Non-umbilical cutaneous metastasis of a pancreatic adenocarcinoma

Christodoulos Kaoutzanis,¹ Myungwon C Chang,¹ Feras J Abdul Khalek,² Edward Kreske¹

¹Department of Surgery, Saint Joseph Mercy Health System, Ann Arbor, Michigan, USA
²Department of Internal Medicine, Saint Joseph Mercy Health System, Ann Arbor, Michigan, USA

Correspondence to
 Dr Christodoulos Kaoutzanis,
 ckaoutzanis@gmail.com

SUMMARY

Pancreatic adenocarcinoma is one of the deadliest human malignancies with the majority of cases diagnosed late in the course of the disease. Cutaneous metastases originating from pancreatic cancer are rare. The most common site reported is the umbilicus. Non-umbilical cutaneous metastases are far less common with only a few cases reported in the literature. Our case involved a 43-year-old man with pancreatic carcinoma who was offered resection and a Whipple procedure was planned. Intraoperatively, the patient was found to have a widely metastatic disease not seen on preoperative imaging. Postoperatively, cutaneous metastasis in the scalp was discovered. Although rare, the recognition of non-umbilical cutaneous metastases of pancreatic adenocarcinoma can be of value because they can not only detect an underlying tumour but also guide management.

BACKGROUND

Pancreatic cancer is the fourth leading cause of cancer death among men and women in the USA, accounting for 6% of all cancer-related deaths.¹ The American Cancer Society estimates that, in 2012, about 43 920 new cases of pancreatic cancer will be diagnosed and about 37 390 people will die of pancreatic cancer in the USA.² The overall 5-year relative survival is estimated to be 5.5%.³ Unfortunately, clinical symptoms and signs are usually absent until the late stages of the disease, resulting in the majority of cases being diagnosed in the locally advanced or metastatic stages. The most frequent sites of metastases are the lymph nodes, peritoneum, liver, lung, adrenal glands, kidney, bone and brain.⁴ Cutaneous metastases are uncommon, and if they do occur, they are generally located in the periumbilical area.^{5 6} Non-umbilical cutaneous metastases from pancreatic malignancies are exceedingly rare with very few reported cases in the literature. Here, we report the case of a 43-year-old man with advanced pancreatic carcinoma who was found to have a metastatic cutaneous lesion in the scalp, and represents only the seventh case in English literature.

CASE PRESENTATION

A 43-year-old Caucasian man, with a history significant for tobacco and alcohol abuse, presented with an acute onset of jaundice associated with dark urine, pale stool and mild epigastric abdominal pain. Laboratory data revealed hyperbilirubinaemia with a total bilirubin of 20.6 mg/dl and elevated liver enzymes. Serum lipase was 41 IU/l. CA 19-9 was elevated at 106 U/ml. Abdominal ultrasound

demonstrated a distended gallbladder and dilation of both intrahepatic and extrahepatic bile ducts. A discrete pancreatic mass was not seen. A prominent lymph node superior to the pancreatic head measuring 15×17×27 mm was noted.

During subsequent endoscopic retrograde cholangiopancreatography, a biliary stricture was found and stented. Cytological brushings were sent but were non-diagnostic. Further work-up with endoscopic ultrasound confirmed the abdominal ultrasound findings, and fine needle aspiration of the pancreatic parenchyma and lymph nodes was successfully performed. Pathological findings demonstrated pancreatic ductal adenocarcinoma and metastatic adenocarcinoma to the sampled lymph node. No metastatic disease was noted on physical examination, or CT of the chest, abdomen and pelvis.

The patient was offered resection, and a Whipple procedure was planned. Upon entering the abdominal cavity, the tumour was noted to involve most of the pancreas, with adenopathy throughout the entire celiac chain, and a malignant omental nodule. Owing to the extent of the disease, the Whipple procedure was aborted. In view of the biliary stricture, palliative bypass with a retrocolic gastrojejunostomy and retrocolic Roux-en-y hepaticojejunostomy was performed.

On postoperative day 6, the patient noticed a painful left occipital scalp mass, whose duration was unknown. Physical examination revealed a reddish, tender, firm 1 cm nodule in the left occipital scalp. It was excised under local anaesthesia. Histology sections revealed a dermal-based, poorly differentiated, infiltrative carcinoma embedded in a desmoplastic background (figure 1A). Higher power showed that the lesion was composed of invasive strands of pleomorphic cells with hyperchromatic, angulated nuclei (figure 1B). By immunohistochemistry, the lesional cells were strongly positive for cytokeratin 7 (figure 2). They were negative for cytokeratin 20. The constellation of findings was consistent with a metastatic carcinoma of pancreatic origin.

The patient recovered uneventfully and was discharged home on postoperative day 8. Despite starting chemotherapy, the disease progressed rapidly. He died 4 months later from complications of his widely metastatic disease.

