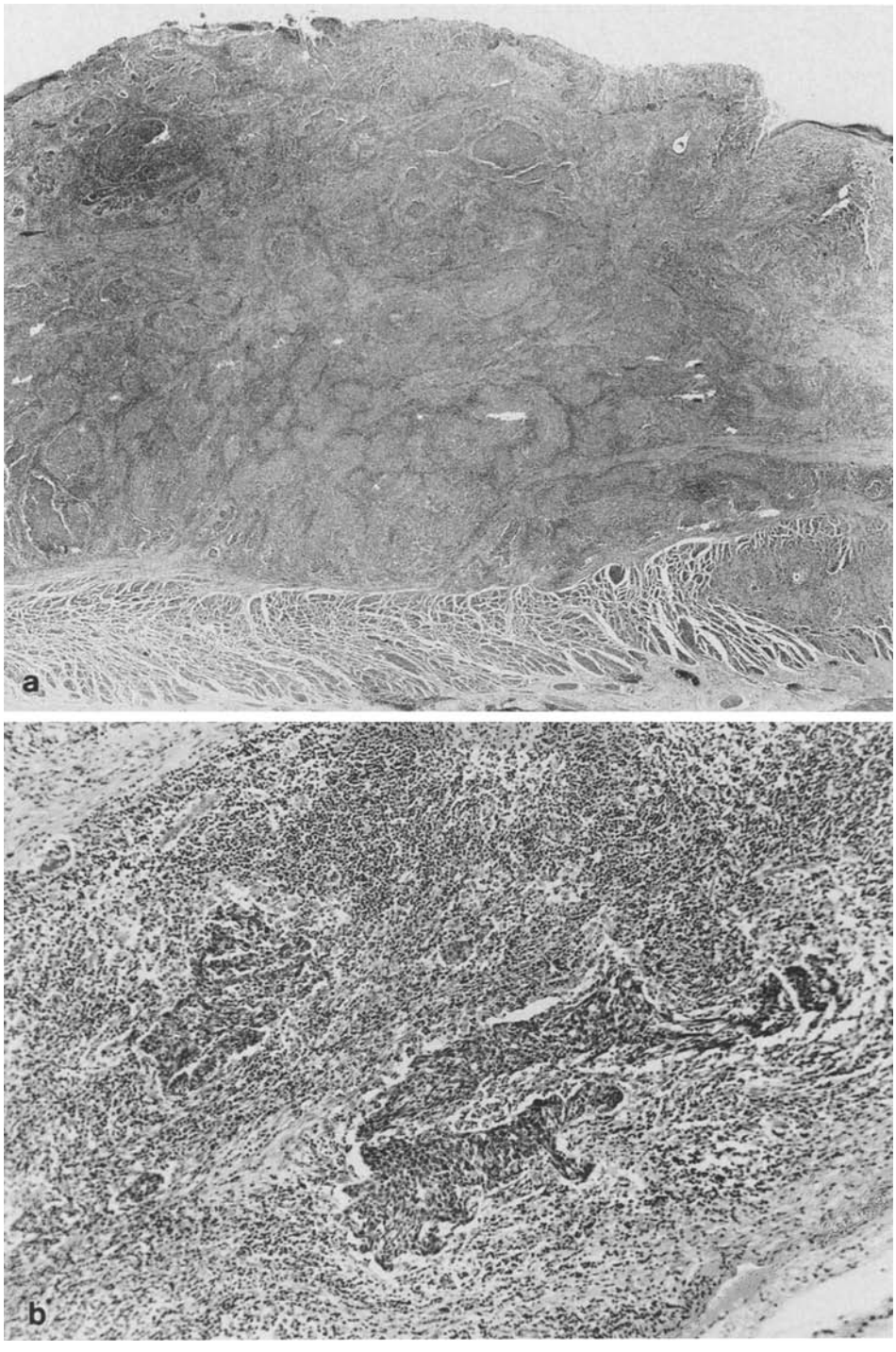
