Korean J Gastroenterol Vol. 68 No. 4, 221-224
https://doi.org/10.4166/kjg.2016.68.4.221
pISSN 1598-9992 eISSN 2233-6869

CASE REPORT

비제대 피부전이로 발견된 췌장암 1예

문지인, 박지영, 전태주, 최정민, 신원창, 성준민, 김영문, 김현정[1]
인제대학교 의과대학 상계백병원 내과학교실, 병리학교실[1]

Non-umbilical Cutaneous Metastasis of Pancreatic Adenocarcinoma as the First Clinical Manifestation: A Case Report

Ji In Moon, Ji Young Park, Tae Joo Jeon, Jung Min Choi, Won Chang Shin, June Min Sung, Young Moon Kim, and Hyun-Jung Kim[1]
Departments of Internal Medicine and Pathology[1], Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea

Non-umbilical cutaneous metastases from pancreatic adenocarcinomas are extremely rare. Only a few cases have been reported in the literature. An 83-year-old Korean woman, with no previous medical history, presented with a painful nodule on her scalp. Histologic examination of the nodule revealed a metastatic adenocarcinoma, and immunohistochemical staining was positive for cytokeratin (CK) 7 and CK 19. These findings were consistent with a metastatic carcinoma of pancreatic origin. An abdominal computed tomography scan identified a mass on the pancreatic head and multiple enlarged lymph nodes. Pathological examination of an endoscopic ultrasound-guided fine needle biopsy of the pancreatic mass determined that it was a poorly differentiated carcinoma. The patient refused any treatment owing to her old age and short life expectancy. Four months later, the disease progressed rapidly, and the patient died. **(Korean J Gastroenterol 2016;68:221-224)**

Key Words: Pancreatic neoplasms; Cutaneous; Neoplasm metastasis; Immunohistochemistry

INTRODUCTION

Cutaneous metastasis from pancreatic cancer is very rare, but usually occurs in close proximity to the umbilicus and is termed 'Sister Mary Joseph's nodule'.[1-3] Non-umbilical cutaneous metastasis from pancreatic cancer is exceedingly rare with very few cases reported in the literature.[2-5] Here, we report a case of non-umbilical cutaneous metastasis as the first clinical presentation of a pancreatic cancer. The case serves as a reminder that pancreatic cancer may be considered in the initial differential diagnosis of patients who present with this clinical sign.

CASE REPORT

An 83-year-old Korean woman, who was in good general health, noticed a small nodule on her scalp two weeks prior. She visited the dermatology department for evaluation of the nodule, which measured approximately 1.0×1.0 cm. It was firm, painful, and non-pruritic, with a central plug (Fig. 1). Around the time the patient discovered the scalp lesion, she developed upper abdominal pain that radiated to her back. Associated features were anorexia and weight loss. A biopsy was obtained, and pathological examination revealed a poorly-differentiated metastatic adenocarcinoma of unknown primary site. Immunohistochemical staining revealed that

Received July 4, 2016. **Revised** July 27, 2016. **Accepted** July 29, 2016.

교신저자: 박지영, 01757, 서울시 노원구 동일로 1342, 인제대학교 상계백병원 소화기내과
Correspondence to: Ji Young Park, Division of Gastroenterology, Department of Internal Medicine, Inje University Sanggye Paik Hospital, 1342 Dongil-ro, Nowon-gu, Seoul 01757, Korea. Tel: +82-2-950-1341, Fax: +82-2-950-1955, E-mail: human@paik.ac.kr

Financial support: None. Conflict of interest: None.

the lesion was positive for cytokeratin (CK) 7 and CK 19, and negative for CK 20, thyroid transcription factor-1 and p63 (Fig. 2). The patient was referred to the gastroenterology department for further investigation of the source of the scalp lesion and the cause of the associated symptoms. On physical examination, no further abnormalities were identified, with the exception of mild tenderness on the epigastric area. Routine blood chemistry tests revealed only a slightly elevated level of amylase (146 U/L; normal range, 22-80 U/L), but there was a remarkable elevation in the serum level of the tumor marker CA 19-9 (348.2 U/mL; normal range, 0-37 U/mL). Abdominal CT was performed, revealing a 1.4-cm, ill-defined, ovoid low-density lesion in the pancreatic head with upstream pancreatic duct dilatation and multiple small lymph nodes in the left gastric, common hepatic, peripancreatic, portacaval, aortocaval, and paraaortic areas (Fig. 3). To confirm histology of the pancreatic lesion, an endoscopic ultrasound-guided fine needle aspiration biopsy was performed. Pathological analysis revealed a poorly differentiated carcinoma (Fig. 4). The patient refused any treatment owing to her old age and short life expectancy. Three months later, she was hospitalized with severe abdominal pain and anorexia. An abdominal CT showed that the size of the pancreatic head mass had increased to 4.1 cm. It also revealed

Fig. 1. Erythematous plaque with a central plug is seen on the scalp.

