Cutaneous Metastasis of Pancreatic Adenocarcinoma After Kidney Transplant: A Case Report and Review of the Literature

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Abstract

Objectives: **Pancreatic cancer is one of the most lethal human cancers. Each year in the United States, about 42 470 individuals are diagnosed with this condition, and 35 240 die, despite advances in imaging, medical treatment, and surgical intervention. Often, 80% to 90% of pancreatic cancers are diagnosed at the locally advanced or metastatic stage. However, cutaneous metastases originating from pancreatic cancer are rare. If cutaneous metastases do indeed occur, it is often near the umbilicus, known as the *Sister Mary Joseph's nodule*. Nonumblical cutaneous metastases are rare, with only several cases reported, but none regarding lesions after organ transplant.**

We introduce the first reported case of a cutaneous metastatic lesion of pancreatic adenocarcinoma after the transplant of an organ. We also performed a literature review and an analysis of reported cases of nonumblical cutaneous metastases of pancreatic adenocarcinoma.

Materials and Methods: **We performed a MEDLINE and PubMed search of reported nonumblical cutaneous metastases of pancreatic adenocarcinoma since 1980 after a literature review and analysis.**

Results: **Our case involved a 76-year-old woman who developed cutaneous pancreatic adenocarcinoma metastases in her surgical wound 2 years after a bilateral kidney transplant. This is the first case of pancreatic adenocarcinoma cutaneous metastases after an organ transplant.**

Conclusions: **The death rate from cancer has increased as the population has aged. This also holds true for transplant recipients. Some believe that cancer will soon surpass cardiovascular disease as the major cause of mortality after transplant. Therefore, it is incumbent upon us to appropriately screen patients with age-appropriate evidence-based examinations. Additionally, those patients with suspicious presentations should be judiciously evaluated to discover a cure for cancer as quickly as possible.**

Key words: *Surgery, Oncology, Nephrology*

Introduction

Pancreatic cancer is 1 of the most-lethal human cancers. Each year in the United States, about 42 470 individuals are diagnosed, and 35 240 die from the disease. It is the tenth most-common type of cancer and the fourth leading cause of cancer-related deaths (1). Unfortunately, the majority of pancreatic cancers are diagnosed at the locally advanced or metastatic stage, while presenting with a paucity of clinical signs and symptoms. The overall 5-year survival rate is 5.5%, despite advances in imaging, medical treatment, and surgical intervention (1).

Pancreatic cancer metastasizes to regional lymph nodes, liver, lungs, celiac plexus, mesenteric vessels, ligament of Treitz, portal vein, and rarely to the skin. If cutaneous metastasis does occur, it is often as a palpable nodule near the umbilicus, known as the *Sister Mary Joseph's nodule*. This nodule most commonly heralds gynecologic or gastrointestinal malignancy. Less than 10% of reported Sister Mary Joseph's nodules originate from pancreatic cancer (2).

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Nonumbilical cutaneous metastases are rare, with only several cases reported. None of these reports is in an organ transplant recipient.

We introduce the first reported case of a cutaneous metastatic lesion of pancreatic adenocarcinoma after transplant of an organ. We performed a literature review and analysis of reported cases of nonumbilical cutaneous metastases of pancreatic adenocarcinoma.

We also performed a MEDLINE and PubMed search of reported nonumbilical cutaneous metastases of pancreatic adenocarcinoma since 1980 after a literature review and analysis.

Case Report

Our case involved a 67-year-old woman who initiated hemodialysis in 2003. In February 2006, she underwent a dual kidney transplant. Her immunosuppression initially consisted of induction with rabbit antithymocyte globulin (total, 350 mg) and total of 500 mg steroids over 5 days; this was continued with chronic immunosuppression of tacrolimus, mycophenolate mofetil, and prednisone. For the 3 years after her surgery, her creatinine ranged from 88.4 μmol/L to 185.6 μmol/L. She never experienced any rejection and did not require additional immunosuppressive therapy. She also did not experience any severe infections or illnesses.

From March 2009 to May 2009, she developed abdominal pain and weight loss of 30 pounds. She also noticed a lesion in her right lower quadrant over the incision site (Figure 1). On May 11, 2009, she underwent biopsy of that lesion, which resulted in metastatic adenocarcinoma, positive for CK7 and CK19. She then underwent a computed tomographic (CT) scan that initially only showed 2 small liver lesions. The CT scan was then repeated on June 2, 2009, which showed a 3.8 × 2.5 × 3.6 cm mass in the pancreatic tail (Figure 2). At this time, the diagnosis of T4N1M1 pancreatic adenocarcinoma was made. Her CA-19-9 level was 103 420. She began chemotherapy in July 2009 consisting of gemcitabine, from which she developed severe dehydration and an elevated creatinine level. After her second dose of gemcitabine, she died from complications of her metastatic disease.

Figure 1. The patient's metastatic lesion in her incision site.

Figure 2. CT scan demonstrating the pancreatic mass.

Results

A MEDLINE search revealed 18 cases of nonumbilical cutaneous metastases of pancreatic carcinoma between 1980 and 2009 (Table 1). The average age of the patient was 61 years. Nine of the 19 cases (47%) reported the metastasis as the presenting sign of cancer. There was 1 case reporting a metastasis to a cholecystectomy incision, but none involving organ transplant.

Discussion

Pancreatic cancer is the fourth leading cause of cancer death. Currently, there is no early diagnostic test or effective treatment for this disease (3). Morbidity and mortality from pancreatic cancer is closely associated with metastasis. Among the sites most-frequently reported are the lymph nodes, the lung, the liver, the adrenal glands, the kidney, and the bones (4). Cutaneous metastases are much less common (5-6), and are often found in the periumbilical area (7).