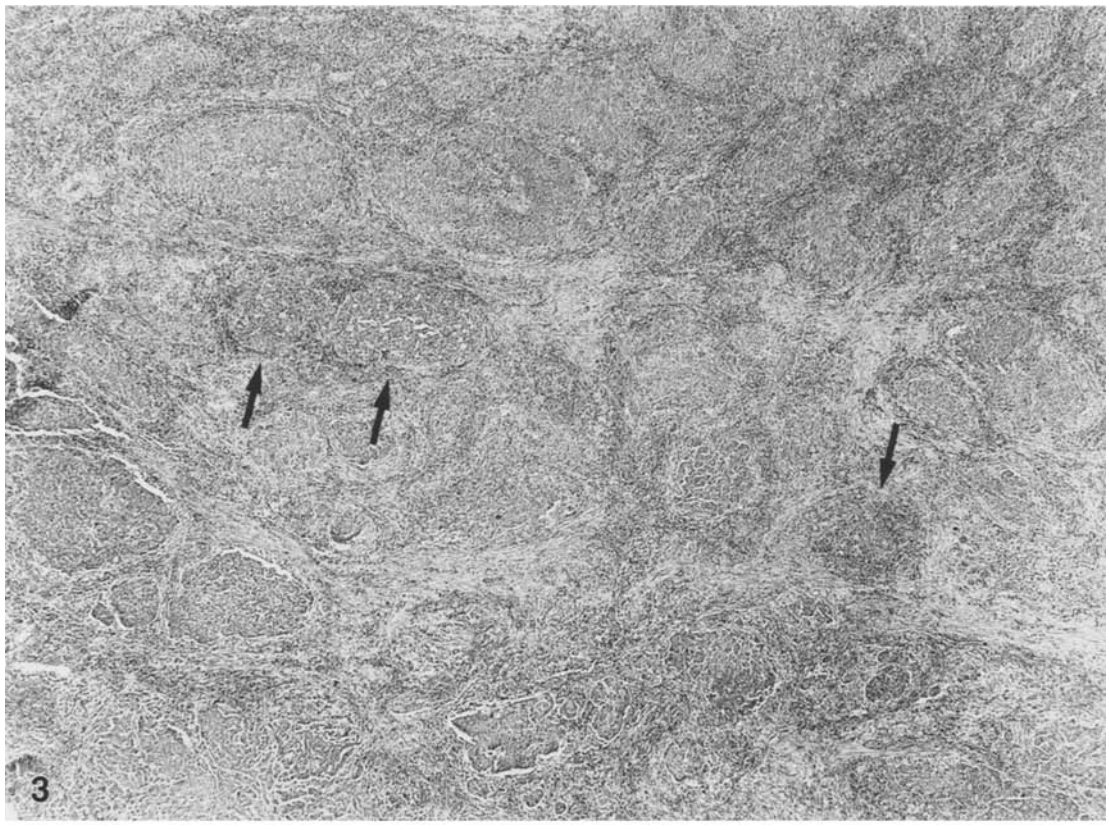


