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Case Report

Osteoclast-like giant cell undifferentiated carcinoma of the pancreas: a case report

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Abstract: The objective was to investigate the diagnosis and related clinical criteria of undifferentiated carcinoma of the pancreas with osteoid giant cells, and to analyze its treatment and prognosis. we report a case of this disease in a A 62 year old male, who had upper left abdominal pain for more than 10 days, had pain that was aggravated 1 day prior to visit. The pancreas showed a mass with volume 10 cm × 8 cm × 6 cm. On cut section, the mass was fish-fleshy like and necrotic with hemorrhage, and had a close relationship to the residual pancreatic tail. Microscopically, tumor was clearly found around osteoclastic giant cells, and tumor cells invaded the colon and spleen. This is a rare pancreatic tumor with no specific clinical manifestation or serologic marker, composed of undifferentiated osteoid giant cells. Rarely, patients may havelymph node metastasis. The diagnosis should rely on imaging data such as CT and MRI combined with immunohistochemistry. The treatment can be surgical resection, but the prognosis is poor.

Keywords: Pancreas, giant cell undifferentiated carcinoma, osteoclast

Introduction

Undifferentiated carcinomas with osteoclast-like giant cells (UC-OGC) are rare tumors first reported in 1968. The age of the affected population is mainly between 60 and 70 years old. UC-OGC is characterized by osteoclast-like giant cells as the main pathologic feature. Pancreatic UC-OGC can occur in almost any part of the pancreas. Tumors often occur in the tail of the pancreas, mostly with giant cell tumor-like metastasis and invasion of adjacent tissues, with few lymph nodes and distant metastases [1]. At present, pancreatic ductal epithelial cells are considered to be the primary tissues of origin of pancreatic ductal UC-OGC. Based on the pathologic phenomenon of pancreatic ductal adenocarcinoma and OGC, the World Health Organization also classified it as a tumor subtype of pancreatic ductal adenocarcinoma [2]. Surgical resection is the main treatment for UC-OGC.

Medical record information

The patient was a 62 year old male who was admitted to the hospital on October 13, 2017 because of pain in the left upper quadrant for more than 10 days. Our study was done with patient consent. This patient had a medical history of gout. At the time of admission, the patient was clear-minded, with a slightly poorer spirit, poor appetite, poor sleep, and normal bowel movements. The patient claimed to have lost 3 kilograms in weight over the past month. The patient had no obvious cause of left upper abdominal pain more than 10 days ago. It was persistent and unbearable. The above symptoms were aggravated without obvious incentives one day ago. Pain was accompanied by radiation pain in the lower back and the patient was sent to a local hospital. Abdominal B-ultrasound showed that the pancreatic tail was low and the echogenic mass was uneven. Considering the source in the peritoneum, it was recommended to conduct further examination and transfer to our hospital for treatment. Total abdominal augmentation of CTA showed a left upper abdominal malignant tumor with bleeding, possibly involving pancreatic tail, thickening of the splenic flexure of colon and intestinal wall, a small amount of pelvic fluid, and abdominal blood hardening. There was no abnormality in routine blood tests and

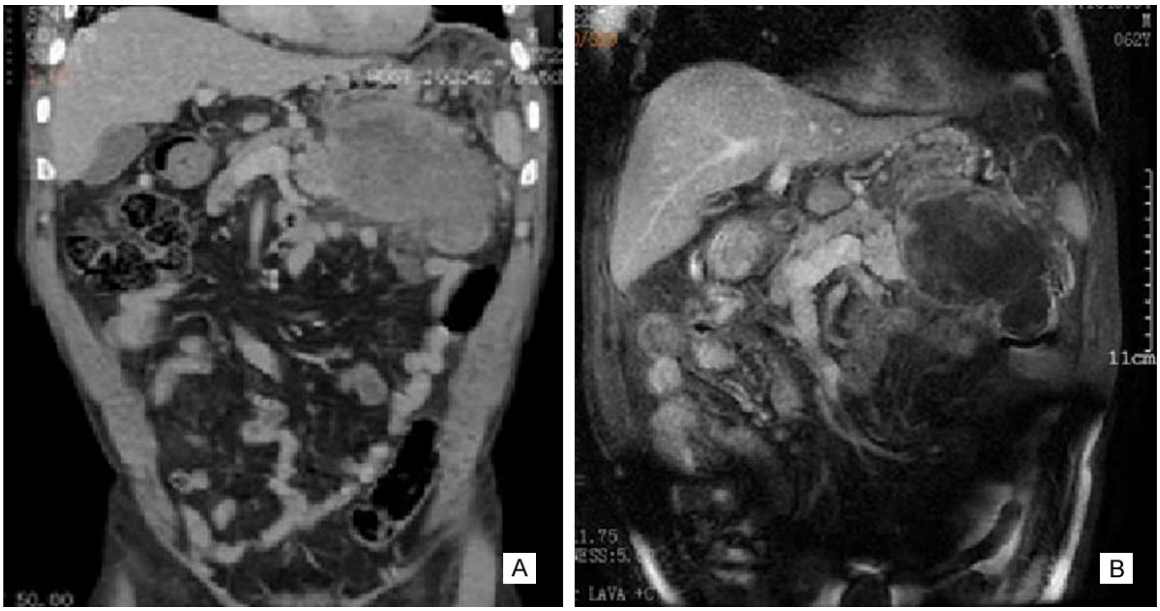

Figure 1. A. Abdominal plain and CTA (256) imaging data. B. Enhanced MRI of the upper abdomen.

hypersensitive CRP. The patient was scheduled to diagnose abdominal masses and gout and was admitted to hospital.

Abdominal plain and CTA (256) imaging data

On October 14th, 2017, the results showed that there was a round-like mass with a size of 9.5*8.5 cm in the left upper abdomen. The boundary was clear, and the unevenness was enhanced after the enhancement. The surrounding fat gap was blurred, and the effusion was visible. The lesion and the tail of the pancreas were unclear, and the adjacent stomach was compressed. The local part of the splenic vein was unclear, and the wall of the colon was thickened. After enhancement, a suspected round mass was seen. The other gastrointestinal tract showed no obvious thickening, stenosis or abnormal enhancement. There was no obvious enlarged lymph node in the abdominal cavity, and a small amount of effusion in the pelvic cavity. Calcification was observed in the abdominal wall, and no obvious abnormal stenosis or filling defects were observed. No abnormal blood supply artery or pathological vascular mass were found (**Figure 1A**). We considered a left upper abdominal malignant tumor with hemorrhage originating from the tail of the pancreas. The splenic flexure of colon was thickened and invaded by the tumor. Abdominal blood vessels showed angiosclerosis.

Enhanced MRI of the upper abdomen

On October 13th, 2017, the results showed that there was a long T1 long T2 signal in the left upper abdomen, the size was about 8.7*9.7 cm. The internal signal was uneven, and DW was high. After enhancement, the arterial phase showed obvious uneven enhancement, the peripheral fat gap was blurred, a small amount of effusion was seen in the abdominal cavity, and it was closely related to the tail of the pancreas. The adjacent stomach was compressed and the splenic flexure of colon was thickened. There was no special manifestation in the bilateral kidneys, and multiple enlarged lymph nodes were seen in the posterior peritoneum. Diagnosis was considered to be a malignancy that invaded the pancreas and thickened the wall of the splenic flexure of the colon (**Figure 1B**). Under general anesthesia, the tumor in pancreas and pancreatic tail, spleen, and partial colectomy were excised. There was more intraoperative blood loss, and blood transfusion and plasma symptomatic treatment were used.

*CT imaging data of the chest results of February 5th, 2018 (see **Figure 2**)*

CT showed that there were multiple nodular density enhancements in both lungs. Diagnosis included multiple space-occupying lesions to

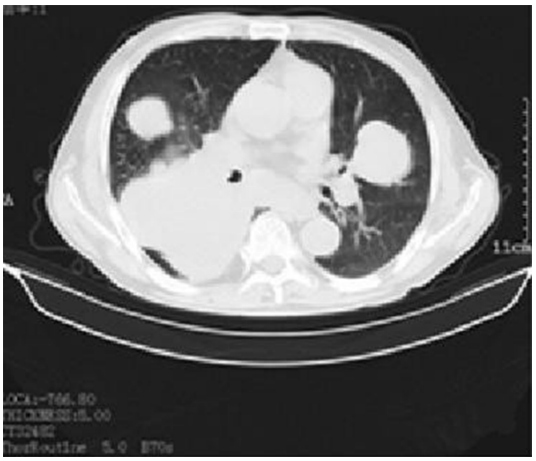

Figure 2. Chest scan on March 25, 2018.

