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Cutaneous pancreatic metastasis: A case report and review of literature

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Abstract
Pancreatic cancer is one of the most lethal human cancers and continues to be a major unsolved health problem as we enter the 21st century. This is the case despite advances in imaging technology and surgical management. Indeed, 80-90% of pancreatic cancers are diagnosed either at the locally advanced stage or metastatic stage. Cutaneous metastases originating from pancreatic cancer are relatively rare. The most common site of cutaneous metastasis is the umbilicus, and it is known as the Sister Joseph's nodule. Very few patients have been reported with cutaneous lesions disclosing pancreatic carcinoma at sites other than the umbilical area. To our knowledge, there were no previous reports on cutaneous pancreatic metastasis in Egypt. This is a report of a patient with cutaneous pancreatic metastases at the neck, followed by a review of reported non-umbilical cutaneous metastases from pancreatic carcinoma in the literature.

Key words: Pancreas cancer, skin metastases

Introduction
Pancreatic cancer is one of the most lethal human cancers and continues to be a major unsolved health problem as we enter the 21st century. This is the case despite advances in imaging technology and surgical management. Indeed, 80-90% of pancreatic cancers are diagnosed either at the locally advanced stage or metastatic stage. Cutaneous metastases originating from pancreatic cancer are relatively rare. The most common site of cutaneous metastasis is the umbilicus, and it is known as the Sister Joseph's nodule. Very few patients have been reported with cutaneous lesions disclosing pancreatic carcinoma at sites other than the umbilical area.

Case Report
A female patient, 55 years old, was referred from the Oncology Department with complaints of multiple asymptomatic, reddish skin nodules at the left side of the neck of 3-week duration.

The condition started 6 months before when the patient was admitted because of jaundice and general fatigue accompanied by multiple enlarged, firm, nontender left cervical lymph nodes. Laboratory tests showed raised total and direct bilirubin and raised liver enzymes; hepatitis markers were negative and renal function tests were normal. Chest X-ray was free. Abdominal ultrasound (US) showed a mass located at the head of pancreas measuring 4.6 × 4.8 cm (AP × W) with multiple enlarged portahepatis lymph nodes with evidence of dilated intrahepatic biliary radicals and dilated common bile duct. A computerized tomography (CT) scan of the abdomen revealed enlarged head of pancreas with heterogeneous, soft tissue mass measuring 5 × 5 cm with multiple portahepatis and para-aortic lymph node enlargements with no evidence of hepatic focal lesions. Metastases elsewhere were not detected by examination and thorough investigations. Abdominal US and CT findings were compatible with a cancer head of pancreas with multiple metastatic abdominal lymph nodes causing common bile duct obstruction. On abdominal exploration, cholecysto-jejunostomy and entero-enterostomy were done, but the surgeons refused to take a biopsy from the unresectable mass for fear of complication by a pancreatic fistula.

Our patient started palliative cytotoxic treatment. During treatment, she developed asymptomatic violaceous
nodules and indurated plaques over the skin on the left side of the neck, and was subsequently referred to the Dermatology Department for consultation. There were no other similar lesions elsewhere in the body. A lymph node biopsy revealed metastatic carcinoma, and a skin biopsy revealed nests of poorly differentiated atypical cells throughout the dermis [Figure 1]. Silver stain and chromogranin were negative, whereas EMA was reactive for tumor cells and CA 19-9 was focally positive [Figure 2]. In light of the patient’s history of a cancer head of pancreas and the positive immunohistochemical stain result with CA 19-9 for skin biopsy, the diagnosis of metastatic pancreatic carcinoma was established.

A month later, while receiving palliative cytotoxic treatment, the reddish, non-tender indurated plaques increased in size to involve the whole left side of the neck [Figure 3]. At that time, a follow-up CT demonstrated decrease in the size of pancreatic mass to reach a 4 cm cranio-caudal diameter.