Fig. 3. Abdominal CT scan shows a 1.4-cm, ill-defined, ovoid, low-density lesion (arrow) in the pancreatic head with upstream pancreatic duct dilatation.

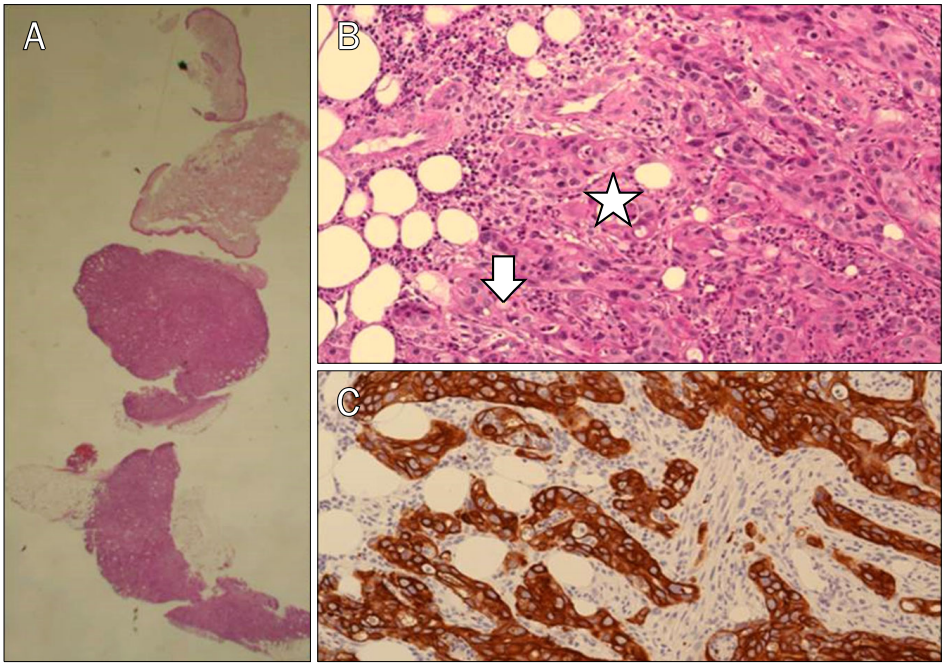

Fig. 2. (A) Histology section of the scalp lesion. The nodule is highly cellular and infiltrating towards the fat lobule. (B) Ductal proliferation with severe nuclear atypia, frequent mitoses, intraluminal necrotic debris (asterisk), and intracytoplasmic mucin vacuoles (arrow), suggestive of high-grade adenocarcinoma. (C) Diffuse and strong staining for cytokeratin 7 in the tumor cells, supportive of a ductal type carcinoma (such as pancreas, breast, or biliary).

