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Case Report

Primary pancreatic leiomyosarcoma initially misdiagnosed as pancreatic adenocarcinoma: a case report and review of the literature

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Abstract: Background: In numerous cases of advanced pancreatic adenocarcinoma, it is possible to make the diagnosis by evaluating clinical symptoms, various tests and radiographic findings. However, there are certain dangerous drawbacks because some other pancreatic neoplastic entities might also mimic pancreatic ductal adenocarcinoma, and this leads to an incorrect diagnosis. Case presentation: A 46-year-old man without any prior history of smoking visited a local hospital in September 2013 with complaints of recurrent upper abdominal discomfort since one-month. An abdominal computer tomography revealed a 44 mm × 36 mm small enhancing mass in the pancreas, along with numerous rim-enhancing lesions in the liver and inflamed lymph nodes in the hepatoduodenal ligament. After receiving the radiographic findings along with abnormal levels of carbohydrate antigen 19-9 concentration, the patient was diagnosed with stage IV pancreatic adenocarcinoma. In order to confirm the diagnosis, patient was advised to undergo for a fine needle aspiration biopsy but his family members did not agree for it. After 11 months, the patient was referred to our specialized cancer hospital due to failure to respond to treatment. This time his family allowed a biopsy of the liver lesions which revealed a metastatic leiomyosarcoma from the pancreas. The patient died two months later because of multiple organ failure. Conclusions: Primary leiomyosarcoma rising from the pancreas is a very rare type of malignancy. The current case indicates that it might appear in a manner parallel to pancreatic adenocarcinoma. Hence, it is extremely important to obtain pathologic confirmation of advanced primary pancreatic neoplasia before beginning the treatment.

Keywords: Leiomyosarcoma, pancreatic adenocarcinoma, misdiagnosis, survival, prognosis

Background

The healthy pancreas is composed of an exocrine component and an endocrine component. The exocrine component contains ductal and acinar cells, and the endocrine component contains small islands of cells known as the islets of Langerhans, while the stroma is tremendously scant. Ductal adenocarcinoma characterizes the furthermost common primary tumor initiating from the ductal epithelium. In various advanced cases, the diagnosis can be assumed intensely from the clinical as well as radiographic findings. Mesenchymal tumors might also involve the pancreas, but then again most of them are secondary lesions from extra pancreatic tumors. Leiomyosarcoma (LMS) is the utmost recurrent primary malignant mesenchymal tumor of the pancreas; however, it is very rare and accounts for only 0.1% of all pancreatic malignancies [1]. Generally, the tumors are revealed at an advanced stage of the disease along with nearby tissue invasion or distant metastasis at the time of diagnosis [2]. Moreover, the clinical and radiographic findings are nonspecific and do not convey the correct diagnosis many times; and recognizing it by means of non-invasive diagnostic method is extremely challenging [3]. Here, a case of misdiagnosed primary pancreatic leiomyosarcoma (PLMS) is reported.

Case presention

A 46-year-old male patient visited a local hospital in September 2013 with a complaint of inter-

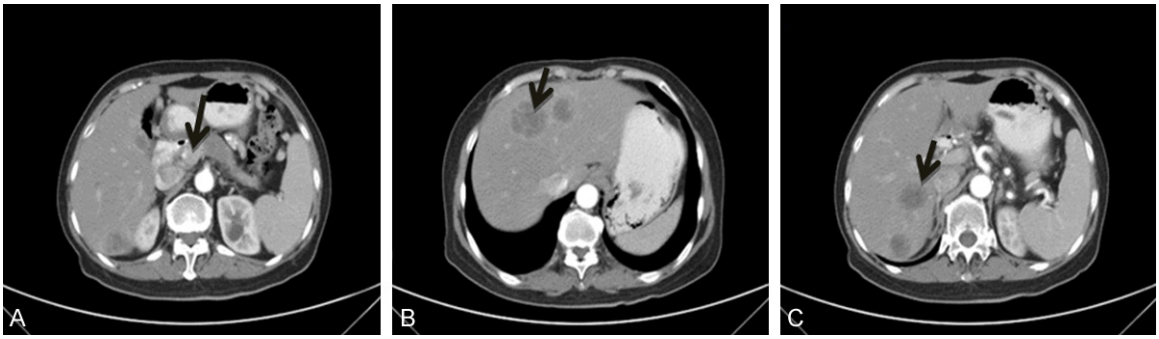

Figure 1. Abdominal contrast-enhanced computer tomography at the time of first visit. A 44 mm × 36 mm slight enhancing mass located in the body of the pancreas, with multiplerim-enhancing lesions in the liver and inflamed lymph nodes in the hepatoduodenal ligament.

