Reprinted from PANCREAS
Vol. 22, No. 1 January 2001
Lippincott Williams & Wilkins Printed in U.S.A.

Benign Variant of Osteoclast-Type Giant Cell Tumor of the Pancreas: Importance of the Lack of Epithelial Differentiation

Osteoclast-like giant cell tumor of the pancreas (OGTP) is an unusual entity originally described by Rosai (1) in 1968, characterized by osteoclast-like giant cells and mononuclear stromal cells identical to those seen in bone giant cell tumors. Since then, there have been only a few reports of tumors containing giant cells in other anatomic locations (2). OGTP can be distinguished from pleomorphic giant cell tumor of the pancreas (PGTP), because of the lack of marked nuclear pleomorphism associated with PGCP.

Often a histologically recognizable pancreatic carcinoma accompanies OGTP, leading to a poor outcome (3,4). Pure forms of OGTP present a better prognosis because it takes much time to develop metastasis, but these forms are very rare, with only a few cases reported in the English literature (3,5,6). We describe a case of a pure OGTP and discuss the diagnosis of benignity of such tumors based on immunohistochemical evaluation.

CASE REPORT

A 68-year-old woman with a 4-week history of abdominal mass incidentally found in routine gynecologic examination was referred for treatment. There was no pertinent medical history. At abdominal examination, a palpable tumor in the right upper quadrant was found. Liver function tests, CA 19-9, and carcinoembryonic antigen (CEA) were within normal limits. Abdominal ultrasound disclosed a cystic tumor in the head of the pancreas measuring 8.5 × 8.1 × 8.0-cm associated with a dilated (9 mm) pancreatic duct. Computed tomography (CT) scan showed a 9-cm cystic tumor in the head of the pancreas with central calcification. The patient underwent a pylorus-preserving duodenopancreatectomy. At laparotomy, there were no lymph nodes or other metastases. The patient had an uneventful postoperative recovery. One month after the surgery, she had lower limb deep vein thrombosis, treated with anticoagulating agents with relief of the symptoms. The patient is alive and without any evidence of disease after 30 months of follow-up.

METHODS

The surgical specimen consisted of pancreatic head and uncinated process and the duodenum and was fixed in buffered formalin, 10%. Multiple cuts were taken

from the cystic mass, representing all tumor surfaces. For light microscopy, 5-μm cut sections from the paraffin blocks were stained with hematoxylin–eosin. For immunohistochemistry, 5-μm cut sections in poly-L-lysine–coated glass slides were submitted to antigen retrieval comprised of domestic microwave treatment, using high power (100%) in citrate buffer, 1 mmol/L. Monoclonal antibodies and their dilutions are listed in Table 1. Incubations were at 4°C overnight (16 hours), and the peroxidase-conjugated streptavidin method was used. Color was developed by incubating slides in 0.06% diaminobenzidine in PBS for 15 minutes.

Pathological findings

The specimen of the pancreatoduodenectomy had a cystic tumor mass measuring 8.5 × 7 × 4 cm, occupying all of the pancreas head (Fig. 1). Cut surface was friable and yellowish, with hemorrhage and necrosis in the central zone. Microscopic examination revealed a proliferation of large spindle cells, with large, eosinophilic cytoplasm and pleomorphic nuclei with dispersed chromatin and evident nucleolus. No mitosis was found. Numbers of multinucleated, osteoclast-like giant cells were intermixed with the spindle cell proliferation. There was no pleomorphism, mitotic activity, and no adenocarcinoma or neoplastic gland inside the tumor (Fig. 2). The stroma was partially sclerotic with focal calcification and deposits of hemosiderin. No osteoid formation was found. The tumor was extensively vascularized, with areas of hemorrhage and necrosis. Pancreatic tissue adjacent to the tumor was unremarkable, and no lymph node metastasis was found. The immunohistochemistry profile is demonstrated in Table 1. The spindle and giant cells were positive for CD68 (Fig. 2), vimentin, and α_1-antitrypsin, suggesting fibrohistiocytic properties. All epithelial markers such as low-weight and high-weight cytokeratin 7, 20, and epithelial membrane antigen were negative.

TABLE 1. *Immunohistochemical profile*

Name	Clone	Dilution	Profile
Vimentin	V9	1/400	+++
α_1-Antitripsin	—	1/100	++
CD68	KP1	1/100	+++
EMA	E29	1/200	–
Cytokeratin high weight	34βE12	1/100	–
Cytokeratin 8, low molecular	35βH11	1/200	–
Cytokeratin 7	OV-TL 12130	1/100	–
Cytokeratin 20	KS 20.8	1/50	–
CD15	C3d-1	1/100	–
CEA	II-7	1/100	–
Factor VIII	F8/86	1/50	–
Anti-human muscle actin	HHF-35	1/80	–
S100	—	1/100	–