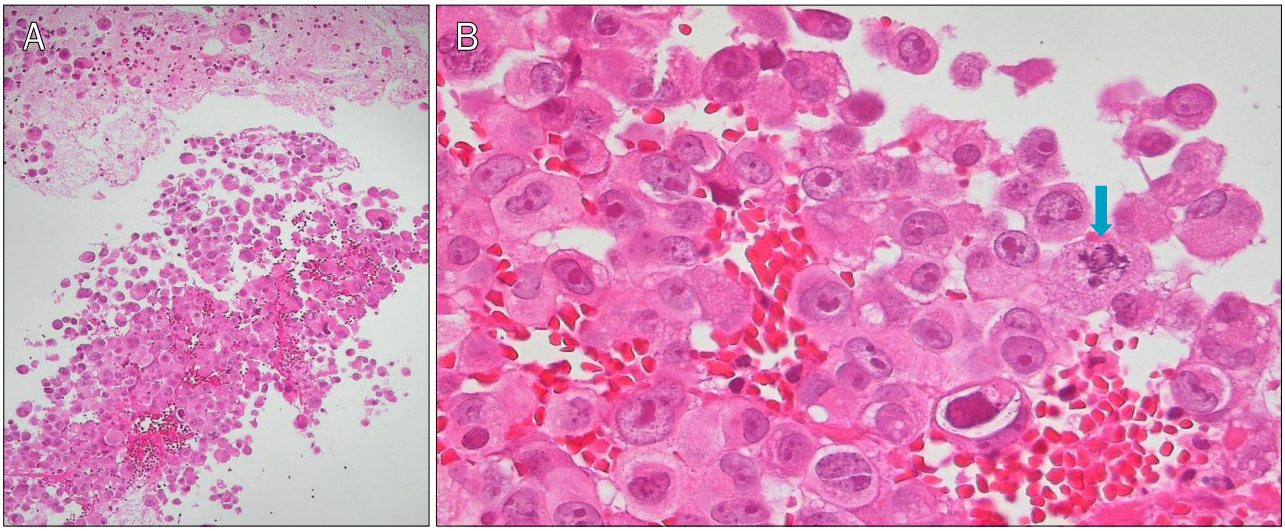

Fig. 4. (A) The needle biopsy from the pancreatic head mass shows loosely cohesive atypical epithelial cells, embedded in a blood-tinged fibrin clot (H&E, ×40). (B) Pleomorphic tumor cells with vesicular nuclei and several prominent nucleoli. Occasional atypical mitoses are indicated (arrow) (H&E, ×400).

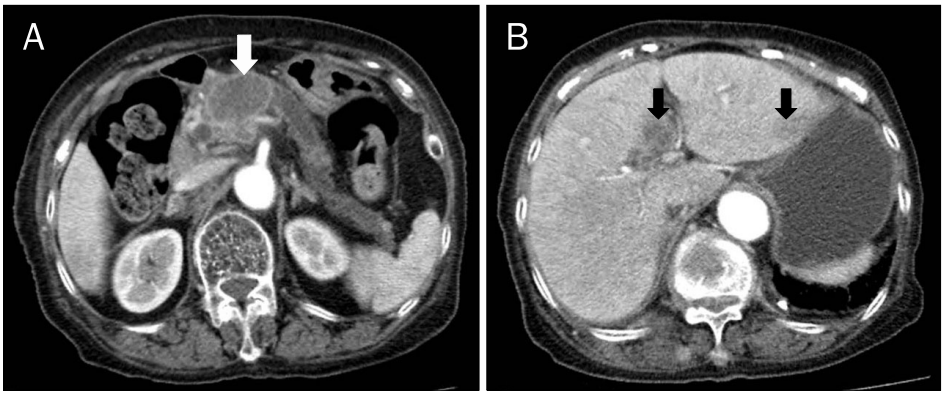

Fig. 5. (A) Abdominal CT scan taken three months after the diagnosis shows the increased size (4.1 cm) of the pancreatic head mass with upstream pancreatic duct dilatation (white arrow). (B) Multiple newly detected metastases to the liver (black arrows).

multiple, newly detected metastases to the liver, adrenal gland, and bones (Fig. 5). The disease progressed rapidly, and one month later, the patient died in the hospital.

DISCUSSION

The incidence of pancreatic cancer has increased over the past few decades and is presently the fifth leading cause of cancer-related deaths in Korea.[6] Unfortunately, clinical symptoms and signs are usually absent until the late stages of the disease.[7] As a result, the majority of cases are diagnosed with advanced stage disease. Indeed, 80% to 90% of pancreatic cancers are diagnosed either at the locally advanced or metastatic stage.[8] The most frequent sites of metastasis are the lymph nodes, peritoneum, liver, lung, adrenal glands, kidney, bone, and brain.[7,9] Cutaneous metastases are uncommon in pancreatic cancer.[1,10-12] The most common site of cutaneous metastasis from the pancreas is the umbilicus; this type of metastasis is known as 'Sister Mary Joseph's nodule'.[1-3,8,13] Non-umbilical metastasis from the pancreas, especially to the scalp, is very rare.[2,14,15] To the best of our knowledge, there have been only seven reported cases of pancreatic cancer with cutaneous metastasis to the scalp in the English literature.[2] Our case demonstrates an extremely rare presentation of pancreatic cancer, in which a metastatic scalp nodule was the first manifestation of the disease.

While several theories regarding cutaneous metastasis have been proposed, no mechanism has been identified.[8] These theories include the soil and seed hypothesis, direct invasion, lymphatic or hematogenous dissemination and the chemotaxis hypothesis.[1,8,16] According to Zhou et al.,[1] the

head of the pancreas is the most common primary tumor site, followed by the tail. However, cutaneous metastases from tumors in the pancreatic head account for a smaller proportion of metastases than those from tumors in the tail.[1] This indicates that tumors of the pancreatic head have a metastatic route different from that of tumors of the pancreatic tail.[1] A recent study reported that the predominant manifestation of cutaneous metastases was a nodule or mass, and that the gross appearance of the cutaneous tumors was oval, firm, and solid.[1,5]

