

Undifferentiated Carcinoma with Osteoclast-Like Giant Cells of the Pancreas (A Case Report)

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Abstract

Introduction: Our aims are to describe a new case of undifferentiated carcinoma of the pancreas with osteoclast-like giant cells (UCPOGC) and to make a PUBMED research of the different publications about it in order to assess the different prognostic factors that haven't been reported in the literature due to the rarity of this tumour.

Case presentation: We describe the case of a 71-year-old patient, with a past medical history of hypertension that was explored for a prostatic adenocarcinoma. An MRI examination was performed in order to search for secondary localizations and showed an asymptomatic mass in the tail of the pancreas. Clinical examination and laboratory tests were normal. Radiological findings showed an irregular and hypoechoic mass in the tail of the pancreas measuring 8 x 8 cm. the pancreatic duct, the common bile duct and intra-hepatic duct weren't invaded. A corpo-caudal spleno-pancreatectomy was performed with a resection of a part of the transverse colon and an end-to-end anastomosis. Histological examination showed a malignant epithelial proliferation invading the colonic mucosa. Tumoral cells were fusiform, epithelioid or polygonal with atypical nuclei. Osteoclast-like giant cells were also observed. Immunohistochemical study allowed to make the diagnosis of undifferentiated carcinoma with osteoclasts-like giant cells. The patient remained asymptomatic during an 18-month follow up period.

Conclusion: Pancreatic carcinoma has a bad prognosis with a 5-year survival inferior to 1%. This article is of interest because we tried to assess the different prognostic factors based on the different publications including our case report.

Introduction

Undifferentiated carcinoma with osteoclast-like giant cells is a rare tumor affecting different organs such as the eye, the skin, the kidney, the liver, the lung, the breast, the thyroid gland, the parathyroid gland and rarely the pancreas [1]. It was initially reported in the pancreas by Juan Rosai in 1968 [2]. In 2000, the world Health Organization defined this tumor as a new variant of the ductal adenocarcinoma [3]. The epithelial origin of this tumor has been proved [4].

Case Presentation Section

The authors describe the case of a 71-year-old patient, with a past medical history of hypertension that was explored for a prostatic adenocarcinoma. An MRI was performed in order to search for secondary localizations and showed an asymptomatic mass in the tail of the pancreas. Clinical examination and laboratory tests were normal. The patient was referred for an endoscopic ultra-sound examination which detected an irregular and hypoechoic mass in the tail of the pancreas measuring 8 x 8 cm. the pancreatic duct, the common bile duct and intra-hepatic duct weren't invaded. A corpo-caudal spleno-pancreatectomy was performed with a resection of a part of the transverse colon and an end-to-end anastomosis. Macroscopic analysis revealed an 8-centimeter tumor, with ill defined borders (Figure 1a). Foci of necrosis were also observed. Histological examination showed a malignant epithelial proliferation invading the colonic mucosa. Tumoral cells were fusiform, epithelioid or polygonal with atypical nuclei. Osteoclast-like giant cells were also observed (Figures 1b and Figure 1c). Ten lymph nodes were analyzed and were normal. The giant cells expressed the CD68, but were negative with cytokeratin antibody (Figure 1d). Tumoral cells expressed the cytokeratin antigen and were negative with the CD68 antibody. The patient remained asymptomatic during an 18-month follow up period.

Literature Review

A critical literature review of 70 cases of undifferentiated carcinoma

of the pancreas was performed (Table 1). Among the 70 cases, the mean age was 55,2 years varying between 25 and 88 years with a sex ratio (M/F) of 0,89. One patient had a past medical history of breast cancer treated surgically. A familial history of carcinoma was noted in 3 other