Fig. 2. (**a**) The main lesion shows a poorly differentiated squamous cell carcinoma invading the muscular layer of the oesophagus. The inflammatory cell infiltration is evident in the tumour stroma (H & E, ×24). (**b**) The tumour cells often showed necrotic change plus inflammatory cell infiltration (H & E, ×92)

There were no changes such as Barret's oesophagus or dysplasia in the non-neoplastic mucosa of the oesophagus.

The infiltrating lymphocytes consisted of a large number of T lymphocytes and a small number of B lymphocytes. T lymphocytes were prominent just around the tumour cell nests and made contact with the nests (Fig. 5a). B lymphocytes were seen in the tumour stroma, and a few were scattered in the tumour cell nests (Fig. 5b). Many granulocytes and monocytes that were recognized by LeuM1 were seen within the tumour cell nests, however, distribution in the stroma was scanty. S-100 protein positive cells were visualized



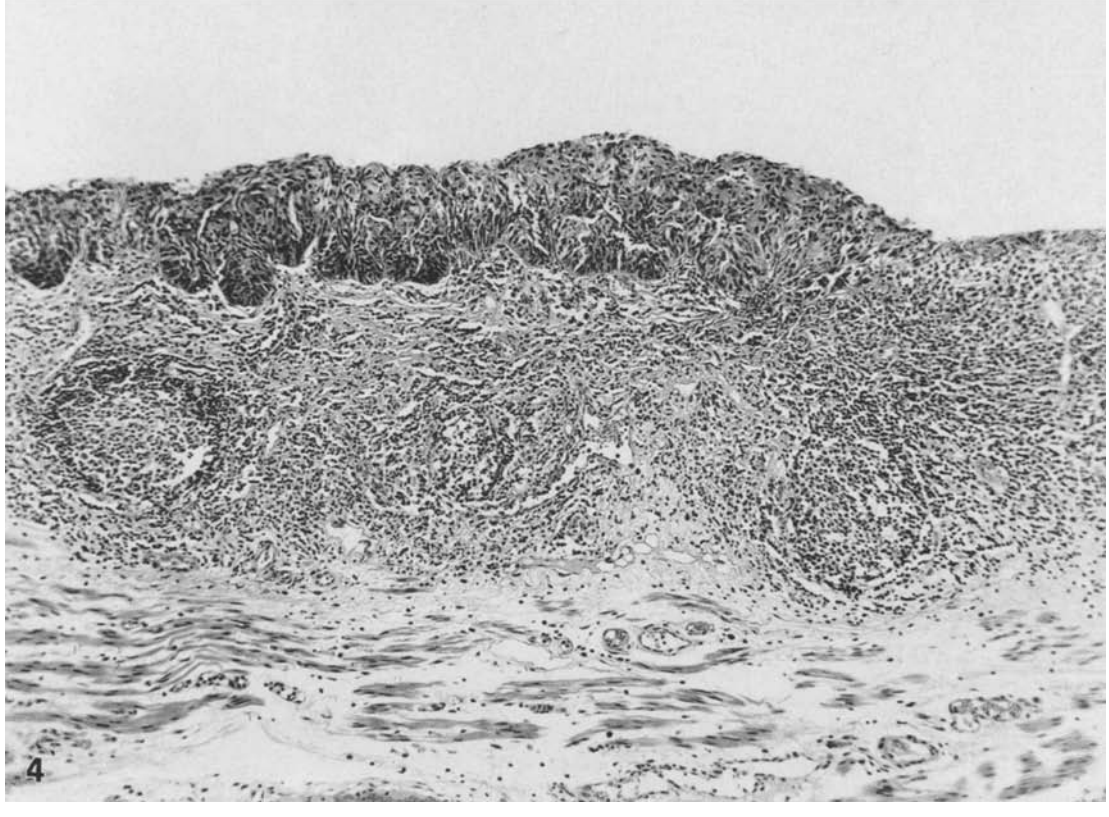


Fig. 3. Lymphoid follicles (*arrows*) are evident within the stroma of the invasive cancer (H & E, × 36)

Fig. 4. Carcinoma in situ conjunct to the main cancerous tissue of the oesophagus. Notice the abundant inflammatory cell infiltration with lymphoid follicles (H & E, × 102)

