Journal of Medical Case Reports and Case Series ISSN: 2692-9880

Case Report Volume 2 Issue 19

Invasive intraductal papillary mucinous neoplasm of the pancreas with multiple metastases: A case report and review

Qingqing Zhu[1], Jin jie[2], Wei Liu[1], Dadao Jing[2*]

[1]Department of Gastroenterology, Hefei BOE Hospital, Hefei, China

[2]Department of Geriatric Gastroenterology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

[*]**Corresponding Author:** Dadao Jing, Department of Geriatric Gastroenterology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Received date: 07 December 2021; **Accepted date:** 16 December 2021; **Published date:** 28 December 2021

Citation: Zhu Q, Jie J, Liu W, Jing D (2021) Invasive intraductal papillary mucinous neoplasm of the pancreas with multiple metastases: A case report and review. J Med Case Rep Case Series 2(19): https://doi.org/10.38207/JMCRCS/2021/0219254

Abstract

Intraductal papillary mucinous neoplasm of pancreas (IPMN) characterized by cystic dilation of the pancreatic duct and papillary projection of the ductal epithelium with rich mucin secretion accounting for around 1 % of all exocrine pancreatic neoplasms, is a relatively rare group of pancreatic cystic neoplasm. IPMN has an orderly progression of dysplastic changes and can be classified as low-grade, medium-grade, or high-grade dysplasia and invasive carcinoma. In this text, we herein report a case of invasive IPMN with lung and multiple lymph node metastases and summary relative literature in order to improve the understanding level of invasive IPMN for clinicians by discussing the diagnosis, treatment, and surveillance.

Keywords: Intraductal papillary mucinous neoplasm of pancreas (IPMN); invasive carcinoma; multiple metastases; case report

Case Report

A 54-year-old male was hospitalized having cough and tachypnea for twenty days, with expectoration of some white sticky and blood-stained sputum, absence of chest pain, or fever. Laboratory data showed: white count 5.04×109/L, hemoglobin 135g/L. Also, the patient had a CT scan of the chest **(Figure 1)** which revealed bronchial obstruction of the right middle lobe of the lung and multiple nodules at the right middle as well as bilateral lower lung; multiple lymph nodes enlargements were present at the bilateral lung hila and over the mediastinum. Chest examination revealed bilateral supraclavicular lymph node enlargement with a normal body temperature and cardiac rhythm. The breath sound over the right lung was weaker than that of the left lung. Coupled with the symptoms and signs and auxiliary examination of the patient, we considered possibly secondary pulmonary malignancy. About history, the patient, 20 years ago, was found to have a pancreatic cystic lesion during a conventional health examination and was diagnosed as "intraductal papillary mucinous neoplasm of the pancreas". He was followed up yearly with no recognizable symptom till 2010, a contrast-enhanced computed tomography scan of the pancreas revealed a cystic lesion, 10cm x 7cm in size, over the pancreatic head. Surgical treatment was suggested but refused by the patient. He had no history of pancreatitis or diabetes, nor a family history of cancer. The patient was then admitted on November 14, 2016.

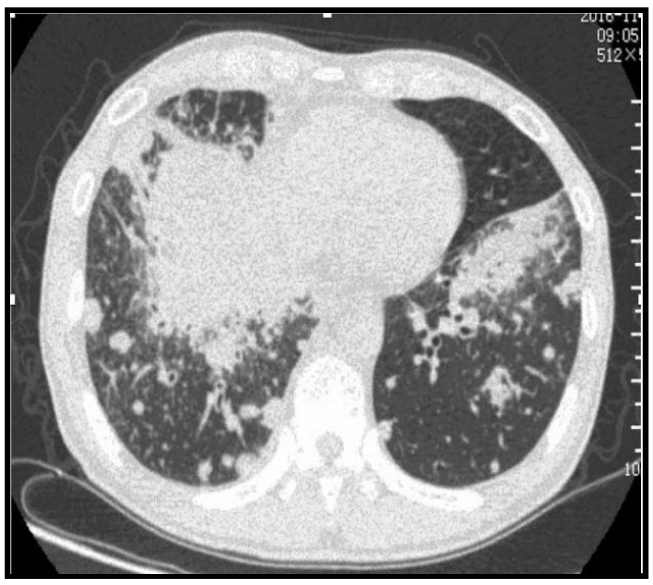

Figure 1: CT scan of the chest revealed bronchial obstruction of the right middle lobe and multiple lung nodules over the bilateral lung bases.