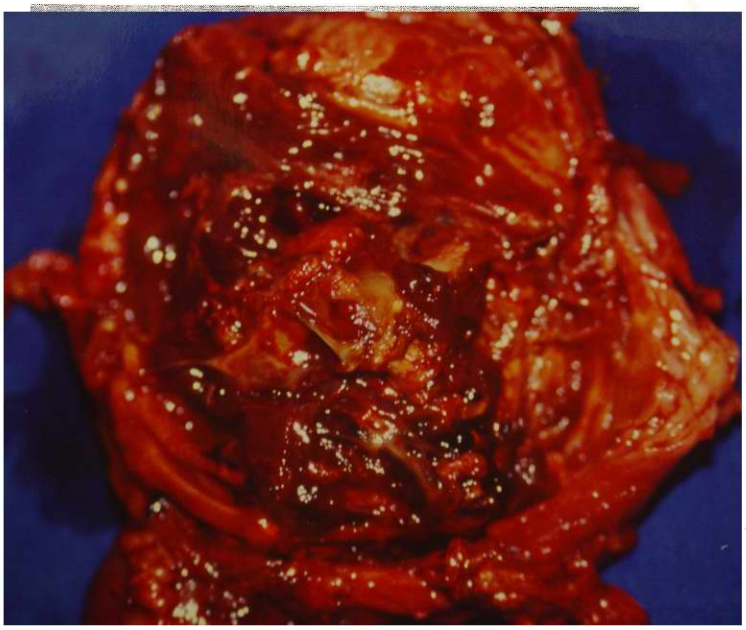

FIG. 1. Macroscopic view of the specimen consisting of pancreatoduodenectomy. Note a cystic tumor mass occupying the pancreas head.

CD 15, CEA, anti-human muscle actin (HHF-35), S100 protein, and factor VIII were also negative.

DISCUSSION

Giant cell tumors of the pancreas are rare nonendocrine neoplasms, and two histopathologic types are generally recognized. The first, osteoclastic giant cell tumor of the pancreas (OGTP), is indistinguishable at light microscopy from giant cell tumor of bone. The second type, pleomorphic giant cell carcinoma (PGCP), is a sarcoma-like tumor with bizarre pleomorphic mononucleated and multinucleated giant cells (1,7).

The histogenesis of these tumors has been regarded as different. PGCP is generally considered a sarcomatous metaplasia of ductal adenocarcinoma that is epithelial in its origin (4). Conversely, the origin of OGTP has been debated, and both mesenchymal and epithelial origins have been reported in the literature (8,9). In favor to an epithelial origin, some authors have reported the presence of glands within the tumor and the coexistence of OGTP with adenocarcinoma (6). In favor to a mesenchymal derivation is the striking resemblance of OGTP to bone giant cell tumors and, in some tumors, the lack of epithelial differentiation (7). Robinson et al. (9) believed that these differences may be the result of different degrees of cellular differentiation within the same type of tumor, rather than an indication of different cell origins.

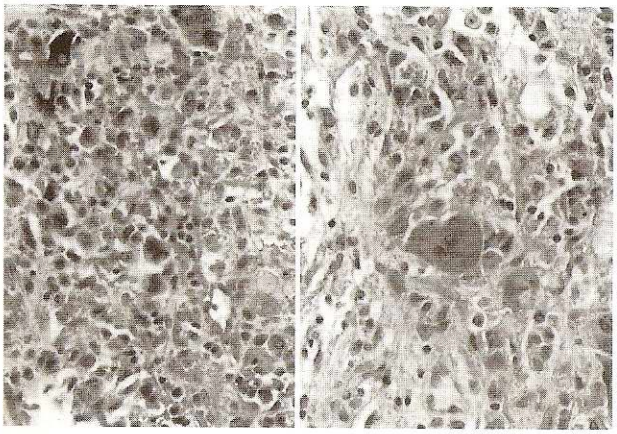

FIG. 2. CD68 antibody staining both spindle and giant tumor cells.

Giant cell tumors of the pancreas may best be regarded as arising from a precursor cell capable of differentiating along divergent lines and giving rise to a spectrum of morphologic, immunohistochemical, and ultrastructural phenotypes (7). As suggested by Cubilla and Fitzgerald (10), OGTP and PGCP may represent opposite ends of the biologic spectrum of a single neoplasm, the latter being biologically more aggressive.

The majority of the reported cases deal with the malignant type of pancreatic giant cell tumor (2). In all reported cases where a poor outcome was observed, an epithelial component within the tumor was found (2,4, 11,12). Therefore the absence of such differentiation is associated with a better prognosis. Indeed, in some reported cases (3,5) and in the present one, a lack of epithelial component in the immunohistochemical study is directly related to a favorable outcome.

Immunohistochemical study has to be considered as of paramount importance to predict the outcome of these patients and to determine whether adjuvant therapy will be necessary. Accurate histologic recognition of the benign variant of osteoclast-type tumor will encourage an aggressive surgical approach, in view of the expectation of a better prognosis. We believe that the absence of staining of epithelial markers in the immunohistochemical study of these patients precludes any type of adjuvant chemo- or radiotherapy.

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