DISCUSSION

A thorough PubMed search, including all articles in the English language since 1950, identified 21 other cases of non-umbilical cutaneous metastases (table 1). To the authors' knowledge, only 6 of 21

To cite: Kaoutzanis C, Chang MC, Abdul Khalek FJ, et al. *BMJ Case Reports* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-007931

A

B

Figure 1 Histology sections of the skin lesion stained with H&E. (A) Low power ($\times 40$) view demonstrates a dermal-based, poorly differentiated, infiltrative carcinoma embedded in a desmoplastic background. (B) Higher power ($\times 200$) view shows invasive strands of pleomorphic cells with hyperchromatic, angulated nuclei.

cases were metastases in the scalp. There was no identifiable pattern of presentation or cancer spread among these six cases. Our case report represents only the seventh case in English literature. In this case, non-umbilical cutaneous metastasis was identified in the immediate postoperative period. One could argue that surgical intervention, which is associated with significant morbidity, could have been avoided if the lesion was recognised prior to the operation.

When cutaneous metastases are present, pancreatic cancer is usually widely disseminated. In some reported cases, it was discovered prior to the primary tumour. In these cases, the use of immunohistochemical staining of cytokeratins (CKs), members of the intermediate filament family, can be helpful in discovering the origin of the primary site.⁷ The majority of pancreatic

Figure 2 Lesional cells are shown to be strongly positive for cytokeratin 7.

cancers will stain positive for CK7; however, the expression of CK20 can be variable. Matros *et al*⁸ used tissue specimens from 103 patients and demonstrated that CK7 and CK20 expression is present in 96% and 63% of pancreatic adenocarcinomas, respectively. Of the pancreatic adenocarcinomas studied, 35% had the same cytokeratin profile as our patient, with positive CK7 staining and negative CK20 staining. Interestingly, the authors found that different levels of CK20 staining are associated with different clinical outcomes. Specifically, they demonstrated that relative to those who had high levels of CK20

Table 1 Case reports since 1950 of non-umbilical cutaneous metastases of pancreatic origin

Author	Age (years)	Gender	Metastatic site
Ambro <i>et al</i> ¹²	63	M	Scalp
Edelstein ¹³	60	M	Face, neck
Florez <i>et al</i> ¹⁴	48	M	Buttock
Gawrieh <i>et al</i> ¹⁵	45	F	Temporal scalp
Horino <i>et al</i> ¹⁶	65	F	Chest wall
Hafez ¹⁷	55	F	Neck
Jun <i>et al</i> ⁷	68	M	Right forearm, chest
Lookingbill <i>et al</i> ⁵	NS	NS	Abdomen
	NS	NS	NS
Miyahara <i>et al</i> ¹⁸	43	M	Scalp
	65	M	Mentum (head)
Nakano <i>et al</i> ¹⁹	80	M	Occipital scalp
	80	M	Chin, arm, chest, thighs
Otegbayo <i>et al</i> ²⁰	59	M	Face, chest, abdomen, back
Puri <i>et al</i> ²¹	45	M	Scalp, face, neck, back
Saif <i>et al</i> ²²	46	F	Chest, abdomen, neck
Sironi <i>et al</i> ²³	72	M	Right thigh
Takemura <i>et al</i> ²⁴	85	M	Left temple
Takeuchi <i>et al</i> ⁹	77	M	Left axilla
Taniguchi <i>et al</i> ²⁵	63	F	Left axilla
Van Akkooi <i>et al</i> ²⁶	59	M	Scalp
Our Case	43	M	Occipital scalp

F, female; M, male; NS, not specified.

staining, less CK20 staining correlated with better clinical outcomes and increased postoperative survival.

Currently, no effective screening modalities are available for pancreatic cancer, and early diagnosis is uncommon. Cutaneous metastases are usually a late finding. Various theories of tumour spread have been proposed, but no specific mechanism has been elucidated. These theories include direct invasion, lymphatic and haematogeneous spread.^{9–10} A recently proposed mechanism is via chemotaxis. He *et al*¹¹ looked at Th17 cells, a subset of CD4 cells that secretes interleukin-17. This has been shown to promote angiogenesis and may be a contributing factor in the haematogeneous dissemination of malignant pancreatic cells.

Non-umbilical cutaneous metastases are rare in pancreatic adenocarcinoma. Although uncommon, they can be the initial physical finding. In these cases, immunohistochemical staining can help to elucidate the origin of the underlying tumour, which can potentially guide further management. More often, the discovery of non-umbilical cutaneous metastases is a late finding, but it still may influence treatment choices. Therefore, when a suspicious non-umbilical cutaneous lesion is identified on physical examination, further investigation is suggested.

Learning points

- ▶ Non-umbilical cutaneous metastases are rare in pancreatic adenocarcinoma but should be considered if a suspicious lesion is found in a patient with either suspected or diagnosed pancreatic cancer.
- ▶ Often, non-umbilical cutaneous metastases have a non-specific clinical appearance and hence, can be confused for commonly occurring cutaneous lesions, and are overlooked by physicians.
- ▶ If a suspicious lesion is identified, further investigation is suggested to avoid delaying diagnosis and treatment.
- ▶ Immunohistochemical staining can help to elucidate the origin of the underlying tumour.