In our case, detection of the primary source of the cutaneous metastasis was not difficult owing to early intervention via CT examination. However, in other reported cases, identification of the primary source of the cutaneous metastasis was more difficult.[2] In such cases, immunohistochemical staining for CKs can be helpful in identifying the primary tumor site.[2] In the pancreas, CK 8 and CK 18 are produced by exocrine acinar cells, endocrine islets, and duct cells.[1,5] CK 17 and CK 19 are usually detected only in the ductal cells.[1,5] Approximately 90% of pancreaticobiliary adenocarcinomas show diffuse positivity for CK 7, while 50% show diffuse positivity for CK 19.[5] However, the expression of CK 20 can be variable.[7] According to Matros et al.,[17] different levels of CK 20 positivity are associated with different clinical outcomes. They demonstrated that a lower degree of CK 20 positivity is associated with better clinical outcome and increased postoperative survival, compared with a higher degree of CK 20 positivity.[2,5,17] In our case, the tumor cells were positive for CK 7 and CK 19, and negative for CK 20, consistent with metastasis from the primary pancreatic adenocarcinoma and a poor prognosis.

Cutaneous metastases have very rarely been reported, especially to non-umbilical areas.[2,14,15,18] Our patient had a metastatic scalp lesion, an extremely rare presentation of pancreatic adenocarcinoma. Therefore, when a suspicious non-umbilical metastatic cutaneous lesion is identified, the clinician should consider pancreatic cancer presenting with cutaneous lesion as initial sign and further investigation such as immunohistochemical staining for CK 7 and CK 19 is suggested.

REFERENCES

1. Zhou HY, Wang XB, Gao F, Bu B, Zhang S, Wang Z. Cutaneous metastasis from pancreatic cancer: a case report and systematic review of the literature. Oncol Lett 2014;8:2654-2660.
2. Kaoutzanis C, Chang MC, Abdul Khalek FJ, Kreske E. Non-umbilical cutaneous metastasis of a pancreatic adenocarcinoma. BMJ Case Rep 2013;2013:bcr2012007931.
3. Bdeiri K, Kamar FG. Cutaneous metastasis of pancreatic adenocarcinoma as a first clinical manifestation: a case report and review of the literature. Gastrointest Cancer Res 2013;6:61-63.
4. van Akkooi AC, Dokter J, Boxma H. Unusual first presentation of metastatic pancreatic cancer as skin metastases in a burn patient. Burns 2010;36:e111-e114.
5. Jun DW, Lee OY, Park CK, et al. Cutaneous metastases of pancreatic carcinoma as a first clinical manifestation. Korean J Intern Med 2005;20:260-263.
6. Lim D, Ha M, Song I. Trends in major cancer mortality in Korea, 1983-2012, with a joinpoint analysis. Cancer Epidemiol 2015; 39:939-946.
7. Pontinen T, Melin A, Varadi G, et al. Cutaneous metastasis of pancreatic adenocarcinoma after kidney transplant: a case report and review of the literature. Exp Clin Transplant 2010;8:273-276.
8. Yendluri V, Centeno B, Springett GM. Pancreatic cancer presenting as a Sister Mary Joseph's nodule: case report and update of the literature. Pancreas 2007;34:161-164.
9. Abdel-Hafez HZ. Cutaneous pancreatic metastasis: a case report and review of literature. Dermatol Surg 2008;34:1580-1583.
10. Gawrieh S, Massey BT, Komorowski RA. Scalp metastases as the first manifestation of pancreatic cancer. Dig Dis Sci 2002;47: 1469-1471.
11. Nakano S, Narita R, Yamamoto M, Ogami Y, Osuki M. Two cases of pancreatic cancer associated with skin metastases. Am J Gastroenterol 1996;91:410-411.
12. Taniguchi S, Hisa T, Hamada T. Cutaneous metastases of pancreatic carcinoma with unusual clinical features. J Am Acad Dermatol 1994;31:877-880.
13. Galvañ VG. Sister Mary Joseph's nodule. Ann Intern Med 1998;128:410.
14. Takemura N, Fujii N, Tanaka T. Cutaneous metastasis as the first clinical manifestation of pancreatic adenocarcinoma: a case treated with gemcitabine. J Dermatol 2007;34:662-664.
15. Takeuchi H, Kawano T, Toda T, et al. Cutaneous metastasis from pancreatic adenocarcinoma: a case report and a review of the literature. Hepatogastroenterology 2003;50:275-277.
16. Brownstein MH, Helwig EB. Patterns of cutaneous metastasis. Arch Dermatol 1972;105:862-868.
17. Matros E, Bailey G, Clancy T, et al. Cytokeratin 20 expression identifies a subtype of pancreatic adenocarcinoma with decreased overall survival. Cancer 2006;106:693-702.
18. Lookingbill DP, Spangler N, Sexton FM. Skin involvement as the presenting sign of internal carcinoma. A retrospective study of 7316 cancer patients. J Am Acad Dermatol 1990;22:19-26.