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Case Report

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Undifferentiated Carcinoma with Osteoclast-Like Giant Cells: Case Report of a Rare Type of Pancreatic Cancer

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ABSTRACT

Undifferentiated pancreatic carcinoma with osteoclast-like giant cells is a very rare type of exocrine pancreatic cancer. Symptoms are often non-specific which leads to misdiagnosis and delay in treatment. Surgery is the first-line treatment and enables better survival rates. In this case report we describe a male adult patient who presented with pancreatitis of unknown cause who was later diagnosed with undifferentiated pancreatic carcinoma with osteoclast-like giant cells. Treatment evolved radical pylorus-preserving pancreaticoduodenectomy and adjuvant chemotherapy.

Introduction

Undifferentiated pancreatic carcinoma is a rare and aggressive type of pancreatic cancer [1,2]. It is more frequently diagnosed in the 6th and 7th decade of life [3].

World Health Organization further distinguishes between undifferentiated pancreatic carcinoma and osteoclast-like giant cells (OGC) undifferentiated pancreatic carcinoma, since they constitute two entities, histologically distinct [1,2].

Clinically, patients with undifferentiated pancreatic carcinoma with OGC can present with jaundice, pruritus, nausea and vomits, fever, weight loss and abdominal pain. Alternatively, patients can be asymptomatic. A cytocholestatic pattern in the blood analysis is usually seen, with elevation of bilirubin, liver enzymes and alkaline phosphatase [1].

Computed tomography (CT) and magnetic resonance imaging (MRI) are exams that often identify the presence of a pancreatic lesion. This type of cancer exhibits particular CT features that can be useful for de diagnosis. The next step is to perform an endoscopic ultrasound, in order to obtain pancreatic tissue and send it to histologic analysis [4].

Surgery is the only curative treatment [1].

Case presentation

A 58 years old man is evaluated in a General Surgery appointment after an hospital admission due to pancreatitis of unknown cause. Medical history included hypertension, dyslipidaemia, ischemic heart failure and Parkinson disease. The patient was not a smoker and didn't consume alcoholic drinks or drugs. A CT of the abdomen and pelvis performed during hospital stay revealed a heterogeneous cystic lesion with 40x32 mm in the head of the pancreas. Magnetic resonance cholangiopancreatography didn't show biliary lithiasis. Analytically, the only alteration identified was an elevated value of Ca19.9 (176 U/mL). An endoscopic ultrasound was performed, revealing an irregular lesion without invasion of adjacent structures and biopsies were obtained. Biopsy was compatible with adenocarcinoma. CT of the chest, abdomen and pelvis showed no distant metastasis. The patient was submitted to radical pylorus-preserving pancreaticoduodenectomy. Post-operative period was complicated with pancreatic type B fistula and abdominal abscess. Histology revealed undifferentiated pancreatic carcinoma with osteoclast-like giant cells of the head of the pancreas with a small area of ductal glandular differentiation

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(pT2N0Mx). Adjuvant chemotherapy with gemcitabine and capecitabine was accomplished. One year after surgery, during follow-up which included medical appointments and abdominal CT regularly, an abdomen CT showed multiple hepatic lesions, compatible with metastases. Palliative chemotherapy was initiated, but the patient died 5 months later.

Discussion

Undifferentiated pancreatic carcinoma is a rare type of pancreatic cancer. It is classified as a subtype of ductal adenocarcinoma because there are common features, such as mutation in KRAS, TP53, CDKN2A and SMAD4 [1,2].

World Health Organization further distinguishes between undifferentiated pancreatic carcinoma and OGC undifferentiated pancreatic carcinoma.

OGC undifferentiated pancreatic carcinoma is more frequent after the 5th decade of life and does not exhibit gender predominance [5]. In fact, the patient was 58 years old, which corroborates these data.

