

MIXED OSTEOCLASTIC AND PLEOMORPHIC GIANT CELL CARCINOMA OF THE PANCREAS

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True mixed giant cell tumors of the pancreas¹ that are composed of osteoclastic² and pleomorphic³ giant cells are quite rare. Three such cases have been reported previously in the English literature, but ours is the first case from Saudi Arabia. The biologic behavior of osteoclastic giant cell tumors (OGCT)⁴ is that of a locally aggressive low-grade malignancy, in contrast to pleomorphic giant cell tumors (PGCT), which behave in a highly malignant fashion. The behavior of true mixed giant cell tumors (OGCT+PGCT) is not known, because of the limited number of cases. Our case, which was a true mixed tumor of giant cells, behaved in a highly aggressive manner. In this report we document that if pleomorphism is seen among giant cell tumors of the pancreas, then such tumors should be regarded as highly malignant and be treated accordingly.

Case Report

A previously healthy 65-year-old Saudi male presented with a four-month history of left upper quadrant pain radiating to the back, and associated with considerable anorexia and recent onset of weight loss. There was no prior history of gastrointestinal disease or pancreatitis. Examination revealed an ill-defined non-tender mass near the left hypochondrium without any evidence of peritoneal irritation. There was no palpable lymphadenopathy or hepatosplenomegaly.

Laboratory evaluation revealed normochromic, normocytic anemia. Liver function tests were normal. Serum chemistry levels such as urea, creatinine, glucose and electrolytes were also within normal limits. Stool examination revealed no parasitic ova or occult blood. The urine examination was normal. An ultrasound examination of the abdomen revealed an ill-defined mass on the posterior abdominal wall related to the body and tail of the pancreas. CT scan demonstrated a tumor arising from the

cardiomegaly with subsegmental left basilar atelectasis. Endoscopy of the upper gastrointestinal tract was normal, however, it was not possible to negotiate beyond the descending colon on flexible colonoscopy. Barium enema showed a cutoff near the splenic flexure. At this point, it was decided to perform an explorative laparotomy through a midline incision, which revealed a tumor arising from the junction of the body and tail of the pancreas. The tumor was firm, dark, hemorrhagic and irregular-shaped, with some cystic areas. There was no evidence of any local invasion or liver metastases. Subtotal distal pancreatico-splenectomy was performed, which resulted in temporary improvement of the patient's condition. The patient was discharged home two weeks after the operation. He was readmitted four months later because of anorexia and continued weight loss. A thorough workup did not reveal any recurrence or metastases from the tumor. Supportive treatment was instituted, but the patient died about five months after the operation.

Histopathological examination (Figure 1) revealed a tumor containing abundant multinucleated osteoclastic giant cells with central nuclei varying from a few to 50 per cell. The nuclei were uniform in size and oval in shape, containing delicate vesicular chromatin with one or two small nucleoli. The cytoplasm in these cells was abundant and eosinophilic. Many of these cells contained clear intracytoplasmic vacuoles. In the background of these osteoclastic giant cells, one could see pleomorphic cells that exhibited bizarre cytological features and hyperchromatic nuclei. The chromatin pattern was coarse and clumped. A few cells contained several nuclei, but most were mononuclear and had high nuclear to cytoplasmic ratio. Their cytoplasm was eosinophilic and varied from scant to abundant. Intermediate cells with features of both pleomorphic and osteoclastic giant cells were also present. There were extensive areas of necrosis and hemorrhage. A few intravascular tumor thrombi were seen. Scattered among the tumor cells were inflammatory cells, mainly lymphocytes and neutrophils. Occasional neutrophilic microabscesses were also present. Among the tumor cells some preserved islets of Langerhans and pancreatic ductules were visible. No osteoid or chondroid elements were noted.