Discussion

Pancreatic cancer is the fourth leading cause of cancer death. Currently, there is no early diagnostic test or effective treatment for this deadly disease. Morbidity and mortality from pancreatic cancer is conspicuously associated with metastasis; the most frequent sites of metastasis are lymph nodes, lung, liver, adrenal glands, kidney and bones. Cutaneous metastasis is rare, and it is generally situated in the periumbilical area. The mechanism of cutaneous metastasis is not well described; early studies mostly focused on the ‘soil and seed’ hypothesis. Tumor seeding during resection is complex as recurrence within the peritoneal cavity commonly occurs after resection for curative intent. Moreover, pancreatic carcinoma is known to metastasize rapidly to the lymphatic system by permeation, embolization and retrograde spread due to lymphatic obstruction in the pancreas. Recently, chemotaxis hypothesis has been paid more attention where cancer cell with high expression of chemokine receptor will spread to specific sites where the legend is highly secreted. Lookingbill et al. reported that cutaneous involvement could occur by three different mechanisms: direct invasion, local metastatic disease or distant metastasis. According to their series, the last mechanism is the most uncommon, and if it happens cutaneous lesions arise as multiple nodules grouped in a body area. Takeuchi et al. stated that the most frequent cutaneous metastatic site is the umbilicus; distant spread showed that pancreatic carcinoma can reach all cutaneous tissues via blood or lymphatic systems.

Miyahara et al. reported five cases and reviewed 17 cases of cutaneous metastasis originating from pancreatic cancer. In 20 cases, cutaneous metastases
were present prior to the diagnosis of pancreatic cancer. In 11 cases, metastatic lesions in the skin were the first symptoms of pancreatic cancer, and in the other nine cases, the lesions were discovered by physical examination. They stated that the most common site of cutaneous metastases originating from pancreatic cancer is the umbilicus. Although such cases are rare, it is important to note that metastatic lesions in the skin may be the first sign and one type of distant metastases originating from pancreatic cancer. Horino et al. [7] reviewed 49 reported cases of pancreatic metastasis from 1950 to 1999. In the majority of cases, skin metastatic lesions were the first signs of pancreatic cancer. Moreover, 90.3% of the cases had multiple organ metastases or peritoneal seeding. Only four cases were alive with skin metastases from pancreatic carcinoma. Two of the four cases underwent resection of the pancreas. In these cases, skin metastatic lesions were first noted on physical examination after resection (details were not described). The other two cases underwent chemotherapy (details were not described). After conducting a detailed PubMed search, Yendluri et al. [10] reviewed the English and Japanese literature published in the last 90 years; they identified 57 cases of Sister Joseph’s nodule originating from the pancreas. Although 70-80% of pancreatic adenocarcinomas arise in the head of the pancreas, in patients presenting with a Sister Joseph’s nodule, the majority (91%) were in the tail and body of the pancreas. This may relate to the propensity for cancers in the tail of pancreas to remain asymptomatic until a later stage when distant metastasis has already occurred.

The authors, after reviewing the published data, have found 16 cases, excluding the present case, with non-umbilical cutaneous metastasis [Table]. Patients with metastases to the skin incision or at sites of drain were excluded from this search. Of the 17 cases reviewed (15 men and 2 women), the location sites of primary pancreatic carcinoma were at the head in 52.8% of cases, 23.7% were located at the body and/or tail, and no details were given about the site of primary pancreatic carcinoma in 23.5% cases. The majority of skin metastases reported in literature occurred after palliative procedures, in which the tumor burden remains. In our case, the first skin metastasis was not at the umbilicus but to the left side of the neck; the metastatic process was confirmed by CT examination; the primary tumor was found at the head of the pancreas. Focal positive staining of skin biopsy with CA 19-9 supported our diagnosis. Based on the relative frequency of this phenomenon, this case represents a scenario that validates that non-umbilical cutaneous pancreatic metastasis arises secondary to a primary pancreatic cancer located at the head of pancreas.
Carcinomas of the pancreas represent less than 5% of human malignant neoplasms, where skin involvement is rare and metastasis is generally situated at the umbilical area. We described here an interesting case of cutaneous pancreatic metastasis. To our knowledge, very few patients have been reported with cutaneous metastasis at the neck, disclosing a pancreatic carcinoma, thus making this case especially interesting. This was the first case of cutaneous pancreatic metastasis to be reported in Egypt.

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References


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