Case Report

Cytological Diagnosis of Undifferentiated Carcinoma of The Pancreas with Osteoclast-like Giant Cells: Report of Three Cases

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ABSTRACT

Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells is a very rare, highly malignant tumor of the exocrine pancreas and only few cases, diagnosed by Fine needle aspiration cytology (FNAC) have been reported till date. This tumor consists of two distinct cell populations composed of numerous multinucleated giant cells resembling osteoclasts of the bone and mononuclear stromal cells. Other heterogeneous cell populations may be present. We report three such cases in young patients with abdominal mass /digestive problems and rapid weight loss. Diagnoses were primarily made by FNAC and eventually confirmed by histopathology in tertiary centers.

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Introduction

Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells (OGCs) is a rare, highly malignant, non-endocrine tumor. It accounts for less than 1% of all pancreatic malignancies. It was first described by Juan Rosai in 1968. [1] In histology, the OGCs remain distributed diffusely in the stroma of the cyst wall, with more than 10 nuclei per cell and lacking features of atypia. [2] Till date only four cases including one from India have been diagnosed by FNAC (Fine Needle Aspiration and Cytology). [3 – 5] We report three such tumors of the pancreas primarily diagnosed by Computed tomography (CT) – guided FNAC (Fine Needle Aspiration and Cytology). Two of the patients were male (age 22 and 30 years) and one was female (age 32 years). All presented with abdominal mass, digestive problems, pain and rapid weight loss. There was an intricate mixture of the adenocarcinomatous component, spindle cells and osteoclast-like giant cells and eventually confirmed by histopathology.

Case Reports

A 30-year-old male presented with the complaints of dull aching abdominal pain in and around the umbilicus for about 18 months. Pain was not related to food intake and was not radiating to the back. He was a known diabetic and hypertensive, both controlled adequately. Clinical examination revealed a firm to hard tender mass involving peri-umbilical region. Plain and intravenous contrast-enhanced computed tomography (CT scan) of the abdomen revealed a large (71 x 48 x 70 mm) well defined heterogeneous solid cystic space occupying lesion at the preaortic and precaval region abutting right psoas showing punctuate calcification and mild enhancement on contrast study [Figure 1a]. Another young male of 22 years also presented with similar features but the mass was at the tail of the pancreas that measured 12 cm in diameter. The third patient was a married 32 years old lady with one 8 years old child. She presented with a vague heaviness in the left hypochondrium with digestive problems. CT scan revealed mass in the tail of pancreas adherent to stomach and measuring 4 cm in diameter with central cystic cavity. In all three cases CT-guided fine needle aspiration was done from the masses [Figure 1b]. The smears were cellular and showed numerous mononuclear stromal cells along with numerous multinucleated osteoclast-type giant cells having 10 to 20 centrally placed, uniform, overlapping nuclei with smooth delicate nuclear membranes, finely granular homogenous chromatin and small nucleoli. The adenocarcinoma component was intermixed with these giant cells and the tumor cells were large, pleomorphic, polygonal with abundant cytoplasm, coarse chromatin and distinct nucleoli [Figures 1c, 1d, 2a, 3a and 3b]. Background contained variable numbers of foamy histiocytes, squames, necrosis, cellular/nuclear debri, chronic inflammatory cells and crystalloid materials in the fluidy background. The smears from the female patient, in addition, contained large papillary fragments of neoplastic glands [Figure. 3a and 3b]. The possibility of undifferentiated carcinoma with osteoclast-like giant cells was offered in all three cases. Histopathological confirmation was done by excisional or open surgical biopsies in some referral centers [Figures. 1e, 2b, 3c and 3d].

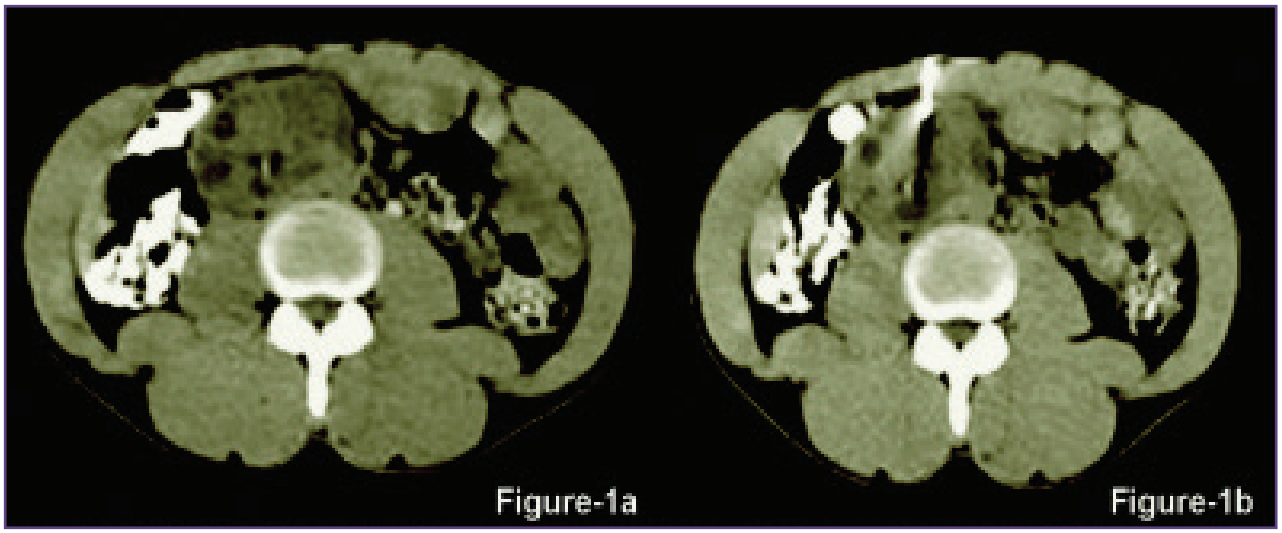

Figure-1a Figure-1b

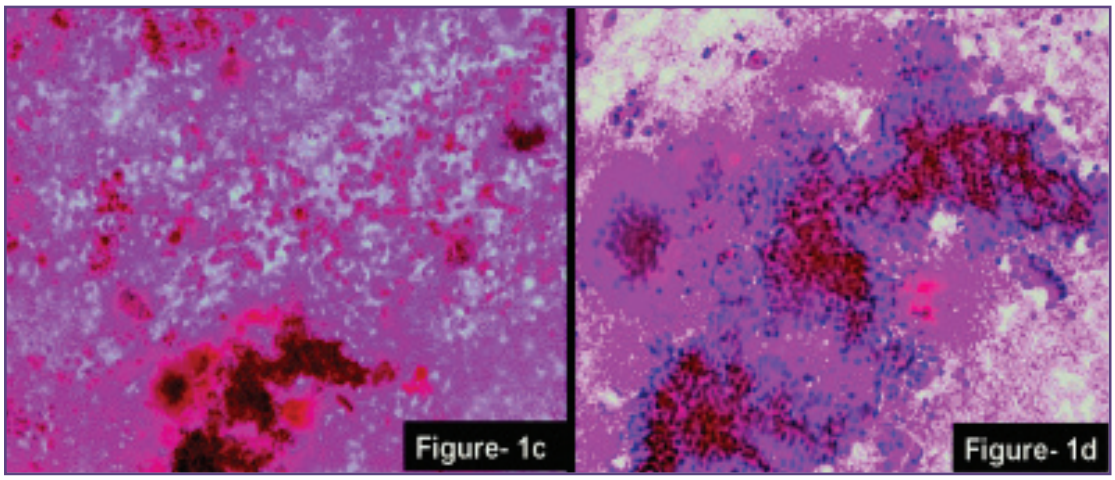

Fig. 1a: CT scan showing the complex SOL in the head of the pancreas
Fig. 1b: CT scan showing the needle in-situ within the SOL
Fig. 1c: 1d: Photomicrograph of the FNA smears show many osteoclastic giant cells, scattered stromal cells and adenocarcinoma component (Geimsa, 100x, 400x)

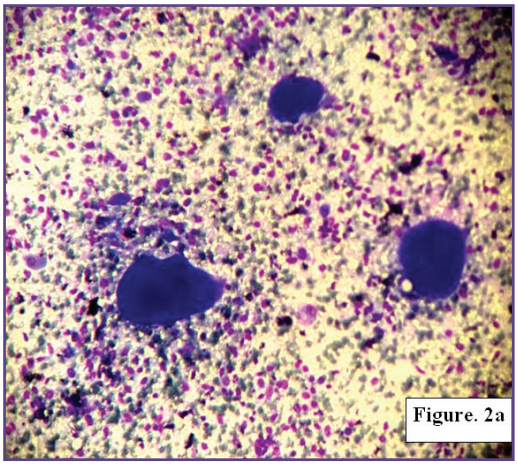

Fig.1e: Corresponding histology of case 1.

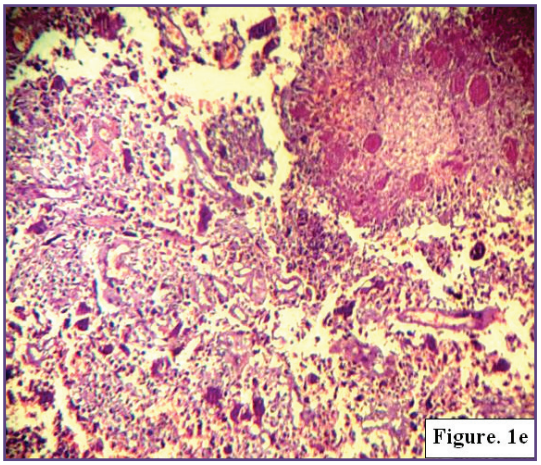

Fig. 2a: FNA smear from case-2 show osteoclastic giant cells and scattered mononuclear spindle stromal cells (MGG, 100x)

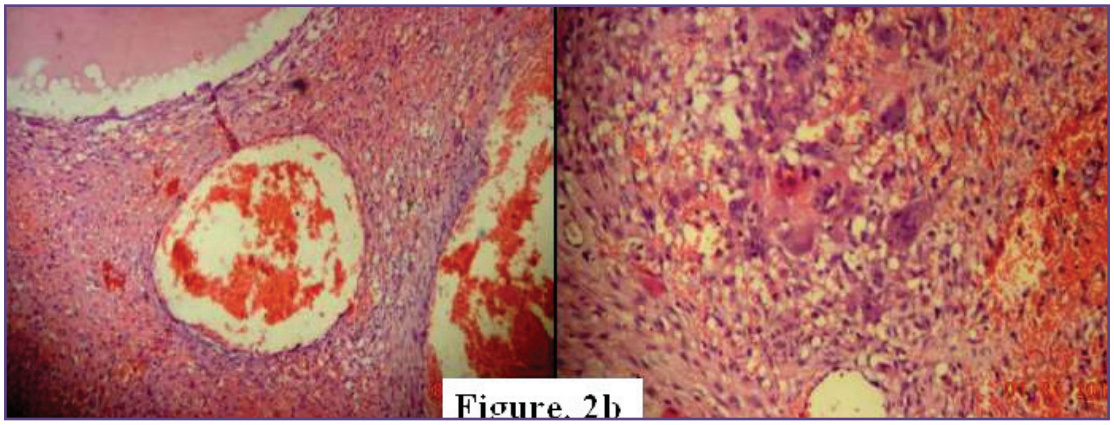

Fig. 2b: Histology of the second case: a mixture of giant cell reparative granuloma / aneurysmal bone cyst (H & E, 100X).