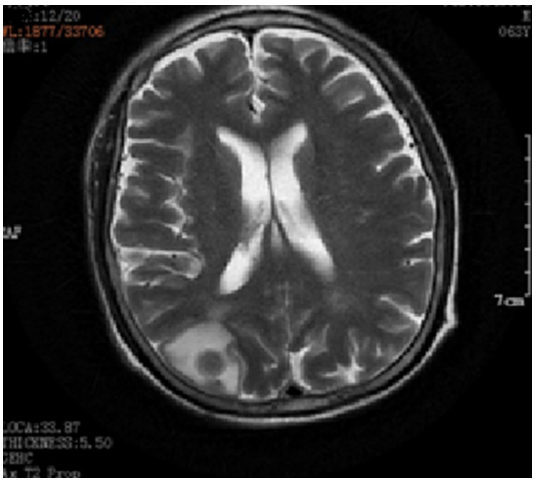

Figure 3. Skull MRI showing occipital lobe occupied.

the lungs. The diameter of the largest lesion was about 3.8*3.8 cm (results of January 13th, 2018) to 7.4*5.3 cm (February 5th, 2018), and it became 8.4*9.9 cm (results of March 25, 2018). Lung lesions progressed quickly. Multiple enlarged lymph nodes were seen in the hilum and mediastinum. More tumor sites can be seen in both lungs, suggesting metastasis. Nodules were found in the body of the stomach, and the tumor may have involved the stomach.

*Skull MR imaging data (see **Figure 3**)*

Nodular and patchy abnormalities were found in the right temporal lobe, occipital lobe, parietal lobe, and left frontal and parietal lobe, and edema signals were found around these sites. Long T2 abnormal signals were seen in the maxillary sinus, ethmoid sinus, and frontal sinus on both sides. Imaging diagnostic imaging diagnoses bilateral maxillary sinus, ethmoid sinus and frontal sinusitis suggesting multiple intracranial metastases.

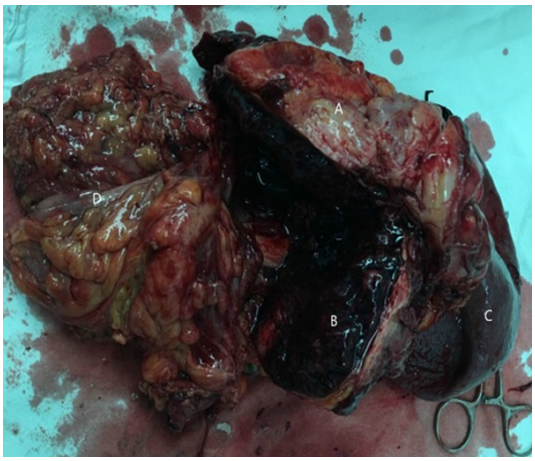

Figure 4. Tissue sample removed during surgery.

Pathologic analysis

At the root of the mesenteric membrane, the middle colonic artery was found to be invaded. About 10 cm away from the mass, the transverse colon was cut off. The mass was closely connected with the stomach wall. The volume of the mass was 10 cm × 8 cm × 6 cm. The mass was fish flesh-like with necrotic hemorrhage, and was closely related to the tail of the pancreas. Microscopic examination showed that most of the tumor was located in the tail of the pancreas (see **Figure 4**). The well-differentiated high-columnar cancer cells and the differentiated cancer cells were diffusely infiltrative. The poorly differentiated cancer cells were various in shape, including oval, fusiform and polygonal. The nucleus is clear and distinct, and it was mostly irregular mononuclear or multinuclear. Eosinophilic and osteoclast-like giant cells were mostly present in poorly differentiated polymorphic cancer cells. The number of nuclei was large, ranging from a few to a dozen, about the same size. The atypia was mild, and there were eosinophils. There was a hemorrhagic necrosis in the tumor, and osteoclast-like giant cells were clearly found around the tumor. The tumor cells invaded the splenic flexure of colon.

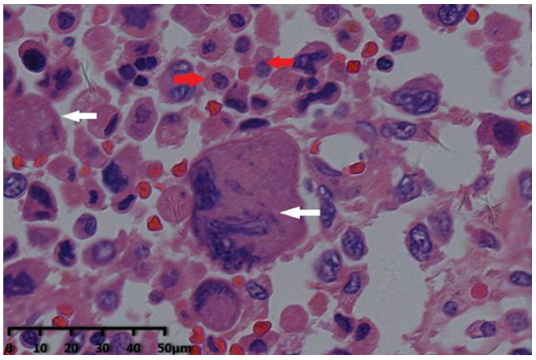

Figure 5. Pathologic results show undifferentiated carcinoma with osteoclasts. The white arrow indicates osteoclast-like giant cells and the red arrow indicates tumor cells. The image is magnified 400 times.