OGC undifferentiated pancreatic carcinomas are usually larger than other pancreatic tumours at the time of the diagnosis (varying from 5 to 10 cm in diameter), and the most frequent location is the body and tail of the pancreas [3]. Despite that, our patient's lesion was in the head of the pancreas and smaller than most of these tumours. OGC undifferentiated pancreatic carcinomas can be presented in the pure form or co-exist with other cancer types such as ductal adenocarcinomas, mucinous cystic tumours, intraductal papillary mucinous neoplasm, adenosquamous carcinoma and cystadenocarcinoma [2-7]. Coexistence of different cancer types usually dictates worse prognosis. Common sites of metastasis include the liver, lung and bone [5].

The pathophysiology of this cancer type is still poorly understood but OGCs are cells recently found to have epithelial origin (derived from macrophages) and several functions related to immune response and antigen presentation [2,3]. Other organs that can develop cancers with OGCs are the skin, breast and lung [6,7].

Symptoms are often absent or are non-specific which can lead to misdiagnosis and delays in diagnosis and treatment [3]. In fact, the patient first presented with pancreatitis of unknown cause. Hence, high suspicion is mandatory, mainly in elder patients who present with pancreatitis of unclear cause. In such cases an abdominal CT is indicated and should be performed in order to exclude pancreatic cancer.

Unlike most pancreatic malignancies, OGC undifferentiated pancreatic carcinomas usually have well defined borders and are mainly cystic [5]. Also, they tend to appear as a heterogeneous mass with both hyper and hypoechoic areas (while adenocarcinoma is typically hypoechoic) [3]. In fact, our patient CT was positive for a heterogeneous cystic lesion and tumour borders were regular.

The role of tumour markers is controversial since in some studies they appear normal but in others they are elevated [1]. In the present case, Ca19.9 was elevated.

Surgery is the only curative treatment. The goal is resection of the tumour with negative margins. However, resection may not be possible at the time of diagnosis (although this is more frequently seen in undifferentiated pancreatic carcinoma). In such cases it is appropriate to start neoadjuvant chemotherapy and reassess the possibility to perform surgery. Surgical options depend on tumour location and local invasion; if the tumour is located in the head of the pancreas without lymph nodes invasion, a cephalic duodenopancreatectomy with pylorus preservation is indicated but if there is nodal involvement an extended cephalic duodenopancreatectomy is necessary. For tumours in the tail of the pancreas, a distal pancreatectomy with or without splenectomy can be performed [1].

To patients who are not candidates for surgery, chemotherapy can be offered and is associated with increased survival. Actual schemes use gemcitabine associated with capecitabine or monotherapy with gemcitabine [1].

Prognosis of these tumours is usually poor. However, pure forms of OGC undifferentiated pancreatic carcinomas seem to have better prognosis than undifferentiated pancreatic carcinoma. This may be explained by the fact that surgical resection often is not possible in undifferentiated pancreatic carcinomas at the moment of diagnosis and are associated to high recurrence rates after surgery [1,3].

According to some studies, KRAS oncogene mutation, p53 mutation, PDL-1 expression and loss of E-cadherin are indicators of poor prognosis [1, 4,7]. Also, male sex, advanced age and positive lymph node metastasis are associated with lower survival rates [3,4]. Better survival rates seem to be observed in patients submitted to surgery [4].

Recent studies revealed that CD74 expression is higher in OGCs undifferentiated pancreatic carcinomas compared with ductal adenocarcinomas. Further research is needed to evaluate if CD74 can become a therapeutic target for OCG undifferentiated pancreatic carcinoma [2].

Conclusions

The case herein reported highlights the importance of high suspicion index when managing acute-onset pancreatitis without obvious cause in elderly patients and the need to exclude pancreatic cancer in such cases.

OGC undifferentiated pancreatic carcinomas is an uncommon and complex type of pancreatic cancer and treatment guidelines are lacking, mainly due to its rarity. Even so, surgery is the first line treatment and overall survival is greater in patients submitted to surgical resection.

Further research is needed to better characterize OGC undifferentiated pancreatic carcinomas, established standardized therapeutic options and identify possible therapeutic targets.

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