Acknowledgments We would like to thank Dr. James Ramirez (Department of Pathology, Saint Joseph Mercy Health System, Ann Arbor, MI, USA) for providing and interpreting the histopathology images.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Jemal A, Siegel R, Xu J, *et al*. Cancer statistics, 2010. *CA Cancer J Clin* 2010;60:277–300.
- 2 Society AC. Pancreatic cancer. What are the key statistics about pancreatic cancer? 13 Jan 2012. 2012. <http://www.cancer.org/cancer/pancreaticcancer/detailedguide/pancreatic-cancer-key-statistics> (accessed 11 Jan 2012).
- 3 Institute NC. SEER Stat Fact Sheets: Pancreas. Nov 2011. 2012. <http://seer.cancer.gov/statfacts/html/pancreas.html> (accessed 11 Jan 2012).
- 4 Brownstein MH, Helwig EB. Patterns of cutaneous metastasis. *Arch Dermatol* 1972;105:862–8.
- 5 Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. *J Am Acad Dermatol* 1993;29(2 Pt 1):228–36.
- 6 Powell FC, Cooper AJ, Massa MC, *et al*. Sister Mary Joseph's nodule: a clinical and histologic study. *J Am Acad Dermatol* 1984;10:610–15.
- 7 Jun DW, Lee OY, Park CK, *et al*. Cutaneous metastases of pancreatic carcinoma as a first clinical manifestation. *Korean J Intern Med* 2005;20:260–3.
- 8 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.
- 9 Takeuchi H, Kawano T, Toda T, *et al*. Cutaneous metastasis from pancreatic adenocarcinoma: a case report and a review of the literature. *Hepatogastroenterology* 2003;50:275–7.
- 10 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;34:161–4.
- 11 He S, Fei M, Wu Y, *et al*. Distribution and clinical significance of th17 cells in the tumor microenvironment and peripheral blood of pancreatic cancer patients. *Int J Mol Sci* 2011;12:7424–37.
- 12 Ambro CM, Humphreys TR, Lee JB. Epidermotropically metastatic pancreatic adenocarcinoma. *Am J Dermatopathol* 2006;28:60–2.
- 13 Edelstein JM. Pancreatic carcinoma with unusual metastasis to the skin and subcutaneous tissue simulating cellulitis. *N Engl J Med* 1950;242:779–81.
- 14 Florez A, Roson E, Sanchez-Aguilar D, *et al*. Solitary cutaneous metastasis on the buttock: a disclosing sign of pancreatic adenocarcinoma. *Clin Exp Dermatol* 2000;25:201–3.
- 15 Gawrieh S, Massey BT, Komorowski RA. Scalp metastases as the first manifestation of pancreatic cancer. *Dig Dis Sci* 2002;47:1469–71.
- 16 Horino K, Hiraoka T, Kanemitsu K, *et al*. Subcutaneous metastases after curative resection for pancreatic carcinoma: a case report and review of the literature. *Pancreas* 1999;19:406–8.
- 17 Hafez HZ. Cutaneous pancreatic metastasis: a case report and review of literature. *Indian J Dermatol* 2008;53:206–9.
- 18 Miyahara M, Hamanaka Y, Kawabata A, *et al*. Cutaneous metastases from pancreatic cancer. *Int J Pancreatol* 1996;20:127–30.
- 19 Nakano S, Narita R, Yamamoto M, *et al*. Two cases of pancreatic cancer associated with skin metastases. *Am J Gastroenterol* 1996;91:410–11.
- 20 Otegbayo JA, Oluwasola OA, Akere A, *et al*. Pancreatic carcinoma presenting as cutaneous nodules in a diabetic Nigerian male. *West Afr J Med* 2005;24:180.
- 21 Puri AS, Saraswat VA, Krishnani N, *et al*. Cutaneous metastases in pancreatic adenocarcinoma. *Indian J Pathol Microbiol* 1995;38:99–101.
- 22 Saif MW, Brennan M, Penney R, *et al*. Cutaneous metastasis in a patient with pancreatic cancer. *JOP* 2011;12:306–8.
- 23 Sironi M, Radice F, Taccagni GL, *et al*. Fine needle aspiration of a pancreatic oxyphilic carcinoma with pulmonary and subcutaneous metastases. *Cytopathology* 1991;2:303–9.
- 24 Takemura N, Fujii N, Tanaka T. Cutaneous metastasis as the first clinical manifestation of pancreatic adenocarcinoma: a case treated with gemcitabine. *J Dermatol* 2007;34:662–4.
- 25 Taniguchi S, Hisa T, Hamada T. Cutaneous metastases of pancreatic carcinoma with unusual clinical features. *J Am Acad Dermatol* 1994;31(5 Pt 2):877–80.
- 26 van Akkooi AC, Dokter J, Boxma H. Unusual first presentation of metastatic pancreatic cancer as skin metastases in a burn patient. *Burns* 2010;36:e111–14.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow