Case Report

"Pancreatic undifferentiated carcinoma with osteoclast-like giant cells (UC-OGC)" on cytology: two case reports on a variant of pancreatic adenocarcinoma

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ABSTRACT

Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells (UC-OGCs) are a rare entity, less than 1% of all pancreatic malignancies. Recent studies quoted that the prognosis of these cancers is more favorable and displays a less aggressive with slow metastasis and lymph node spread compare to patients with an associated conventional pancreatic ductal adenocarcinoma. Here, we describe a case series of two reports as of undifferentiated carcinoma with OGCs of the pancreas in the duration of 10 years. Both the cases presented with complaints of abdominal pain and weight loss. Laboratory investigation revealed a normal level of amylase and lipase. One of the cases showed mild elevation of CA19-9. Endoscopic ultrasound-guided fine-needle aspiration was performed and diagnosis of undifferentiated carcinoma with OGCs of pancreas made on aspiration cytology and cell block. Due to the rarity of the tumor, there is a lack of prospective studies on treatment options. However, surgical *en bloc* is currently considered first-line treatment. The role of chemotherapy and radiotherapy has not been established.

Key words: Amylase, Lipase, Osteoclast-like giant cells, Pancreatic malignancies

Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGCs) of the pancreas were first described by Rosai in 1968 [1]. UC-OGC is an exceedingly rare distinctive tumor type that accounts for less than 1% of all pancreatic malignancies [1]. Microscopically, the neoplasm is mainly composed of two cellular components: The presence of bland osteoclast-like GCs and ovoid-to-spindle-shaped mononuclear tumor cells are a distinct cytomorphological feature of this rare tumor [2]. Less than 100 cases have been published so far. The data on the prognosis of UC-OGCs are fairly limited. The overall impression in the literature is that it is a highly aggressive tumor, with an even worse prognosis than ordinary pancreatic ductal adenocarcinoma (PDAC) although some observers noted a more protracted course [3,4].

Here, we presented a case series of two case reports of UC-OGC of the pancreas, which was diagnosed on aspiration cytology and on cell block. There have been relatively few reports, primarily based on case reports, regarding the clinical and histopathological features of this rare tumor in the literature.

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CASE SERIES

Case 1

A 70-year-old woman presented with complaints of self-resolving epigastric pain radiating to the back and vomiting which were increased for a few days and not managed by medication. There was a decreased appetite and 6 kg weight loss for the past 3 months. No other significant past/family/social/allergic history were noted. On general examination, the patient had pallor with a body mass index of 22 kg/m^2. The palpation of the area showed mild tenderness. Vitals were stable. No jaundice or palpable abdominal mass was noted.

Laboratory results revealed anemia (hemoglobin – 9.8 g/dl). Serum amylase and lipase levels were normal with mild elevated CA19-9. On computed tomography abdomen, a heterogeneous enhanced space-occupying lesion measuring 40 × 35 mm with necrotic changes was seen in the head and uncinate process of the pancreas (Fig. 1). On guided fine-needle aspiration (FNA) and cell block, predominantly scattered pleomorphic round to spindle malignant cells with hyperchromatic nuclei, prominent nucleoli, and scant to moderate amount of cytoplasm were seen along with benign looking multinucleate osteoclastic GCs (Fig. 2). A

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diagnosis of UC-OGC was suggested. The patient was unfit for surgery and chemotherapy due to poor general condition. The patient was advised for supportive therapy (antiemetic and pain management).

Case 2

A 50-year-old male presented with complaints of dull paroxysmal manageable abdominal pain and 4 Kg weight loss for 2 months (BMI – 31 kg/m^2). He had a history of hypertension for the past 1 year and well controlled by antihypertensive. There was no significant abnormality seen in general examination with stable vitals.

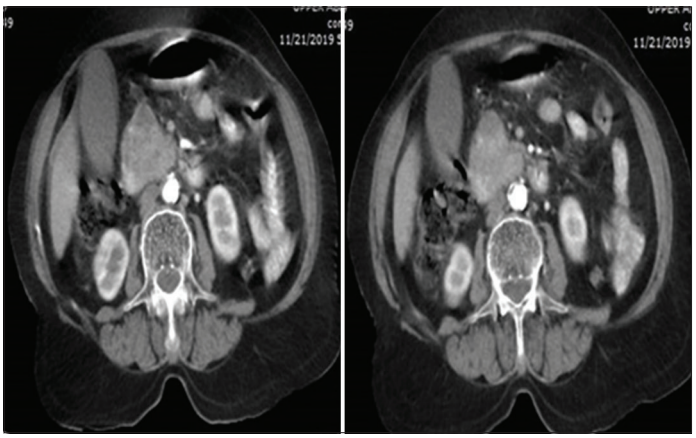

Figure 1: CECT scan of the upper abdomen reveals large heterogeneously enhancing SOL measuring 40 × 35 mm with necrotic changes in the head and uncinate process of pancreas. It is not separately defined from the second and third parts of the duodenum causing common bile duct dilatation (Case 1)

On ultrasonography, a pancreatic mass identified in the head region approximately 91 × 70 mm with peripancreatic lymph nodes suggested malignant nature. Laboratory investigation revealed a normal level of amylase, lipase, and CA19-9. Endoscopic ultrasound (EUS)-guided FNA was performed. Aspirate was highly cellular, composed of singly scattered and loose clusters of ovoid pleomorphic cells with hyperchromatic, enlarged nuclei, and abundant pale cytoplasm. In addition, a large number of multinucleated osteoclast-like GCs seen. Overall morphology suggested UC-OGC. The patient was lost to follow-up.

DISCUSSION

Undifferentiated carcinoma of the pancreas is a rare, aggressive tumor. A variety of other terms has been used to describe this; however, a duct epithelial origin is now established and recognized as a variant of pancreas ductal adenocarcinoma (PDAC) [5]. These tumors can be generally subdivided into two categories: Pure osteoclast-like GC tumors and those with a component of a more conventional neoplasm. Most often, the more conventional component is a PDAC, although intraductal papillary mucinous neoplasm, mucinous cystadenocarcinoma, and PanIN-3 have also been reported. Notable, studies have found that patients with pure UC-OGC survived longer than patients with an associated conventional PDAC [6,7]. Muraki *et al*. also reported a trend toward better survival for patients with pure UCOGC [8]. Their case series support a favorable prognosis with a 5-year survival rate of 59.1%, and median survival of 7.67 years, which was incomparably better than that of PDACs (15.6% and 1.59 years). Thus, a lack of ductal differentiation seems to predict an improved prognosis.

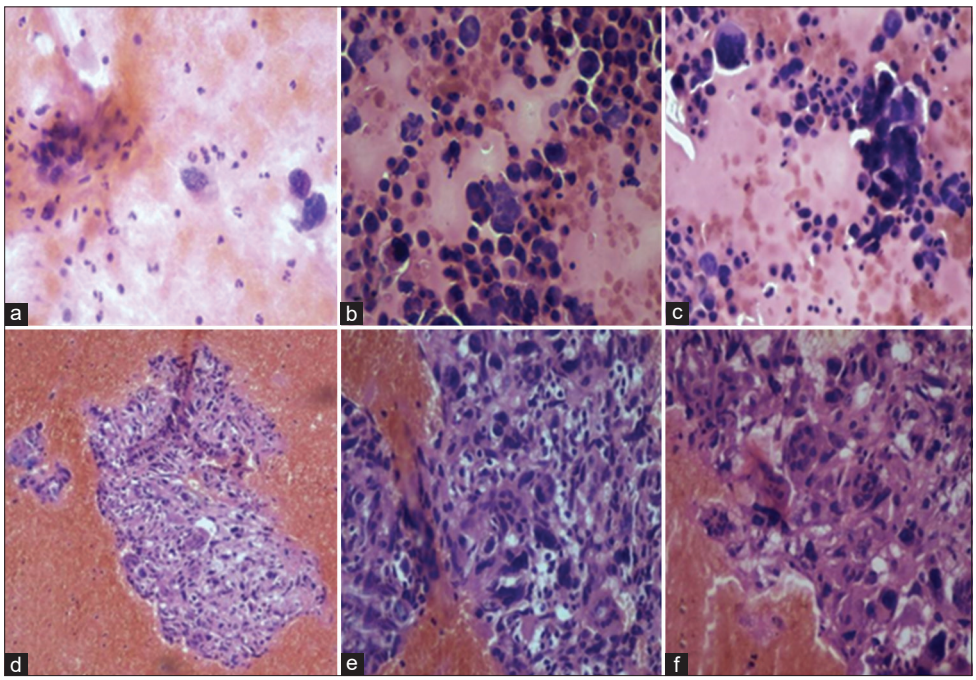

Figure 2: (a-c) Fine-needle aspiration cytology shows combination of pleomorphic malignant mononuclear cells with multinucleated osteoclast-like giant cells with hemorrhagic background. Malignant cells demonstrate marked nuclear pleomorphism and hyperchromasia. (d) Low-power view of cell block preparation demonstrating malignant mononuclear cells admixed with abundant osteoclast-like bland giant cells. (e and f) Photomicrograph of cell block preparation – a mixture of numerous pleomorphic malignant cells with numerous scattered osteoclast-like giant cells (H&E) (Case 1)

In addition to female predominance, UC-OGCs also occur a decade younger than PDACs. The clinical symptom varies from abdominal pain, loss of appetite, nausea, and steatorrhea to rarely asymptomatic individuals diagnosed incidentally. The body and tail of the pancreas are the most common sites for UC-OGCs, however, they can arise from any portion of the pancreas. The size ranges from 3 to 12 (mean – 5 cm). Despite being larger tumors, they appear to be less invasive than PDACs, with less likelihood of perineural invasion and nodal metastasis.

Tumor markers, CEA and CA 19-9, are indistinct as they are less commonly elevated and not significant to arriving at a diagnosis. The diagnosis is usually made on a surgical specimen. In some cases, EUS-FNA has shown to be effective, and an accurate diagnosis had been achieved by cytology test [9,10]. Cytological findings for pancreatic aspirate composed of an obviously malignant cellular proliferation containing benign appearing osteoclast-like GCs. Smears are typically hypercellular with two cell populations; atypical mononuclear cells and osteoclast-like GCs. The mononuclear cells appear singly or in small clusters and range from medium-sized polygonal epithelioid cells with clear cytoplasm to large bizarre sarcomatoid cells with dense and/or spindled cytoplasm [11]. The mononuclear cells intermingled with the OGCs which may be few in number or can be numerous. The GCs often contain 10 or more bland appearing, centrally clustered, and slightly overlapping nuclei with even chromatin and occasionally prominent nucleoli. The cytoplasm is abundant and dense and may contain phagocytic material [11].

In the majority of reports, the mononuclear cell population expresses immunostaining for epithelial membrane antigen and keratin which demonstrates an epithelial origin. Conversely, epithelial markers are rarely express by osteoclastic GCs and show staining consistent with a histiomonocytic origin (CD68) [8]. Genetically, UC-OGC of the pancreas resembles PDAC, with both entities harboring frequent KRAS, TP53, CDKN2A, and SMAD4 mutations [8,12,13]. However, the low proliferative index of the GCs by Ki67 staining and their lack of driver mutations, it is safe to conclude that these osteoclastic cells are innocent recruits to this peculiar neoplasm [14,15].

Metastases are less likely in UC-OGC and when they do occur, it is through lymphatics or direct peritoneal extension. Accordingly, early diagnosis and complete surgical resection represent the best chance to cure this rare tumor. However, the effectiveness of chemotherapy and radiotherapy is not established. Lacunae in our cases were the lack of standard care of treatment and follow-up due to poor general condition and financial constraints.