The mechanism of cutaneous metastasis is not well understood. There have been many reports of recurrence within the peritoneal cavity occurring after resection for curative intent (8). Lookingbill and associates (9) reported that cutaneous involvement could occur by 3 different mechanisms: direct invasion, local metastatic disease, and distant metastasis. According to their series, the last mechanism is the most uncommon. Takeuchi and associates (10) stated that the most-frequent

Table 1. All Reported Cases of nonumbilical cutaneous metastases of pancreatic carcinoma between 1980 and 2009.

Author (Ref No.)	Year	Site of cutaneous lesion	Age/sex	Lesion as the presenting sign of pancreatic adenocarcinoma
Our case (20)	2009	Kidney transplant incision	67 F	Yes
Ulla et al. (26)	2008	Plantar aspect of feet	76 F	Yes
Takemura et al. (25)	2007	Scalp	85 M	Yes
Hafez (16)	2007	Neck	55 F	No
Ambro et al. (27)	2006	Scalp	63 M	Yes
Jun et al. (18)	2005	Forearm, back	68 M	Yes
Tacheuchi et al. (24)	2003	Axilla	77 M	No
Florez et al. (14)	2000	Buttock	48 M	Yes
Horino et al. (17)	1999	Chest wall	65 F	No
Miyahara et al. (19)	1996	Scalp; mentum	43 M; 65 M	No; Yes
Siriwardena etal. (22)	1993	Cholecystectomy incision	71 M	Yes
Bergenfeldt et al. (12)	1988	FNA biopsy site	N/A	No
Fröhlich et al. (15)	1986	FNA biopsy site	N/A	No
Rashleigh-Belcher et al. (21)	1986	FNA biopsy site	68 F	No
Burlefinger et al. (13)	1985	FNA biopsy site	N/A	No
Smith et al. (23)	1980	FNA biopsy site	N/A	No

Abbreviations: FNA, fine needle aspiration

cutaneous metastatic site is the umbilicus, but distant spread shows that pancreatic carcinoma can reach all cutaneous tissues via blood or lymphatic systems.

Miyahara and associates (7) reported 5 cases and reviewed 17 cases of cutaneous metastasis originating from pancreatic cancer. In 20 cases, cutaneous metastases were present before the diagnosis of pancreatic cancer. In 11 cases, metastatic lesions in the skin were the first symptoms of pancreatic cancer, and in the other 9 cases, the lesions were discovered by physical examination. The authors stated that the most-common site of cutaneous metastases originating from pancreatic cancer is the umbilicus. Yendluri and associates (10) reviewed the English and Japanese literature published in the last 90 years and identified 57 cases of Sister Joseph's nodule originating from the pancreas. Although 70% to 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. After reviewing the published data, the authors found 16 cases, excluding the present case, with nonumbilical cutaneous metastasis. Of the 17 cases reviewed (15 men and 2 were women), the locations of primary pancreatic carcinoma were at the head of the pancreas in 52.8% of cases, 23.7% were located at the body and/or tail of the pancreas, and no details were given about the site of primary pancreatic carcinoma in 23.5% cases. The majority of skin metastases reported in the literature occurred after palliative procedures, in which the tumor burden remains. 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.

In 2008, there were 27 963 transplants performed in the United States. In total, there were 16 518 kidney transplants, and 10 551 of those were from deceased donors (3). Organ transplant is associated with significant complications, such as rejection, infection, hypertension, diabetes mellitus, cardiovascular disease, and increasingly more prevalent cancer (3). Kidney transplant is associated with nearly a 20-fold increased risk of nonmelanoma skin cancer, non-Hodgkin lymphoma, and Kaposi sarcoma. However, other malignant associations are a source of controversy (3). It has become widely accepted that transplant patients, in general, are at a high risk of developing many types of cancer. The increased risk can, in part, be explained by cancer associated with viral cause, immunosuppression altering surveillance of neoplastic cells, which may lead to impaired DNA repair mechanisms and ultimately DNA damage (3).

With the improvements in posttransplant management and immunosuppression, patients receiving solid-organ transplants have seen an increase in life expectancy. However, this elucidates malignancy as one of the leading causes of death in these patients (1). It provides evidence that the cumulative effects of immunosuppression in these patients are correlated, to some degree, to the incidence of malignancy. In general, there appears to be at least a 3 times the increased risk of developing cancer in patients with a solid-organ transplant compared with their respective age- and sex-matched general population. According to the Israel Penn International Transplant Tumor

Registry, the increase in incidence is applicable to nearly all types of cancer (except breast and prostate, in women and men).

Specific to our case, the Australia-New Zealand Dialysis and Transplant Registry states that the risk ratio for pancreatic cancer after renal transplant is 2.77 compared with the general population; however, there are few documented cases of pancreatic adenocarcinoma following transplant (11). It appears that immunosuppression impairs surveillance of tumor cells allowing them to replicate unchecked. With this in mind, we must determine an efficient means of screening transplant patients for malignancy and attempt to minimize immunosuppression in older transplant recipients (11).

We believe that the death rate from cancer has increased as the population has aged. This also holds true for transplant recipients. Some believe that cancer will soon surpass cardiovascular disease as the major cause of mortality after transplant. Therefore, it is incumbent upon us to appropriately screen patients with age-appropriate evidence-based examinations. Additionally, those patients with suspicious presentations should be judiciously evaluated to discover a potentially undiagnosed cancer quickly as possible.

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