Physical examination revealed a palpable mass, 10cm×8cm in size with tenderness was found in the right lower quadrant, which was somewhat fixed. Rectal examination was non-revealing. Laboratory data showed: serum glucose 4.8mmol/L, total bilirubin 13umol/L (reference range, 3.4-17.1umol/L), γ-glutamine acylase 11.8U/L (reference range, 7-59U/L), alkaline phosphatase 77U/L (reference range, 35-129U/L), amylase 64U/L, carcinoembryonic antigen 9.68ng/ml (reference range, 0-5ng/ml), carbohydrate antigen (CA) 19-9 >1000U/ml (reference range, 0-39U/ml), neuron-specific enolase 22.94ng/ml (reference range, 0-16.3ng/ml), cytokeratin-19-fragment 84.14ng/ml (reference range, 0-3.3ng/ml). The electrolytes, liver, and renal function were only natural. Then contrast-enhanced pancreatic CT scans **(Figure 2A-2B)** were performed. 10.8cm x 7.8cm cystic lesions with multiple cystic wall nodules over the pancreatic head were found together with strong enhancement of the cystic wall nodules and the septation. The main pancreatic duct was expanded and there were multiple lymph nodes enlargements over the peritoneum, retroperitoneum, and lesser omentum. To investigate further the distribution of the tumors, the patient had a positron emission tomography / computed tomography (PET-CT, **Figure 3A-3B**), which showed an irregular multiple cystic mass, 10.9 cm× 7.7cm× 17.9cm in size with multiple papillary processes at the head of the pancreas and the SUV value was 10.1. The density and radioactivity of the rest of the pancreatic tissue were normal. The mesenteric, retroperitoneal, hila of lungs, mediastinum, right diaphragm, and bilateral supraclavicular lymph nodes were all enlarged. Glucose metabolism activity of the diffuse lung nodules, multiple lung ground-glass opacities, and the enlarged lymph nodes was increased in varying degrees. To further define the nature of the tumors, bronchial brushing was performed. Heterotrophic cells with deep nuclear staining were discovered. The patient also had bilateral supraclavicular lymph node biopsy and cytology **(Figure 4)**, which revealed clustering cells scattered in a blue-purple mucin-like background, with deep nuclear staining of the heterotrophic cells, these might originate from metastasis of the mucinous adenocarcinoma. The presence of pancreatic cystic neoplasms, lung nodules, and multiple enlarged lymph nodes can be identified as invasive IPMN with multiple metastases, which can be further verified if the patient consented to dispose of endoscopic ultrasonography (EUS).

The patient was finally diagnosed as having invasive intraductal papillary mucinous carcinoma of the pancreas with multiple metastases, of which surgery was not recommended. The patient had the first chemotherapy on December-24, 2016, which consisted of gemcitabine (D1, D8) 1.6g and cisplatin 120 mg. Unfortunately, the patient refused further chemotherapy and died at home in January 2017.

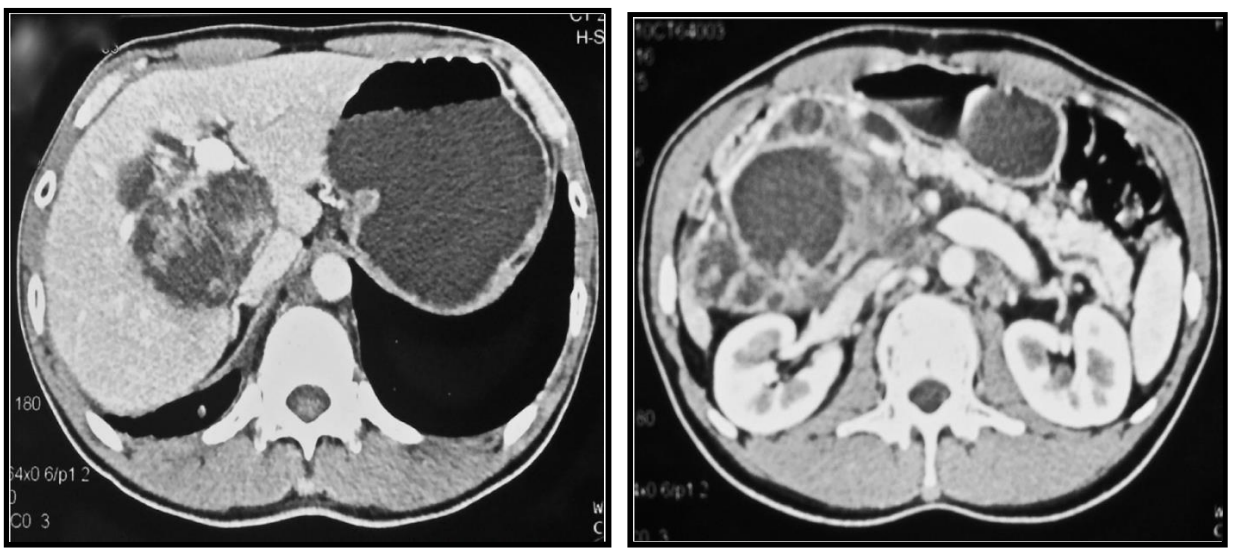

Figure 2A-2B: Contrast-enhanced CT of a pancreatic cystic lesion with multiple cystic wall nodules over the pancreatic head and sharp enhancement of the cystic wall nodules and septation. The main pancreatic duct was extended. The abdominal, retroperitoneal, lesser omentum with multiple enlarged lymph nodes.