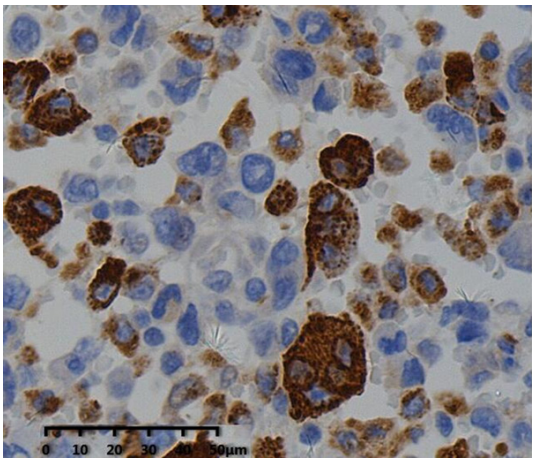

Figure 6. CD68 (+) (EnVision method was used for immunohistochemistry, and the image is magnified 400 times).

Immunohistochemistry

Immunohistochemical results showed that cytokeratin, EMA and vimentin were positive (+) in poorly differentiated multi-shaped cancer cells; CD68 and vimentin were positive (+) in osteoclast-like giant cells (see **Figures 5**, **6**). The pathologic diagnosis was an undifferentiated carcinoma of the pancreas with osteoclast-like giant cells.

The patient developed a wound infection after surgery and recovered well after dressing. The patient had a large mass, and the pathologic results showed that there was lymph node metastasis, and many organs such as the lungs and brain had metastases in the next 3 months after surgery. Metastatic tumors increased rapidly (the patient refused a biopsy). With gemcitabine 1.4 g IVGTT chemotherapy, the effect was poor and the disease continued to progress.

Discussion

At present, it has been reported that pancreatic UC-OGC has not been diagnosed before an operation. Because it is very similar to bone giant cell tumor in tumor cell morphology, clinical diagnosis input is needed as well as postoperative pathology. The disease mainly occurs in the pancreas and mammary glands of the elderly, as a rare subtype of ductal adenocarcinoma [3]. At present, research has mainly used retrospective methods to analyze the clinical and pathologic manifestations and progress of individual patients. It is worth noting that imaging studies on pancreatic UC-OGC are rare. According to Li's research, pancreatic UC-OGC can occur in almost any part of the pancreas, and its tumor volume is relatively large. The image usually shows a solid cyst with a clear boundary. There is often hemorrhage and necrosis in the cyst, and there is little calcification. MRI examination has obvious specificity for identifying the disease, but it still needs to be confirmed by pathology with immunohistochemistry. The current study has more imaging data, so it can be further explored based on this analysis.

Clinical manifestations

There is no characteristic clinical manifestation of UC-OGC in the pancreas. Because there are few case studies, there are no reports showing statistical significance with gender, but the average age is 60 years. General symptoms were abdominal pain, bloating, fatigue and significant weight loss. It may be palpated with abdominal examination. The imaging examination showed that the boundary was clear and the pancreas was occupied. Jaundice caused by pancreatic UC-OGC was also reported [4]. According to the above symptoms, patients are easily misdiagnosed with intestinal and pancreatic inflammatory diseases. This patient was admitted to the hospital due to abdominal pain. The abdominal CT scan showed a small amount of effusion in the abdominal cavity, which was closely related to the tail of the pancreas. Examination showed that the adjacent

stomach was compressed and the splenic flexure of colon was thickened, consistent with pancreatic UC-OGC.

Pathologic features

Special features of pancreatic UC-OGC include greater invasiveness, involvement of surrounding organs, and poor prognosis. According to relevant research results, about two-thirds of patients die within one year after tumor resection. The mass is large, with frequent hemorrhage and necrosis, and K-ras and P16 gene mutations or deletions are also characteristic of pancreatic UC-OGC [5]. The pancreatic UC-OGC tumor mass contains monocytes, pleomorphic cells, and osteoclast-like giant cells. According to the malignant or benign cytology of pleomorphic giant cells, it is classified into pleomorphic carcinoma and osteoclast-like tumor. According to related research, S-100 protein, actin, and cytokeratin are negative in osteoclast-like giant cells. CD68, acid phosphatase, non-specific esterase, and lysozyme are characteristic enzymes in osteoclast-like giant cell expression. Immunophenotype and ultrastructure show that osteoclast-like giant cells are very similar to histiocytic mononuclear cells and osteoclasts. Hemorrhage and necrosis at the tumor site are usually closely related to the formation of giant cells from osteoclasts [6]. In this study, patients were diagnosed with undifferentiated carcinoma of the pancreas with osteoclasts based on H&E morphology and immunohistochemistry, combined with small ductal adenocarcinoma components. Osteoclast-like giant cells existed at the tumor necrosis site, accompanied by hemorrhage and tumor necrosis. The splenic parenchyma was not involved, and the incisional margin and pancreatic margin were negative. We see group 8 lymph nodes 2/4, considered metastatic cancer. but no macrophage phagocytosis and hemoglobin were observed, which may be due to tumors producing related chemokines and growth factors [7]. The immunophenotype of cell-like monocytes and osteoclast-like giant cells in this patient's tumor tissue is consistent, and the occurrence of osteoclast-like giant cells may be due to the interstitial reaction of tissue-like mononuclear cells aggregated at the tumor. The monocyte fusion reaction produces osteoclast-like giant cells, which are involved in tumor cell response changes.