mittent upper abdominal discomfort since one-month. He denied previous history of smoking, drinking, any sort of radiation exposure, or family history of cancer. Findings from routine blood test, stool test, urine test, as well as blood coagulation function were all within normal limits. There was a mild elevation of Carbohydrate antigen 19-9 (CA199) concentrations with the value of 82.9 U/ml (Normal range < 39 U/ml). However, the concentration of carcinoembryonic antigen (CEA) was normal.

An abdominal computer tomography (CT) showed a slight enhancing mass (44 mm × 36 mm in size) in the pancreas, with multiple rim-enhancing lesions in the liver as well as inflamed lymph nodes in the hepatoduodenal ligament (**Figure 1**). The patient was diagnosed with stage IV pancreatic adenocarcinoma based on the radiographic findings along with abnormal carbohydrate antigen 19-9 concentration. A fine needle aspiration biopsy (FNAB) was recommended to confirm the diagnosis but his family members refused to comply. Without FNAB, it was difficult to confirm the diagnosis of the condition. From October 1, 2013 onwards, the patient was started on gemcitabine as well as cisplatin. Once the patient received two courses of this treatment, CT was done again to evaluate the tumor response. CT revealed the patient's condition as progressive disease (PD). From November 7, 2013 onwards, the treatment schedule was changed and the patient was started on a combination of albumin-bound paclitaxel and gemcitabine. After completing the six courses of the new treatment, a partial response (PR) was observed. Furthermore, because of this PR, the patient was maintained on gemcitabine monotherapy. However, a PD was again observed following the two cycles of the monotherapy with gemcitabine and thus the treatment was changed to immunotherapy with reinfusion of dendritic cells as well as cytokine-induced killer cells reinfused into the body. Because of an augmentation of size as well as number of liver metastasis, the patient was required to undergo trans-catheter arterial chemoembolization (TACE) followed by a treatment of S-1 plus irinotecan. After two cycle, response evaluation was reported as PD.

Around one year later, on October 20, 2014, the patient was referred to our specialized cancer hospital. This time his family members agreed for him to undergo a CT-guided FNAB of the liver lesions (**Figure 2**). This exposed fascicles of spindle cells along with adequate nuclear pleomorphism (**Figure 3A**). Next, the immunohistochemical analysis indicated a strong positive staining for smooth muscle actin (SMA) (**Figure 3B**). Nonetheless, AE1/AE3, S-100, CD-34, and CD117 were all negative. The concluding diagnosis was that the patient was suffering from pleomorphic leiomyosarcoma (PLMS) with metastasis to the liver. When genetic testing was done, mutations of PDGFRα and c-Kit were negative. At this stage, there was not any specifically targeted medicines for the patient. Thus, he was given two cycles of palliative chemotherapy comprising doxorubicin and dacarbazine, and this was repeated every three weeks. On November 27, 2014, he presented with numerous lung metastases (**Figure 4**). On December 11, 2014, the patient died due to multiple organ failure. The overall duration of the survival for the patient was 15 months.

