Giant cell tumour (osteoclastoma) of the pancreas—an epithelial tumour probably of pancreatic acinar origin

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SUMMARY A case of giant cell tumour of the pancreas has been studied. The light microscopical appearance of the tumour is indistinguishable from osteoclastoma of bone. Electron microscopy of the tumour shows many typical desmosomes between stromal cells. This is strong evidence of its epithelial nature. The cytoplasm of both the osteoclast-like giant cells and stromal cells contain abundant rough endoplasmic reticulum, many with dilated cisternae containing prominent dense granules. There are also some larger homogeneous granules, some of them electron-dense, in the cytoplasm of the cells. These findings when compared with the features of other cases of giant cell tumour of the pancreas studied by electron microscopy support the view that this epithelial tumour is of acinar origin.

Carcinomas of the exocrine pancreas are more common than is generally realised because of the great difficulty in clinical diagnosis. A total of 5339 people died of cancer of the pancreas in England and Wales in 1973 (from the Registrar General Statistical Review of England and Wales for the year 1973, Part 1 (A); London, 1975); and it ranks fifth in order of frequency of cancer causing death. The rising incidence of cancer of the pancreas throughout the Western World is well documented. Histologically the great majority of these cancers are adenocarcinomas, usually well-differentiated and of ductal origin. Other histological types occasionally seen are adenoacanthomas and squamous cell carcinomas. There are also rare pancreatic cancers with unusual light microscopic appearances. These have been divided into four groups¹:

- 1 Spindle cell carcinoma consisting of malignant spindle cells and undifferentiated round cells.
- 2 Malignant giant cell carcinoma composed of osteoclast-like giant cells and malignant stroma.
- 3 Pleomorphic giant cell carcinoma composed of malignant mononucleated and multinucleated giant cells with sarcomatous stroma and usually showing mucin secretion.
- 4 Round cell anaplastic carcinoma composed of monotonous sheath of round cells with only occasional giant cells.

This paper reports a case of primary giant cell tumour of the pancreas with metastases to other organs. The tumour falls into group 2.

The clinical presentation of this case, the age of the patient, the mean survival time from onset of symptoms to time of death and the gross appearance of the tumour were very similar to that of the usual adenocarcinoma of the pancreas. On light microscopy, however, the appearance is identical to that of giant cell tumour of bone (osteoclastoma), with typical osteoclast-like giant cells intimately associated with stromal cells both in the primary and the metastases.

Case report

A 72-year-old woman was admitted into hospital because of upper abdominal and back pain, anorexia and weight loss. She had experienced her symptoms for the last six to eight months. Her past medical history included pulmonary tuberculosis in 1937. On examination she was a thin lady who was obviously in pain. She was not jaundiced. Her abdomen was distended and the liver enlarged and hard. She was suspected of having metastatic liver disease with the primary tumour in the alimentary tract. She died 10 days after admission.

PATHOLOGY

At necropsy a tumour of the pancreas was found.

The tumour was in the head of the pancreas and measured 6.5 cm × 6 cm × 5 cm. It had infiltrated the wall of the duodenum. The cut surface was greyish-white, moderately firm and variegated with multiple foci of necrosis. The body and tail of pancreas were free of tumour. The peripancreatic lymph nodes were enlarged, grey and firm. The liver weighed 2050 g and was extensively replaced by umbilicated nodules of metastatic tumour. The left adrenal gland also contained a small greyish-black nodule of metastatic tumour. The other organs were unremarkable and the skeletal system was normal.

MICROSCOPICAL FINDINGS

The tumour has the appearance of giant cell tumour of bone (Fig. 1). It has a diffuse pattern, is very cellular and consists of two types of cells—osteoclast-like giant cells and mononuclear stromal cells. The multinucleate giant cells appear benign and are diffusely distributed throughout most of the tumours and are intimately associated with the stromal cells. They contain numerous central nuclei,

Fig. 1 Representative field of the tumour showing two types of cells—mononuclear cells and giant cells. Haematoxylin and eosin ×250.

up to one hundred in some. The nuclei are oval and vesicular and contain one or two nucleoli. The cytoplasm is abundant and eosinophilic but also vacuolated in places.

The stromal cells are oval or spindle-shaped. They have round to oval vesicular nuclei with prominent nucleoli and eosinophilic cytoplasm. The nuclei of the giant cells and stromal cells are very similar. These stromal cells do not generally show features of malignancy except in areas of degeneration where their nuclei appear hyperchromatic. In some areas the tumour consists predominantly of mononuclear stromal cells and where they are spindle-shaped give the appearance of a sarcoma (Fig. 2). There was no evidence of gland formation in any of the numerous blocks of tissue examined. Stains for mucin were negative. Both the giant cells and stromal cells are present in blood vessels (Fig. 3) and in the metastases in the liver (Fig. 4). The metastasis in the adrenal consists of mononuclear cells only (Fig. 5).

