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 groups:

1. Spindle cell carcinoma consisting of malignant spindle cells and undifferentiated round cells.
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, 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
Giant cell tumour (osteoclastoma) of the pancreas

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. Extraskeletal "osteoclas-
tomas" are very rare. The giant cells in osteoclas-
toma 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 Dahlin13 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 pan-
creas.
2 Metaplastic carcinoma of the pancreas.
3 Adenocarcinoma of the pancreas with reactive
osteoclast-like giant cells.
4 A true extraskeletal osteoclastoma arising from
mesenchymal tissue in the pancreas—that is, a sar-
coma.
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 his-
tological 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 desmo-
somes 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 dis-
tended cisternae some containing dense granules.
Mitochondria were not seen. This is in contrast to
Robinson and Damjenov13 who found much ultra-
structural similarity between the giant cells in their
pancreatic tumour and those of osteoclastoma of

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Fig. 2 Sarcoma-like appearance of tumour; a field show-
ing spindle-shaped stromal cells only with a few mitoses.
Haematoxylin and eosin ×160.

Fig. 3 Vascular permeation by tumour; blood vessel con-
tains both giant and stromal cells. Haematoxylin and eos-
in ×100.
Fig. 4 Extensive replacement of liver by metastatic tumour—cords of liver cells can be seen at top right hand corner. Haematoxylin and eosin ×80.

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

Fig. 6 Typical desmosomes between two stromal cells. Haematoxylin and eosin ×19000.
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. 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.

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References


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