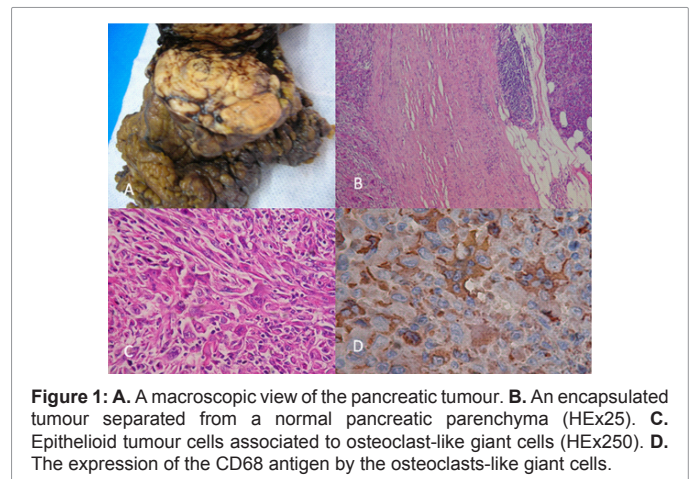


Figure 1: A. A macroscopic view of the pancreatic tumour. B. An encapsulated tumour separated from a normal pancreatic parenchyma (HEx25). C. Epithelioid tumour cells associated to osteoclast-like giant cells (HEX250). D. The expression of the CD68 antigen by the osteoclasts-like giant cells.

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Publication year	Title	Number of cases	Journal	Authors
2010	Undifferentiated carcinoma with osteoclast-like giant cell tumor of the pancreas: a discussion of rare entity in comparison With pleomorphic giant cell tumor of the pancreas	1	Indian J Pathol Microbiol	Mannan R (54)
2010	Giant cell tumor of the pancreas: a pathological diagnosis with poor prognosis.	2	Hepatobiliary Pancreat Dis Int	Singhal A (53)
2009	Undifferentiated carcinoma with osteoclast-like giant cells of the pancreas diagnosed by endoscopic ultrasonography-guided fine-needle aspiration.	1	Chin Med J (Engl)	Gao L (52)
2009	Pathomorphologic study of undifferentiated carcinoma in seven cases: relationship between tumor and pancreatic duct epithelium	7	J Hepatobiliary Pancreat Surg	Naito Y (51)
2009	Undifferentiated pancreatic carcinoma with osteoclast-like giant cells: report of a case with osteochondroid differentiation.	1	Pathol Res Pract	Manduch M (50)
2008	Undifferentiated carcinoma with osteoclast-like giant cells arising in a mucinous cystic neoplasm of the pancreas.	1	Pathol Int.	Hirano H (49)
2007	Endoscopic ultrasound-guided fine-needle aspiration of undifferentiated carcinoma with osteoclast-like giant cells of the pancreas: a report of 2 cases with literature review.	2	Diagn Cytopathol.	Chopra S (48)
2007	[Rapidly progressing cyst of the pancreas as a manifestation of an undifferentiated pancreatic carcinoma with osteoclastic giant cells]	1	Dtsch Med Wochenschr	Breidert M (47)
2007	Huge pseudocyst of the pancreas caused by poorly differentiated invasive ductal adenocarcinoma with osteoclast-like giant cells: report of a case.	1	Hepatogastroenterology	Yamaguchi T (46)
2006	Non-differentiated carcinoma with osteoclast-like giant cells of the pancreas: a case report	1	Cancer Radiother	Charfi S (5)
2006	Follicular dendritic cell sarcoma mimicking giant cell carcinoma of the pancreas.	1	Pathol Int	Shin Che S (17)
2006	An unusual case of undifferentiated carcinoma in situ with osteoclast-like giant cells of the pancreas	1	Pancreas	Koji T (18)
2006	Undifferentiated carcinoma with osteoclast-like giant cells of the pancreas	1	Korean J Gastroenterol	Jang HW (19)
2005	Adenosquamous carcinoma of the pancreas with an acantholytic pattern together with osteoclast-like and pleomorphic giant cells	1	J Clin Pathol	Alwaheeb S (20)
2005	Osteoclast-like giant cell tumor in mucinous cystadenocarcinoma of the pancreas: an immunohistochemical and molecular analysis.	1	Cancer Detect Prev	Sedivy R (21)
2005	A case of osteoclast-like giant cell tumor of the pancreas with ductal adenocarcinoma: Histopathological, immunohistochemical, ultrastructural and molecular biological studies	1	J Korean Med Sci	Young Eun J (22)
2005	Osteoclast-like giant cell tumor of the pancreas associated with mucus-secreting adenocarcinoma. Case report and discussion of the histogenesis	1	Pancreatology	Gisele A (23)
2005	Pancreatic carcinoma with osteoclast-like giant cell tumor and portal vein fistula.	1	Chirurgia	Ionescu M (24)
2005	Osteoclastic giant cell tumour of the pancreas	1	Gastroenterol Clin Biol	Beaufour A (1)
2005	A case of osteoclast-like giant cell tumor of the pancreas	1	Korean J Gastroenterol	Cho SH (25)
2004	A case of osteoclast-type giant cell tumor of the pancreas with high frequency microsatellite instability	1	Pancreas	Osaka H (26)
2004	Combined osteoclastic giant cell and pleomorphic giant cell tumor of the pancreas: A rarity. An immunohistochemical analysis and review of the literature	1	J Pancreas	Anand C (7)
2004	Undifferentiated carcinoma with osteoclast-like giant cells of the pancreas. A case report	1	Ann Chir	Bedioui H (27)
2003	Non-differentiated carcinoma with osteoclast-like giant cells of the pancreas	1	Ann Pathol	Valmary S (13)
2003	Osteoclast-like giant cell tumor of the pancreas associated with a mucinous cystadenocarcinoma	1	Surgery	Sarnaik A (29)
2002	Osteoclast-like giant cell tumor of the pancreas	1	Int J Clin Oncol	Shiozawa M (28)
2001	Benign variant of osteoclast-like giant cell tumor of the pancreas: Importance of the lack of epithelial differentiation	1	Pancreas	Machado M (10)
2001	An osteoclast-like giant cell tumor pattern in a mucinous cystadenocarcinoma of the pancreas with lymph node metastasis in a patient surviving over 10 years.	1	Virchows Arch	Koichi S (30)
2001	Osteoclastic giant cell tumor of the pancreas. Case report and literature review	1	Am J Clin Oncol	Leighton CC (11)
1999	Immunohistochemical and molecular analysis of giant cell carcinoma of the pancreas: A report of three cases	3	Pancreas	Yasuo I (31)
1998	Osteoclast-like giant cell tumor of the pancreas with metastases to gallbladder and lymph nodes. A case report	1	Pathol Res Pract	Sun AP (32)
1998	Undifferentiated carcinoma with osteoclast-like giant cells of the pancreas and periampullary region	10	Cancer	Molberg K (14)
1998	Osteoclast-type giant cell tumor of the pancreas. Am J Roentgenol	1	Am J Roentgenol	Noboru S (33)
1997	Mixed osteoclastic/pleomorphic-type giant cell tumor of the pancreas with ductal adenocarcinoma: Histochemical and immunohistochemical study with review of the literature	1	Pancreas	Mika W (15)