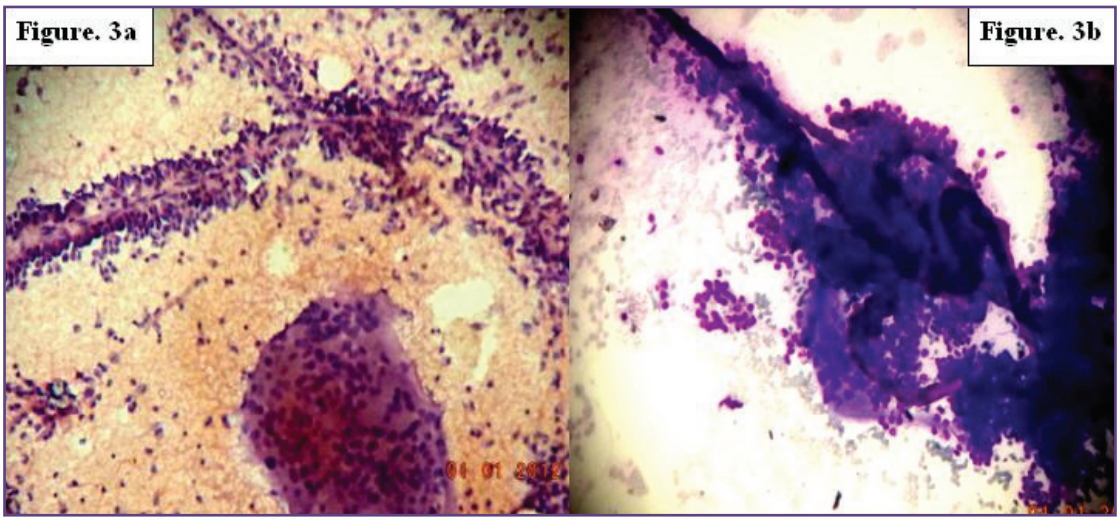

Fig. 3a/3b: Cytosmears from the third case show papillary clusters of neoplastic glandular epithelial cells and osteoclastic giant cells in the background (PAP and MGG, 100x).

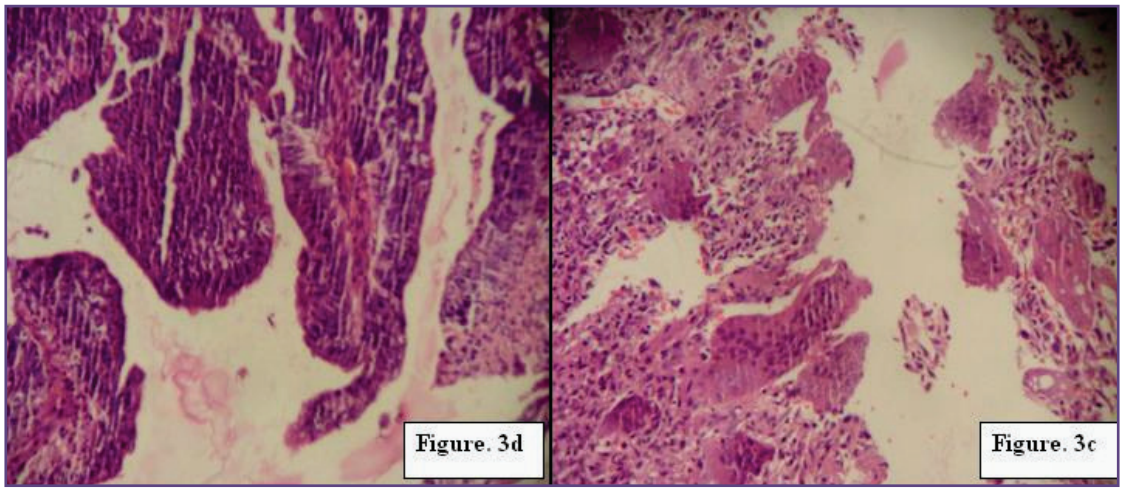

Fig. 3c/3d: Histology from the third case showed well-formed papillary glands at one end of the tumor and other areas showed features those of giant cell tumor of bone (H & E 100x).