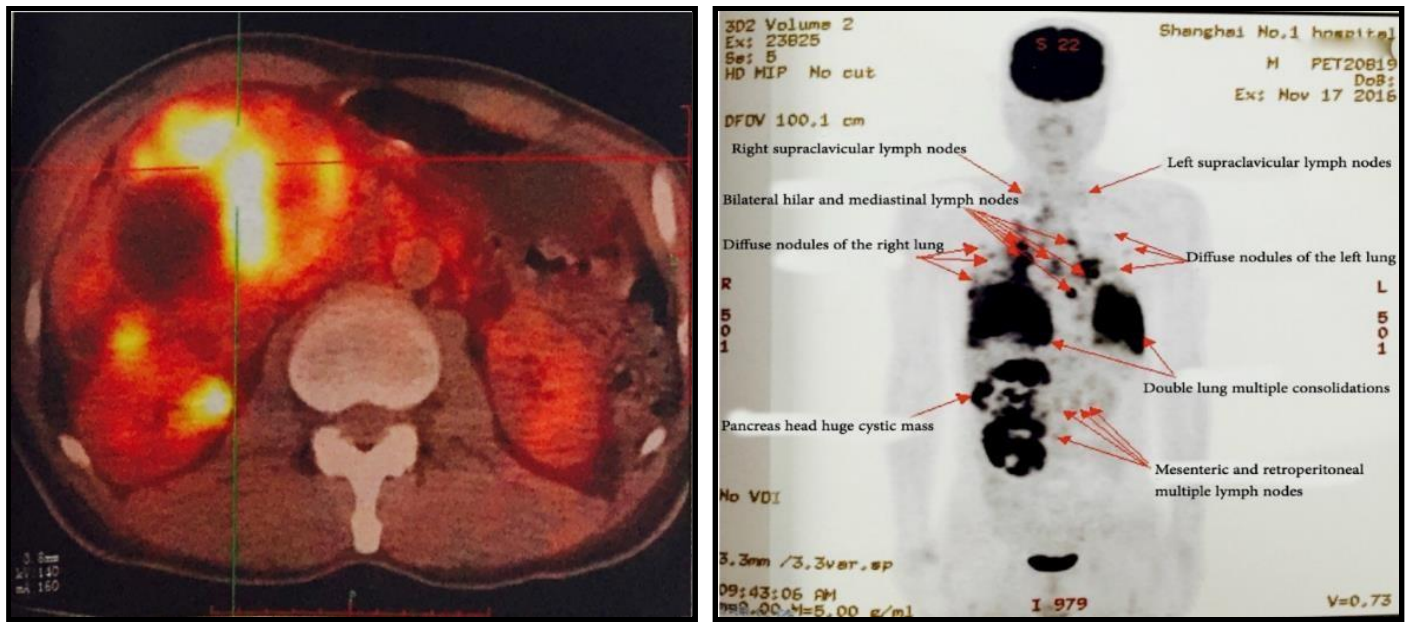

Figure 3A-3B: PET-CT revealed a 10.9cm×7.7cm 17.9cm irregular multiple cystic masses with multiple papillary processes over the pancreatic head. The mesenteric, retroperitoneal, lung hila, mediastinum, right diaphragm, and bilateral supraclavicular lymph nodes were enlarged. Glucose metabolism activity of diffuse lung nodules, multiple lung opacity, and enlarged lymph nodes was extended in varying degrees.