Discussion

LMS generally originates from the soft tissues of the extremities, gastrointestinal tract, retro

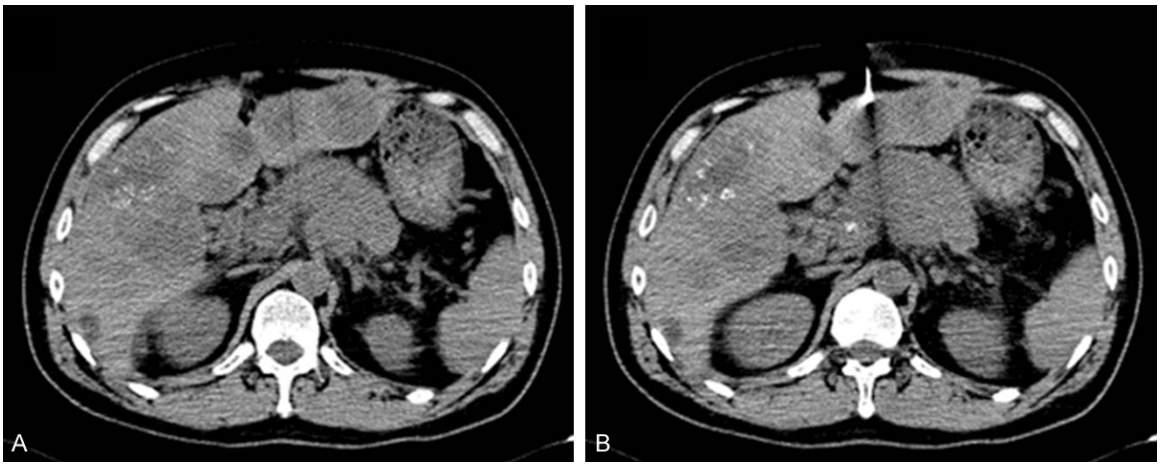

Figure 2. Computer tomography guided fine-needle aspiration biopsy of the liver lesions. A fairly circumscribed mass affecting the pancreatic body and multiple liver metastases were present.

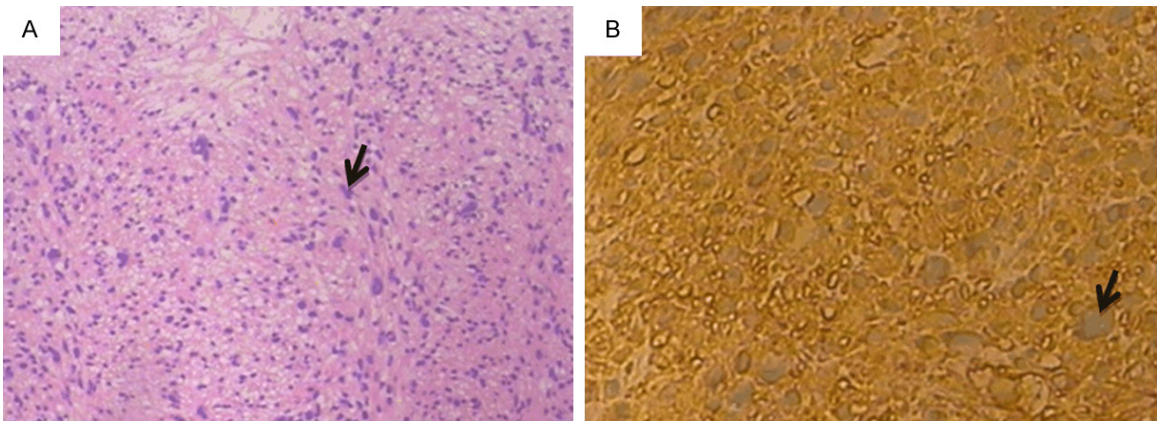

Figure 3. Histopathologic and immunohistochemical analysis. A: Histological examination of the liver lesions showed fascicles of spindle cells, with varying degrees of pleomorphism and atypia (HE, × 100). B: Immunohistochemical examination showed strongly positive staining for smooth muscle actin (SP, × 200).