Discussion

Undifferentiated tumors of the pancreas with osteoclast-like giant cells (OGCTs) are considered as a rare variant of adenocarcinoma and are currently classified as undifferentiated carcinoma with osteoclast-like giant cells by the World Health Organization.[6] Others have classified it into two histopathological subtypes: one with pleomorphic multinucleated giant cells and sarcomatoid growth pattern, the other with osteoclast-like giant cells, resembling a giant cell tumor of the bone presenting osteoclast-like giant cells.[4, 7, 8] Presently, the cases of two males were just the classical cases of undifferentiated carcinoma with osteoclast-like giant cells (second type). The case of the female patient belongs to the first category. This rare neoplasm was composed of pleomorphic to spindle-shaped cells and scattered non-neoplastic or reactive osteoclast-like giant cells with usually more than 20 uniformly small nuclei. There was also an invasive papillary adenocarcinoma component attached to the giant cell component. Mucinous carcinomatous component was found in the first case. The osteoclast-like giant cells are often concentrated near areas of hemorrhage or the cyst wall and may contain hemosiderin and occasionall phagocytosed mononuclear cells. Mucin is common. Osteoid-like material may also be found but no chondroid material.[6]

The mean age of patients with osteoclast-like giant cell tumors is 60 years but there is a wide age range from 32 to 82 years. Some tumors are found in association with mucinous cystic neoplasms as is one case here. In the early reports on this tumor it was suggested that they

may have a more favorable prognosis than the usual ductal adenocarcinoma. More recently a mean survival of 12 months has been reported. [6] In the present cases the individuals are relatively younger and died within 24 months of surgery.

OGCTs usually involve the body and tail of the pancreas in contrast to pancreatic adenocarcinoma which mainly involves the head. [6] In present cases one of the tumors was near the head of the pancreas. Others were located in the tail region. Non-specific upper abdominal pain (likely related to the rapid growth of tumor), abdominal distension and a palpable mass are the prominent initial symptoms in patients with OGCTs, whereas jaundice is the most common presentation in patients with pancreatic adenocarcinoma. They commonly present as large cystic neoplasm with variable areas of hemorrhage and necrosis. [5] The nature and origin of osteoclast-like giant cells remain controversial: Epithelial, histiocytic or mesenchymal metaplasia has been suggested. [7- 10]

Other differential possibilities are metastatic tumors, benign cysts, solid pseudopapillary neoplasm of the pancreas (SPN), and undifferentiated carcinoma / sarcoma. Clinico-radiological correlation and detailed history along with FNAC findings are sufficient to exclude secondaries and benign cysts. In SPN, the smears are highly cellular and the most conclusive criterion for identification of SPN is the pseudopapillary arrangement with bland appearing tumor cells and the absence of multinucleated giant cells. A mixture of benign as well as malignant components excludes undifferentiated carcinoma / sarcoma and other complex neoplasms. [4, 7 – 10]

The histology of OGCTs in the three cases was variable. They resembled osteoclastic giant cell of bone with cystic central component in the first case, a mixture of giant cell reparative granuloma / aneurysmal bone cyst in the second case and papillary carcinoma well segregated from giant cell component in the third case. Primary undifferentiated carcinoma with osteoclast-like giant cells of the pancreas also needs to be differentiated from non-neoplastic giant-cell containing lesions of the pancreas and giant cell containing neoplasms not arising within the pancreas. Non-neoplastic osteoclast-like giant cells remain the histological hallmark of this tumor. [4]

Conclusion

Pancreatic biopsies are difficult to perform because of its critical location and associated complications. Fine Needle Aspiration and Cytology has revolutionized the diagnostic approach to these cases. The presence of bland OGCs and the mononuclear cells in the absence of bizarre pleomorphic cells is a distinct cytomorphological feature of this rare tumor. Identifying these features on the smears helps in the differentiation of these pure OGCTs from undifferentiated carcinoma with OGCs. Very young adults should also be suspected if clinical and radiological features correlate and FNAC may confirm the diagnosis. In summary, CT guided FNAC is an effective and accurate means for cytological diagnosis of undifferentiated carcinoma with osteoclast-like giant cells of the pancreas.

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