Imaging performance

At present, there are few studies on the imaging findings of UC-OGC in the pancreas. According to comprehensive research, a CT of pancreatic UC-OGC shows obvious hemorrhagic necrosis of tumor mass, and the tumor shows uneven cystic solidity with a clear boundary and no separation [8]. An MRI of pancreatic UC-OGC can reflect the pathologic changes of the tumor. In this case, the long T2 abnormal signal is seen in the maxillary sinus, ethmoid sinus and frontal sinus, which is consistent with the results of Togawa. Yang [9] reported that tumor T2W1 had a patchy high signal. Wei reported that pancreatic UC-OGC tumor T2W1 showed a high signal-based mixed signal. Pancreatic UC-OGC is very similar to giant cell tumor of bone. Giant cell tumor of bone mainly occurs in the blood-rich areas, so pancreatic UC-OGC may also occur in similar areas, so this tumor often has bleeding and necrosis [1]. MRI often exhibits characteristic changes such as high T1W1 patchy signal and low signal of T1W1 and T2W1 caused by deposition of lutein. CT, PET-CT, and MRI can reflect progression of the tumor and whether the tumor has hemorrhage and necrosis to some extent [10], but it cannot confirm a pancreatic UC-OGC. This patient complained that he did not feel abdominal discomfort six months ago, indicating that his tumor volume developed rapidly. Because pancreatic UC-OGC has the same cystic structure as pancreatic cystadenocarcinoma and pancreatic pseudocyst, it is difficult to identify. Imaging as an auxiliary examination requires combination with clinical diagnosis.

Treatment

The main treatment for pancreatic UC-OGC is surgical, and this tumor usually needs to be diagnosed after surgery. There are relatively few studies on whether or not to use chemotherapy. In some studies, there have been trials of trial chemotherapy drugs such as gemcitabine, but no conclusive evidence has been found [11]. This patient had no significant effect with gemcitabine 1.4 g IVGTT chemotherapy and the disease is still progressing.

Prognosis

Pancreatic UC-OGC develops rapidly and has a high degree of malignancy, but it is uncommon.

This is because the diagnosis is usually made late, and it can veryeasily relapse after resection, and there have been several cases of metastasis and reoperation after two years of surgical resection [12]. Togawa's findings show that patients with pancreatic UC-OGC have a higher postoperative survival rate than patients who have failed surgery for various reasons. The average survival time of patients after surgery was 19.6 months, and that of unoperated patients was 6.5 months. Therefore, from a prolonged survival period, surgical removal of tumors should be actively performed. There are individual differences in the survival times of patients with pancreatic UC-OGC, and the time from diagnosis to death varies from 4 months to 10 years. Kobayashi found that women with young age, small tumor size, and non-invasive tumors had a good prognosis after pancreatic UC-OGC surgery. This patient in this study had tumor invading lymph nodes, and there was no obvious effect of using gemcitabine. Unfortunately the patient died in April 2018.

Conclusion

Pancreatic UC-OGC has no specific clinical manifestations and serological indicators. It is a rare tumor. Diagnosis depends on imaging data such as CT and MRI combined with immunohistochemistry. The treatment is mainly surgical resection, but the degree of malignancy is high, and the prognosis is poor. Further research on the pathogenesis and biologic characteristics of the disease should be carried out to find a better treatment plan and prolong survival. In this study, there was only one patient in the study, and it may not be representative of pancreatic UC-OGC. Further studies are needed with more samples. With the development of molecular targeted therapy and immunotherapy, better treatment may emerge.

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Disclosure of conflict of interest

None.

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