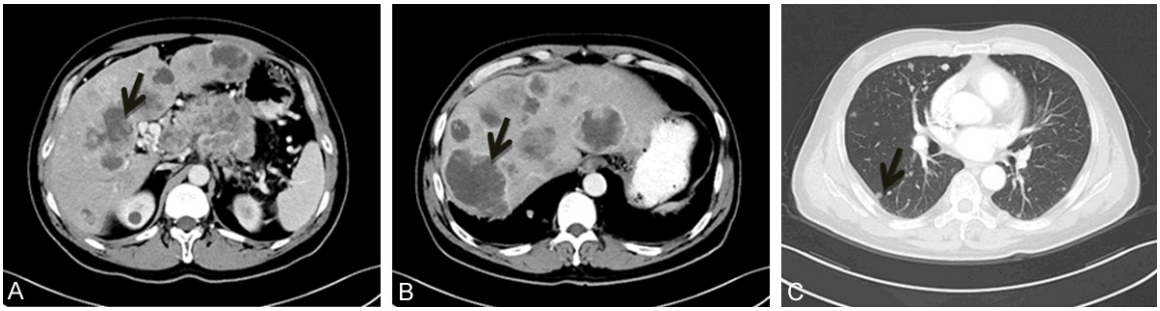

Figure 4. Abdominal contrast-enhanced computer tomography at the time of last visit. The tumor had invaded both the head and body of the pancreas, with multiple liver and pulmonary metastases.

peritoneum as well as female genital tract [1]. Nevertheless, the origination of LMS from the pancreas is extremely rare, responsible for only 0.1% of all pancreatic malignancies [1]. Whenever, LMS originates from the pancreas, it is believed to originate either from the smooth

muscle region of the pancreatic ducts or from blood vessels which are present in the pancreas [4]. Previous studies have exhibited that PLMS has an overall equivalent occurrence rate in both males and females and has an augmented trend during older age [5]. The average age at the time of the diagnosis of PLMS has been reported as 53.9 ± 14.7 years [5]. PLMS occur in the similar manner among the head and body-tail of the pancreas [5]. The furthermost general symptoms at the time of diagnosis include weight loss, abdominal mass, distention, and pain; however, these symptoms are non-specific [5]. Minor tumors generally do not show any symptoms and can be identified during regular physical examination. Previous studies have reported that the overall survival rate of PLMS at 1, 3 and 5 years is 66.6%, 51.2% and 43.9%, respectively [5]. Moreover, the overall prognosis of PLMS is better than pancreatic ductal adenocarcinoma (PDAC).

Conservative radiological investigations may be done to evaluate the association between tumor and pancreas; nevertheless there are not any precise imaging clinical features to identify this type of abnormalities. Abdominal CT scans usually demonstrate an equally circumscribed, an irregular boundary, with or without any cystic component mass, which generally gets presented in homogeneous improvement of the arterial phase [6]. As the size of the tumor increases, there would be hemorrhage, necrosis, as well as cystic degeneration [4-7]. Studies have also reported that some of the large masses presented little reduction in tumor central areas as well as a peripheral improvement following the contrast injection which characterize the cystic degeneration [8, 9]. In those types of cases, it is difficult to make accurate differential diagnosis among PLMS and mucinous cystadenoma or pseudocyst [6]. Under these types of circumstances, the principal solid element of the mass can be detected by clinicians to differentiate it from cystic lesions [6]. Additionally, fluorodeoxyglucose-positron emission tomography FDG-PET has been extensively preferred to distinguish malignant from benign while associated with liquefying necrosis. In this patient, patchy and focal necrosis was detected, but there was not any cystic alteration. PDAC seems to have a robust capability of distant metastasis and nearby tissue invasion, comprising adjoining lymphatic participation. It is generally described by prevalent metastases along with omental and peritoneal numerous nodules propagation when the primary tumor develops around 5-6 cm in the size, and this might be beneficial in the process of differential diagnosis [10]. Previous studies have reported that the average diameter of PLMS is around 11.4 cm [5]. Hence, a single tumor in the pancreatic region greater than 6 cm in the size without any distant metastasis might not be a PDAC and further probable stroma tumors comprising PLMS ought to be considered. In the present case, multiple liver metastasis at the early visit mainly reinforced the diagnosis of PDAC, and this lead to a misdiagnosis of the disease. Furthermore, metastasis of the lymph nodes in PLMS simply happens on exceptional instances even regardless of the tumor's large size, and this might be additional vital point in differential diagnosis of PDAC [6]. During the first clinical visit of the patient, abdominal CT was done and it revealed that there were several inflamed lymph nodes in the hepatoduodenalligamen; and this also supported the diagnosis of PDAC. Additionally, some studies have also revealed that the strong development of the tumor mass along with the lack of pancreatic duct dilatation were clinical features which pointed out a doubtful diagnosis of a mesenchymal tumor, together with PLMS [11].