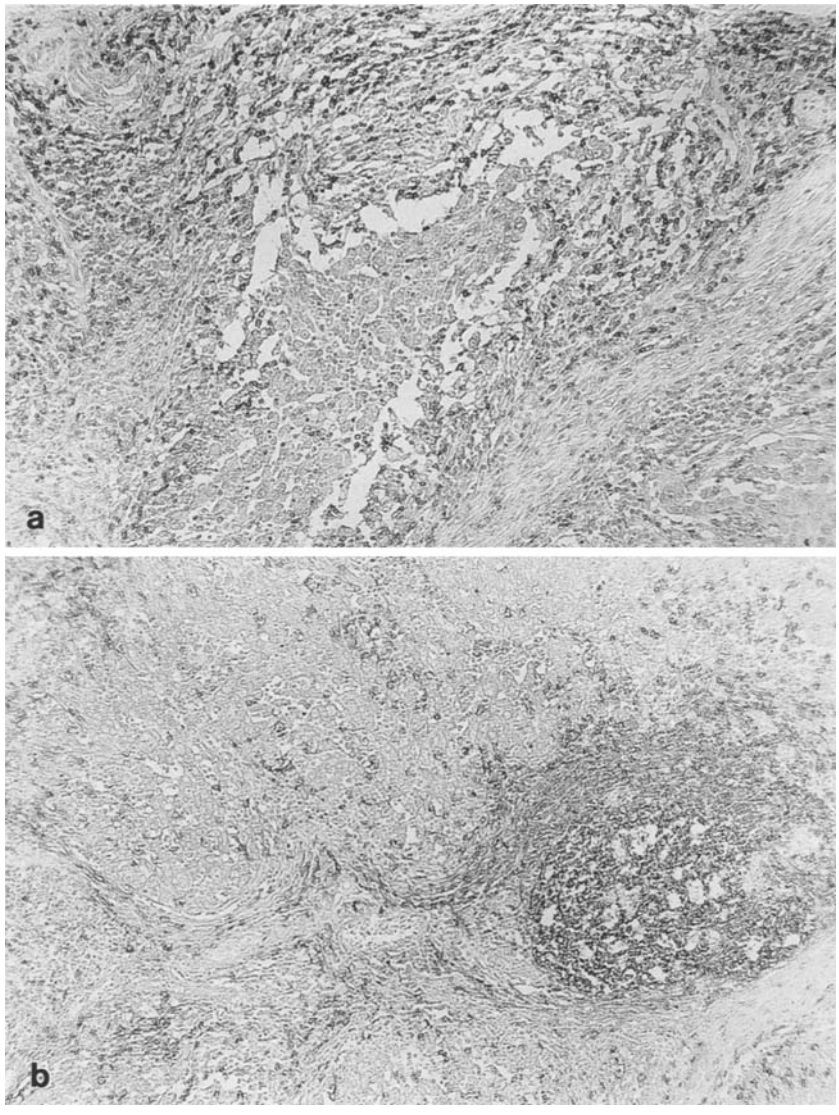


Fig. 5 (**a**) T lymphocytes have diffused, mainly in the tumour stroma of the oesophageal carcinoma (ABC method for UCHL1, ×124). (**b**) B lymphocytes are less frequently present mainly in the tumour stroma, but were also seen in the tumour cell nests. A lymphoid follicle with many B lymphocytes is present on the right. (ABC method for MX-Pan B, ×92)