CONCLUSION

UC-OGCs of the pancreas are a distinct entity and classified separately. UC-OGCs have a better prognosis than the current impression in the literature than ordinary PDACs without osteoclastic cells (PDCs), but further studies in larger cohorts are needed to confirm this observation. These results suggest the importance of extensive histological sampling of UC-OGCs to exclude associated PDAC, which significantly impacts prognosis and awareness, and recognition of these can affect patient care. These cases were being reported as it is a rare entity and FNAC was instrumental in diagnosing it.

REFERENCES

1. Rosai J. Carcinoma of pancreas simulating giant cell tumor of bone. Electron-microscopic evidence of its acinar cell origin. Cancer 1968;22:333-44.
2. Bauditz J, Rudolph B, Wermke W. Osteoclast-like giant cell tumors of the pancreas and liver. World J Gastroenterol 2006;12:7878-83.
3. Luka's Z, Dvora'k K, Kroupova I, Valaskova I, Habanec B. Immunohistochemical and genetic analysis of the osteoclastic giant cell tumor of the pancreas. Pancreas 2006;32:325-9.
4. Osaka H, Yashiro M, Nishino H, Nakata B, Ohira M, Hirakawa K. A case of osteoclast-type giant cell tumor of the pancreas with high-frequency microsatellite instability. Pancreas 2004;29:239-41.
5. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO Classification of Tumours of the Digestive System. 4th ed. Lyon: International Agency for Research on Cancer; 2010.
6. Hirano H, Morita K, Tachibana S, Okimura A, Fujisawa T, Ouchi S, *et al*. Undifferentiated carcinoma with osteoclast-like giant cells arising in a mucinous cystic neoplasm of the pancreas. Pathol Int 2008;58:383-9.
7. Wada T, Itano O, Oshima G, Chiba N, Ishikawa H, Koyama Y, *et al*. A male case of an undifferentiated carcinoma with osteoclast-like giant cells originating in an indeterminate mucin-producing cystic neoplasm of the pancreas. A case report and review of the literature. World J Surg Oncol 2011;9:100.
8. Muraki T, Reid MD, Basturk O, Jang KT, Bedolla G, Bagci P, *et al*. Undifferentiated carcinoma with osteoclastic giant cells of the pancreas: Clinicopathological analysis of 38 cases highlights a more protracted clinical course than currently appreciated. Am J Pathol 2016;40:1203-16.
9. Gao HQ, Yang YM, Zhuang Y, Liu P. Locally advanced undifferentiated carcinoma with osteoclast-like giant cells of the pancreas. World J Gastroenterol 2015;21:694-8.
10. Moore JC, Hilden K, Bentz JS, Pearson RK, Adler DG. Osteoclastic and pleomorphic giant cell tumors of the pancreas diagnosed via EUSguided FNA: Unique clinical, endoscopic, and pathologic findings in a series of 5 patients. Gastrointest Endosc 2009;69:162-6.
11. Gupta RK, Wakefield SJ. Needle aspiration cytology, immunohistochemistry and electron microscopic study of unusual pancreatic carcinoma with pleomorphic giant cells. Diagn Cytopathol 1992;8:522-7.
12. Koorstra JB, Maitra A, Morsink FH, Drillenburg P, ten Kate FJ, Hruban RH, *et al*. Undifferentiated carcinoma with osteoclastic giant cells (UCOCGC) of the pancreas associated with the familial atypical multiple mole melanoma syndrome (FAMMM). Am J Surg Pathol 2008;32:1905-9.
13. Luchini C, Pea A, Lionheart G, Mafficini A, Nottegar A, Veronese N, *et al*. Pancreatic undifferentiated carcinoma with osteoclast-like giant cells is genetically similar to, but clinically distinct from, conventional ductal adenocarcinoma. J Pathol 2017;243:148-54.
14. Dhall D, Klimstra DS. The cellular composition of osteoclastlike giant tumors of the pancreatobiliary tree. Am J Surg Pathol 2008;32:335-7.
15. Sakai Y, Kupelioglu AA, Yanagisawa A, Yamaguchi K, Hidaka E, Matsuya S, *et al*. Origin of giant cells in osteoclast-like giant cell tumors of the pancreas. Hum Pathol 2000;31:1223-9.

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