It is very difficult to make a correct diagnosis just by relying on the non-invasive methods. Until now there has not been any earlier described cases of patients who were diagnosed correctly without any pathological support. Hence, for the first time this study demonstrates the importance of gaining a pathologic validation of pancreatic mass lesions whenever possible. If the patient was not diagnosed correctly and if pathologic diagnosis were not obtained, even the strong and aggressive treatment would not provide any beneficial results or improvements. CT or US-guided FNAB or tissue core fine-needle biopsy (FNB) of the pancreas are well-known techniques with greater diagnostic accurateness. Lately, Hebert-Magee et al. [12] described the first case of PLMS that was diagnosed by EUS-FNAB cytology. This technique requires the mass to be restricted to the head of the pancreas or nearby to the duodenum. If it is very difficult to conduct a biopsy of the pancreatic mass, it may be effective to obtain a biopsy of the liver metastasis as described in the above mentioned case.

It has been established that LMS is somewhat resistant to both chemotherapy as well as radiotherapy [14]. One of the recent systematic reviews on PLMS has specified that non-radical resection is the only autonomous risk of negative consequences [5]. To be precise, as long-term survival has been documented in cases of PLMS with tumor size over 15 cm in diameter, it is safe to say that tumor size is not a limitation for radical resection [11]. Hence, either a comprehensive surgical resection or a prolonged radical resection with total free margin such as a pancreatoduodenectomy or a distal pancreatectomy with splenectomy is the only cure for the patients suffering from PLMS. This should be performed on each patient as there are not any evidences of macrovascular invasion as well as distant metastasis. It is noteworthy that only limited nodal metastases can be detected in clinic even if the tumor size is very large [6]. On the basis of this feature, performing a local radical resection is a conventional practice rather than an extensive node dissection [6]. Nonetheless, several cases are generally diagnosed at an advanced stage with an inclination to affect the adjacent tissues or macrovascular. It is still unclear whether palliative resection of primary tumor and/or metastasis focus will have any beneficial effects in patient or not.

In the present case study, the patient was misdiagnosed for 11 months before being admitted to our hospital. Even though he received a series of wide-ranging treatments, his condition continued to get worse. By the time a conclusive diagnosis was attained, surgery could not be executed on him due to several liver metastases. Additionally, there were not any specific and suitable targeted medicines for him as per his genetic testing. Therefore, for this patient, the only remaining treatment option was palliative chemotherapy because of his poor physical condition. If the pathological diagnosis by needle biopsy of liver lesions would have been executed to eliminate PDAC during his first clinic visit, the extended radical resection along with radiofrequency ablation of the liver lesions would have helped him significantly.

Conclusions

Even though primary LMS arising from the pancreas is rare, the present case suggests that this tumor might appear in a manner analogous to PDAC, with nearby tissue invasion, distant metastasis, or regional lymph node participation. In other words, it is very important to consider PLMS in the differential diagnosis of suspected pancreatic adenocarcinoma in any case. Furthermore, for pancreatic malignant neoplasms, even if the imaging results or clinical presentations constantly support the diagnosis of PDAC, it is extremely important to obtain pathologic confirmation before starting any sort of aggressive treatment (such as chemotherapy or radiotherapy). Otherwise, the consequences of aggressive treatments would be disastrous leading to either financial burden or inappropriate prognosis.

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Written informed consent was obtained from the family of patient for publication of this case report and any accompanying images.

Disclosure of conflict of interest

None.

Abbreviations

LMS, leiomyosarcoma; PDAC, pancreatic ductal adenocarcinoma; PLMS, primary pancreatic leiomyosarcoma; CT, computer tomography; CA-199, carbohydrateantigen 19-9; CEA, carcinoembryonic antigen; FNAB, fine-needle aspiration biopsy; PD, progression disease; PR, partial response; SMA, smooth muscle actin.

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