1997	Osteoclast-like giant cell tumour of the pancreas presenting as a pseudocyst-like lesion	1	Virchows Arch	Oehler U (35)
1996	Osteoclastic giant cell tumor of the pancreas	1	Arch Pathol Lab Med	Dizon MA (34)
1996	"Osteoclastic" giant cell carcinoma of the pancreas, report of a case with aspiration cytology	1	Acta cytol	Mullick S (36)
1994	Giant-cell tumours of the pancreas.	1	Chirurgie	Bahnini J (37)
1992	Adenocarcinoma of the pancreas with osteoclast-like giant cells: a case report with immunocytochemistry	1	Pancreas	Newbould.MJ (38)
1991	Osteoclast-like giant cell tumor of the pancreas: immunophenotypic similarity to giant cell tumor of bone	1	Hum Pathol	Goldberg RD (39)
1990	Giant cell tumor of the pancreas of mixed osteoclastic and pleomorphic cell type: Evidence for a histogenetic relationship and mesenchymal differentiation	1	Hum Pathol	Lewandrowski KB (40)
1989	Malignant fibrous histiocytoma (Giant cell type) of the pancreas, a distinctive variant of osteoclast-type giant cell tumor of the pancreas	1	Cancer	Suster S (41)
1987	Osteoclast-type giant cell tumor of the pancreas: Case report.	1	Acta Chir Scand	Baniel J (8)
1987	The osteoclast-type giant cell tumor of the pancreas	1	Arch Pathol Lab Med	Berendt RC (42)
1986	Fine needle aspiration of pleomorphic giant-cell carcinoma of the pancreas, case report with ultrastructural observations	1	Acta Cytol	Marguerite M (43)
1983	Giant cell tumour (osteoclastoma) of the pancreas. An epithelial tumour probably of pancreatic acinar origin	1	J Clin Pathol	Jalloh SS (44)
1983	Osteoclast-type giant cell tumor of the pancreas	1	J Clin Pathol	Iona J (16)
1983	Osteoclast-type-giant cell tumor of the pancreas.	1	Acta cytol	Walts AE (6)
1981	Giant cell tumor (« Osteoclastoma ») of the pancreas: A tumor of epithelial origin.	1	Cancer	Trepeta RW (45)
1969	Unusual pleomorphic carcinoma of the pancreas featuring production of osteoid	1	Cancer	Kay S (4)
1968	Carcinoma of pancreas simulating giant cell tumor of bone. Electron-microscopic evidence of its acinar cell origin	2	Cancer	Rosai J (2)