ELECTRON MICROSCOPY

Electron microscopy was done on tissues which had previously been fixed in formalin. The findings confirmed the similarity of the nuclei in both the giant and stromal cells (Figs. 6, 7). The nuclei contain one or two small nucleoli and condensed chromatin attached to the nuclear membrane. Both cell types are rich in rough endoplasmic reticulum with dilated cisternae containing dense granules. There are also typical desmosomes between stromal cells. These fine structural features are similar to those described by Rosai² in his study of a similar pancreatic tumour.

Discussion

Tumours with osteoclast-like giant cells have been described in many organs and tissues: breast,³ thyroid,⁴⁻⁶ colon,⁷ lung,⁸ bladder⁹ and soft tissues.¹⁰⁻¹¹ These giant cell tumours like the giant cell tumour of the pancreas reported here are very rare. Areas of giant cell and/or sarcomatoid changes are not uncommonly seen in pancreatic adenocarcinomas. In the pancreas when the tumour consists of malignant mononucleated and multinucleated giant cells it is then referred to as pleomorphic carcinoma. The giant cells in this type of tumour usually have an epithelial appearance; cannibalism of cells by the giant cells is common and mitoses are frequent. Distinct areas of mucin-secreting adenocarcinomas are usually present, if not in the primary tumour, then in the metastases. This type of pleomorphic carcinoma should be distinguished from pleomorphic rhabdomyosarcoma, liposarcoma, choriocarcinoma and malignant melanoma. It

Fig. 2 Sarcoma-like appearance of tumour; a field showing spindle-shaped stromal cells only with a few mitoses. Haematoxylin and eosin $\times 160$.

Fig. 3 Vascular permeation by tumour; blood vessel contains both giant and stromal cells. Haematoxylin and eosin $\times 100$.

differs from the "osteoclastoma" reported here by its obvious anaplasia. In our case the giant cells lack the features of malignancy and the stromal cells for the most part appear benign. There was no evidence of gland formation in the numerous sections examined of both the primary tumour and the metastases. Mucin secretion was absent. In fact, the light microscopic appearance of our case is identical to osteoclastoma of bone. Extraskelatal "osteoclastomas" are very rare. The giant cells in osteoclastoma are considered to be formed by fusion of the mononuclear stromal cells which are the important tumour cells. There is much speculation about the cell of origin of this tumour and Dahlin¹² considers it unknown. With regard to our case there are five possibilities as to the origin of this tumour:

- 1 Giant cell tumour of bone metastatic to the pancreas.
- 2 Metaplastic carcinoma of the pancreas.
- 3 Adenocarcinoma of the pancreas with reactive osteoclast-like giant cells.
- 4 A true extraskelatal osteoclastoma arising from mesenchymal tissue in the pancreas—that is, a sarcoma.
- 5 An epithelial tumour (carcinoma) of pancreas in which the tumour cells have undergone "peculiar metaplasia".²

There was no clinical evidence of any bone tumour and at necropsy the skeletal system was normal. Metaplastic carcinoma in which an epithelial tumour contains areas where the stroma has undergone metaplasia to bone or cartilage is excluded on histological grounds. The absence of gland formation and mucin secretion on histological examination excludes the third possibility and the presence of giant cells in the primary tumour, in blood vessels and in the metastases is evidence that they are a component part of the tumour and not reactive.

True sarcomas of the pancreas are extremely rare and the electron microscopic appearance also excluded that possibility. We therefore consider this tumour to be an epithelial tumour which on light microscopy cannot be identified as such but which showed features of its epithelial nature on electron microscopy—the presence of many typical desmosomes between the stromal cells. Unfortunately, we were not able to demonstrate true microvilli on cell surfaces. This may have been due to autolytic changes. Desmosomes have not been demonstrated in skeletal osteoclastoma. Like Rosai² we also found abundant rough endoplasmic reticulum with distended cisternae some containing dense granules. Mitochondria were not seen. This is in contrast to Robinson and Damjenov¹³ who found much ultrastructural similarity between the giant cells in their pancreatic tumour and those of osteoclastoma of

Fig. 4 Extensive replacement of liver by metastatic tumour—cords of liver cells can be seen at top right hand corner. Haematoxylin and eosin $\times 80$.

Fig. 5 Metastatic tumour in adrenal consists of mononuclear cells only. Haematoxylin and eosin $\times 100$.

Fig. 6 Typical desmosomes between two stromal cells. Haematoxylin and eosin $\times 19000$.

Fig. 7 Giant cell—although the material is poorly preserved abundant rough endoplasmic reticulum and electron-dense granules can be seen. Haematoxylin and eosin $\times 2500$.

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bone. In skeletal osteoclastoma, the endoplasmic reticulum is poorly developed while the cells are rich in mitochondria. The presence of abundant granular endoplasmic reticulum containing intracisternal granules presumably of protein nature are said to be features of pancreatic acinar cells.² These are features which we also observed in our tumour. This study therefore gives further support to the view that “osteoclastoma” of the pancreas is of acinar origin.

In conclusion, the possibility of giant cell tumour from other sites apart from bone should be considered in the differential diagnosis of metastatic tumour with the light microscopical appearance of osteoclastoma.