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Accepted for publication 30 November 1997. Received 6 July 1997. junction of the body and tail of the pancreas, measuring about 20 cm. A roentgenogram of the chest showed mild

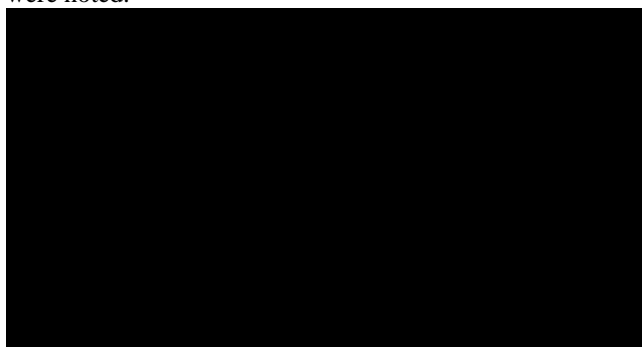


FIGURE 1. Mixed giant cell tumors of the pancreas containing many multinucleated osteoclastic giant cells. Pleomorphic giant cells are seen in the background exhibiting bizarre cytological features and hyperchromatic nuclei. Intermediate cells with features of both pleomorphic and osteoclastic giant cells are also present.

Discussion

Cancer of exocrine pancreas comprises approximately 85% of all cases of pancreatic malignancy.⁵ It is the fourth most common cause of death from cancer in the United States and its incidence is increasing.⁶ The most common type of exocrine pancreatic tumor is the classical adenocarcinoma, but fairly distinct variants of this tumor have been described, such as adenosquamous carcinoma, oncocytic carcinoma, clear cell carcinoma, and signet ring carcinoma.⁷ The OGCT is considered to be a special duct-derived variant of anaplastic carcinoma that contains relatively uniform mesenchymal cells and multinucleated giant cells having an appearance and histochemical profile indistinguishable from that of bone osteoclasts. It is important that this type of tumor be separated from PGCT, which has a worse prognosis.

The histogenesis of OGCT and PGCT is controversial. Being in favor of an epithelial origin, some authors have reported the presence of glands within some tumors and its coexistence with adenocarcinoma.⁸ Those in favor of a mesenchymal derivation point to the striking resemblance of OGCT to osteoclastic giant cell tumor of bone.⁹ Lewandrowski et al.¹ carried out ultrastructural and immunohistochemical studies on a mixed osteoclastic and pleomorphic giant cell tumor of the pancreas, and their results strongly supported a mesenchymal line of differentiation. However, this may very well be a collision tumor, or a dual growth of two distinct malignancies.

With the introduction of fine-needle aspiration (FNA) cytology, the diagnosis by this method has become very popular. Pinto et al.¹⁰ have described the cytological features of pleomorphic giant cell carcinoma of the pancreas through fine-needle aspiration. Gupta and Wakefield¹¹ reported three cases of PGCT in which FNA was carried out for the purpose of diagnosis, electron microscopy and immunocytochemistry.

The first line of treatment of this disease is surgical if the lesion is resectable. The choices of surgery depend upon site and size of the lesion. Neoplasms of body and tail are treated with distal pancreaticosplenectomy.¹²

Neoplasms of pancreatic head and ampullary region are generally treated with pancreaticoduodenectomy (Whipple operation), the alternative being total pancreatectomy.¹³ Mortality from these operations has decreased from 20% to 2% in specialized centers in recent years.¹⁴ Because of the fact that very few cases of mixed OGCT and PGCT have been reported in the literature, and considering the remarkable difference in biological behavior of the two types, long-term merits of each surgical procedure cannot be determined. Pancreatic cancer is generally considered chemoresistant, although many chemotherapy regimens have been described.¹⁵ Other therapies include external beam radiation, brachytherapy, as well as pain management. Experimental studies have shown a significant inhibition of adenocarcinoma of the pancreas by gonadoliberin (luteinizing hormone-releasing hormone) and somatostatin.¹⁶ Gene insertion therapy has also shown promise in animal models.¹⁷

We have described a unique case of mixed giant cell tumor of osteoclastic and pleomorphic type, the treatment of which is a dilemma, due to the marked difference in biological behaviors of the two types. It is our opinion that such tumors will behave according to the most malignant portion of the tumor, that is, the pleomorphic component.

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