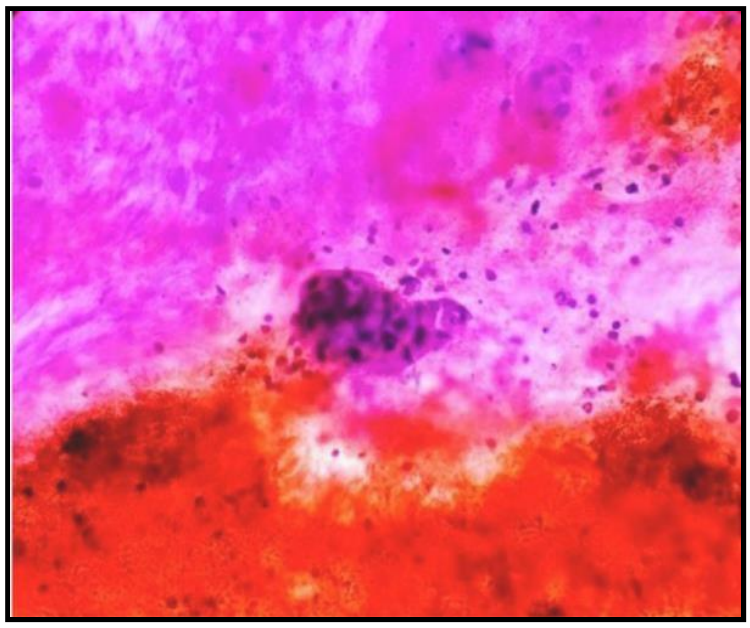

Figure 4: Bilateral supraclavicular lymph node biopsy and cytology showed (Olympus BX53, X400): clustered cells with deep nuclear staining of the heterotrophic cells.

Discussion

IPMN is morphologically classified into 3 subtypes based on the location of pancreatic duct involvement: main duct (MD), branched duct (BD), and mixed-duct IPMN. According to the statistics, the prevalence of invasive carcinoma during the diagnosis has been reported to be higher in the main duct IPMN (23–57 %) and lower in the branched duct IPMN (0– 31 %) **[1]**. In our case, the patient was MD IPMN according to the image of pancreatic contrast-enhanced CT and diagnosed with invasive IPMNs due to the presence of multiple metastases and the cytologic characteristics of the supraclavicular lymph node. We were unable to sample the cystic fluid for analysis due to refusal by the patient.

Most patients with IPMN are diagnosed incidentally with radiographic and endoscopic imaging for another purpose. When appears symptoms, it is usually invasive carcinoma and presents with no typical symptoms, including back pain, abdominal pain, and obstructive jaundice **[2]**.

Magnetic resonance imaging(MRI) or magnetic resonance cholangiopancreatography(MRCP) is the preferred method in diagnostics of IPMN, pancreatic protocol computed tomography(CT) and endoscopic ultrasound(EUS) are excellent adjuncts to another imaging choice **[3,4]**. Routine examination as elevated serum CA19-9 levels > 37U/ml are associated with an increased likelihood of invasive IPMN, worse overall, and disease-free survival **[5]**. High MUC5AC expression in an extracellular vesicle can predict the presence of invasive carcinoma **[6]**.

MD-IPMN and MT-IPMN carry a high rate of malignancy or malignant transformation, so both patients who are fit for surgery should undergo resection universally. As for BD-IPMN, the predictive risk factors of malignant IPMN lesion include a solid component or an enhancing mural nodule(> 5mm), positive cytology for high-grade dysplasia or cancer, or MPD dilatation >10mm, and should be evaluated in all patients fit for surgery **[3]**.

The features associated with invasive cancer include appearing symptoms, larger solid lesions (> 30mm), mural nodule(> 10mm), MPD dilatation(>10mm), and elevated serum cancer antigen 19-9

levels **[3,7]**. When an invasive carcinoma is suspected, pancreatectomy with lymph node dissection is necessary. It is always unclear to assess preoperatively the grading of invasiveness. Whenever any doubt exists, a typical resection (pancreatoduodenectomy or left pancreatectomy or total pancreatectomy with lymph node dissection depending on the site and the extension of the disease) must be required **[1]**. High-risk lesions in the remnant pancreas after surgical resection for IPMN may progress to malignant or develop new PDCA over 5 years, then second surgery for these high-risk lesions may improve survival **[8]**.

Adjuvant therapy improves overall survival only in invasive IPMN patients with the nodal disease or tubular differentiation **[9]** and may not improve overall survival in patients with resected invasive IPMN **[10]**.

All patients with all kinds of IPMN should undergo surveillance. Patients with resected invasive IPMN do have a high risk of recurrence, 17-65 % in the remaining pancreas **[11,12]**. Patients with high-grade dysplasia or invasive IPMN should be followed up every 6 months for the first 2 years, followed by yearly surveillance. MRI or EUS is recommended for follow-up imaging **[4]**.

A study **[13]** showed the median cancer-specific survival time of 1178 invasive IPMN patients with no metastases, isolated lung, isolated liver, and multiple metastases were 19 months, 7 months, 4 months, and 3 months, respectively, and most of them(83.4 %) did not undergo surgery or radiotherapy. In our case, the patient with invasive IPMN had missed the time of surgery and could only be given chemotherapy. Unfortunately, the patient refused to cooperate with additional chemotherapy and died.

Intraductal papillary mucinous neoplasm of the pancreas, with the characteristic of slow disease progression, can be diagnosed clinically, improvement in the understanding of the disease will contribute to early diagnosis and effective treatment.

Author contributions: Zhu QQ wrote the manuscript; Jin J, Wei L, and Jing DD revised the manuscript.

Conflicts of interest: The authors disclose no conflicts.

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