Table 1: A critical literature review of 70 cases of undifferentiated carcinoma of the pancreas.

patients. 20% presented jaundice, 45% presented abdominal pain, 27% presented a deterioration of the general state and 16% presented digestive trouble. Abdominal ultra-sound examination was performed in 35 patients revealing a pancreatic mass in 30 ones. The echogenicity was reported in 11 cases. The mass was cystic in 2 patients, solid in 4 patients and mixed in 5 patients. The mass size was reported in 18 patients with a mean of 8, 6 cm (average, 2,5- 22 cm). A dilatation of the biliary duct was noted in 6 patients, a hepatic localization in 3 patients. The CT-scan was performed in 25 patients. The echoendoscopy was performed in 2 patients revealing intra-cystic vegetations in one case and a gastric tumor in the second one. The MRI was performed in 1 patient revealing a cephalic tumor with a hyposignal on T2 weighted images. The endoscopic retrograde cholangiopancreatography (ERCP) was performed in 3 patients revealing in the first case a dilatation of the pancreatic canal, a compression of the pancreatic duct in the second one and irregularity in the third one. Laboratory tests were reported in 24 patients showing cholestasis in 7 patients, cytotoxicity in 5 patients proved by an increase in the AST and ALT enzymes, increased level of pancreatic enzymes in 3 patients, hyperleukocytosis in 3 patients and anemia in 6 patients. The CA19-9 level was reported in 8 patients and was increased in 4 patients. The carcinoembryonal antigen level was reported in 3 patients and was normal. The tumor's localization was reported in 49 patients. It was located in the head of the pancreas in 29 patients, in the tail in 16 cases and in the body in 4 cases. Hepatic localizations were noted in 3 patients. Concerning histological findings, macroscopic features were reported in 38 patients. The tumor was solido-cystic in 20 patients and encapsulated in 6 ones. Intra-tumoral haemorrhagic and necrotic foci were reported in 28 patients.

Microscopic Findings

Microscopic findings consisted in osteoclast-like giant cells in all tumours. Tumoral cells were mononucleated in 85% of the cases, plurinucleated in 11% and pleomorphic in 42%. Glandular structures were noted in 31% of the cases. Immunohistochemical findings were

reported in 40 patients. The table 2 shows the positivity to the different antibodies.

Treatment

Therapeutic procedures weren't reported in 5 patients. Eleven patients weren't operated. Among these patients, 2 presented hepatic localizations, one patient died one month after the establishment of the diagnosis and 5 patients were treated by a chemotherapy or radiation therapy because of an important local extension. In the 3 remaining patients, the cause of the abstention wasn't reported. Thirty nine patients had a surgical treatment. The procedures were different depending on the tumor's localization. The follow up was available for 20 patients. One patient presented infectious complications secondary to the surgical treatment. 19 patients died after a mean period of 4,5 months (range, 10 days, to 12 months).

Prognostic Factors

We tried to study different factors in order to assess their impact on the survival using the Log Rank tests. They showed that sex, jaundice, abdominal pain, deterioration of the general status and cephalic or caudal localizations of tumors aren't prognostic factors. In the other hand, corporal tumors and hepatic metastases deal with a worse prognosis. Regarding histological findings, the log rank showed that among the different tumour cells, only the presence of pleomorphic cells is statistically relevant and correlated with a poor prognosis.