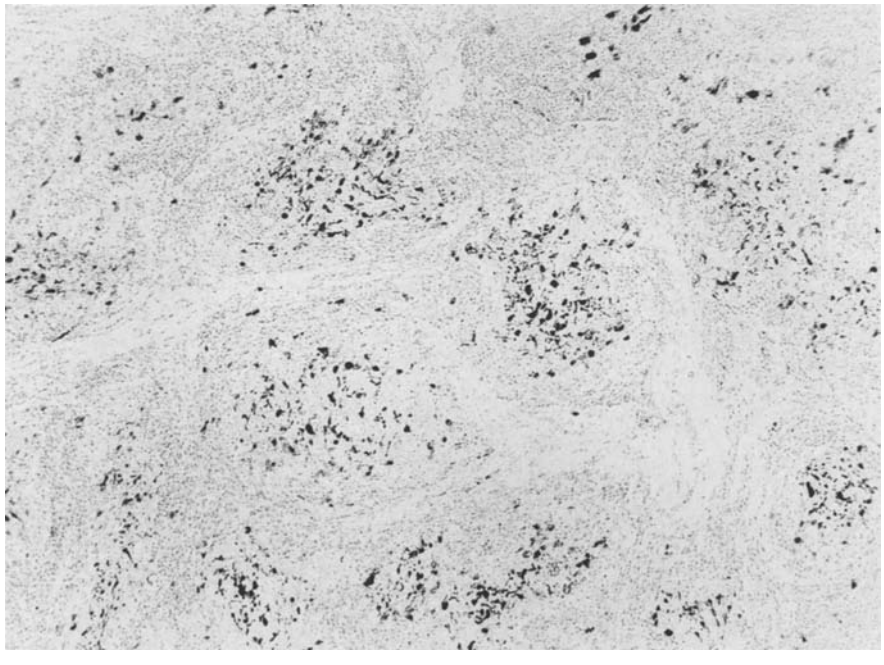


Fig. 6. S-100 protein positive cells are marked, mainly within the tumour cell nests of the oesophageal squamous cell carcinoma (ABC method for S-100 protein, ×92)

as dendritic, using the ABC method. These cells were abundant mainly within the tumour cell nests and were scanty in the stroma (Fig. 6). The distribution was markedly different from that of T and B lymphocytes but was similar to that of LeuM1 positive cells. These cells were also present around the lymphoid follicles, but were rare in the surrounding normal oesophageal tissue.

Discussion

Watanabe et al. (1976) reported a peculiar carcinoma of the stomach termed gastric carcinoma with lymphoid stroma. This type of carcinoma is characterized histologically as having a uniform distribution density of cellular infiltration, mainly comprised of lymphocytes and plasma cells, throughout the entire area of the tumour, with little collagenous element within the stroma. The favorable prognostic significance of this type is another intrinsic feature. This type of carcinoma with its particular histological appearance has also been reported in the breast (Moore and Foote 1949) the uterine cervix (Hasumi et al. 1974) and in the nasopharynx (Micheau 1986).

The current case may be the first report of this type of carcinoma in the oesophagus. The histological feature of the tumour stroma was similar to gastric carcinoma with lymphoid stroma. With regard to nomenclature, we prefer "carcinoma with lymphoid stroma" to "inflammatory carcinoma". The term inflammatory carcinoma is used for a special carcinoma of the breast (Lucas and Perez-Mesa 1978), and is characterized by an inflammatory clinical appearance and/or pathological findings demonstrating widespread carcinomatosis of the dermal lymphatic vessels. Inflammatory cell infiltration in the tumour stroma was not evident. The tumour we report here is characterized by a dense inflammatory cell infiltration in the stroma and for this reason we prefer the term carcinoma with lymphoid stroma according to Watanabe et al. (1976).

The main infiltrating cells in the tumour were lymphocytes that consisted of a large number of T lymphocytes and a small number of B lymphocytes. The characteristic finding in this case was that many S-100 protein positive cells infiltrated the tumour. S-100 protein positive cells are regarded as members of a dendritic cell system capable of antigen processing and potent accessory cell function in the immune response (Stingl et al. 1980; Van Voorhis et al. 1982). While the lymphocytes infiltrated massively mainly around the tumour, S-100 protein positive cells were largely present within the tumour cell nests. As S-100 protein positive cells were practically non existent in the adjacent normal tissue, those cells may have infiltrated selectively toward the malignant cells. These findings might support a role for S-100 protein positive cells which would infiltrate selectively toward the tumour and present tumour-specific antigen to the T-lymphocytes, which would then infiltrate.

Infiltration of S-100 protein positive cells within tumours has been reported to be correlated with a benign prognosis in lung carcinoma (Furukawa et al. 1985) nasopharyngeal carcinoma (Nomori et al. 1988) gastric carcinoma (Tsujitani et al. 1987; Mori et al. 1988) colorectal carcinoma (Ambe et al. 1989) thyroid carcinoma (Schroder et al. 1988) and others. This suggests an important role for S-100 protein positive cells in host defense mechanisms. We can expect a favorable prognosis for our patient.

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