Discussion

Undifferentiated carcinoma of the pancreas are rare neoplasms which have been classified into 2 histopathological subtypes: one with pleomorphic multinucleated giant cells and sarcomatoid growth pattern and a poor prognosis and the other with osteoclasts-like giant cells resembling a giant cell tumor of the bone presenting reactive giant cells and a good prognosis. The authors describe a new case of

	Osteoclast-like giant cells	Tumoral cells
CD68	30	4
Vimentin	16	21
lysozyme	9	2
A1 antitrypsin	5	5
CD45	3	0
Cytokeratin	0	18
Desmin	1	0
ACE	1	1
CAM5,2	0	8
EMA	0	12
Melan A	1	0

Table 2: Immunohistochemical findings.

undifferentiated carcinoma with osteoclast-like giant cells which is a rare tumor affecting different organs such as the eye, the skin, the kidney, the liver, the lung, the breast, the thyroid gland, the parathyroid gland and rarely the pancreas. In 2000, the world Health Organization defined this tumor as a new variant of the ductal adenocarcinoma [3]. This tumour is rare accounting for less than 1% of the pancreatic tumours [2]. There are many predisposing factors such as the familial and genetic factors. Environmental factors, such as the tobacco, the alcohol, have also been reported. The diabetes mellitus, the mucoviscidosis and the chronic pancreatitis have also been mentioned.

According to the literature, these tumors are observed in patients with an average age of 60 years varying from 32 to 82 years and they are more frequently observed in women [1]. The symptoms are non specific consisting mainly in hepato-biliary signs, digestive signs or abdominal pain. Our patient was asymptomatic. Physical examination consists generally in an abdominal mass or signs related to the location and extension of the tumor (hepatomegaly, ascitis, lymph nodes) [2]. Radiological examination is based on the endoscopic ultra-sonography and the MRI examination. Tumors of the body and the tail are more easily identifiable because they induce a deformation of the gland [4,5]. The CT-scan shows a well-limited heterogeneous mass enhanced by the contrast product [6]. The endoscopic ultra-sonography has proved its efficiency in detecting tumors of 1 to 2 cm. It also allows detecting local or distant localizations. This technique was helpful in our case. Li and coworkers reported a case diagnosed by EUS and liquid-based cytology test [7]. Laboratory tests show generally cholestasis. Tumoral markers are useful in the diagnosis and the follow up (CEA, CA19-9, LDH). The diagnosis is generally made on surgical specimen. The pancreatic puncture-biopsy has also been reported. It can be useful in case of suspicion of a benign cystic tumor or an invading malignant tumor. Macroscopic findings consist generally in a yellow tumor, lobulated, multi-cystic infiltrating sometimes the surrounding organs [6]. Microscopic examination shows generally two distinct cell types: Fusiform mononucleated cells and pleomorphic multi-nucleated giant cells [6]. The undifferentiated carcinoma with osteoclast-like giant cells can be pure or mixed with foci of ductal adenocarcinoma or a preexisting mucinous cystic tumor. Fusiform and pleomorphic cells express the cytokeratin, the EMA and the vimentin antigens. The osteoclast-like giant cells express the CD68 and rarely the Vimentin. The expression of the CD68 antigen made some authors suppose their possible histiocytic origin. A ductal adenocarcinoma, an anaplastic carcinoma and a secondary localization are the main differential diagnoses. The ductal adenocarcinoma doesn't contain fusiform cells and contains fewer osteoclasts-like giant cells, the anaplastic carcinoma contain multinucleated cells that don't express CD68. Sometimes, especially in case of multiple localizations it can be hard to distinguish

the primary site and the clinical history can allow making the difference. The oncogenesis of the pancreatic tumors remains unclear but the responsibility of the oncogene K-ras and the deficiency of the gene p53 have been proved [8]. Treatment consists in duodenopancreatectomy for tumors of the head and caudal splenopancreatectomy for tumors of the tail. Sometimes, the treatment consists in total pancreatectomy or a simple tumor excision. The radiation therapy and the chemotherapy haven't proved their efficiency.

Conclusion

Undifferentiated carcinoma with osteoclast-like cells has a better prognosis than the anaplastic carcinoma which remains the major differential diagnosis. Anaplastic carcinoma has a bad prognosis with a 5-year survival inferior to 1%. Prognostic factors haven't been studied in the literature because of the rarity of this carcinoma.

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