

Case Report

A Case of Rare Cutaneous Metastasis from Advanced Pancreatic Cancer

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Keywords

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Abstract

A 71-year-old woman presented to a nearby hospital with an occipital scalp ulcer with exudate. Thoracoabdominal enhanced computed tomography (CT) was performed due to suspected cancer. The imaging results showed tumors in the pancreatic tail and at multiple sites in the lung, whereupon she was referred to our hospital for further investigation. Histological analysis of the occipital scalp ulcer and the pancreatic tumor led to the diagnosis of pancreatic adenocarcinoma with cutaneous metastasis and multiple lung metastases. Combination chemotherapy (gemcitabine and nab-paclitaxel) was started, and about 4 months later the patient experienced right lower back pain. Abdominal CT showed partial sclerosis of the right iliac bone and multiple spinal lesions, which were diagnosed as multiple bone metastases. Narcotic analgesia was started for the right lower back pain. Since then, FOLFIRINOX has been introduced as second-line chemotherapy against tumor growth, and treatment has been ongoing for 10 months since the initial chemotherapy. Pancreatic cancer is a rapidly growing cancer and can show early metastasis to other organs, lymph node metastasis, and peritoneal dissemination; therefore, the prognosis of pancreatic cancer is very poor. Cutaneous metastasis from pancreatic cancer is rare, and only a few cases have been reported. Here, we report an unusual case of pancreatic adenocarcinoma with cutaneous metastasis and multiple lung and bone metastases.

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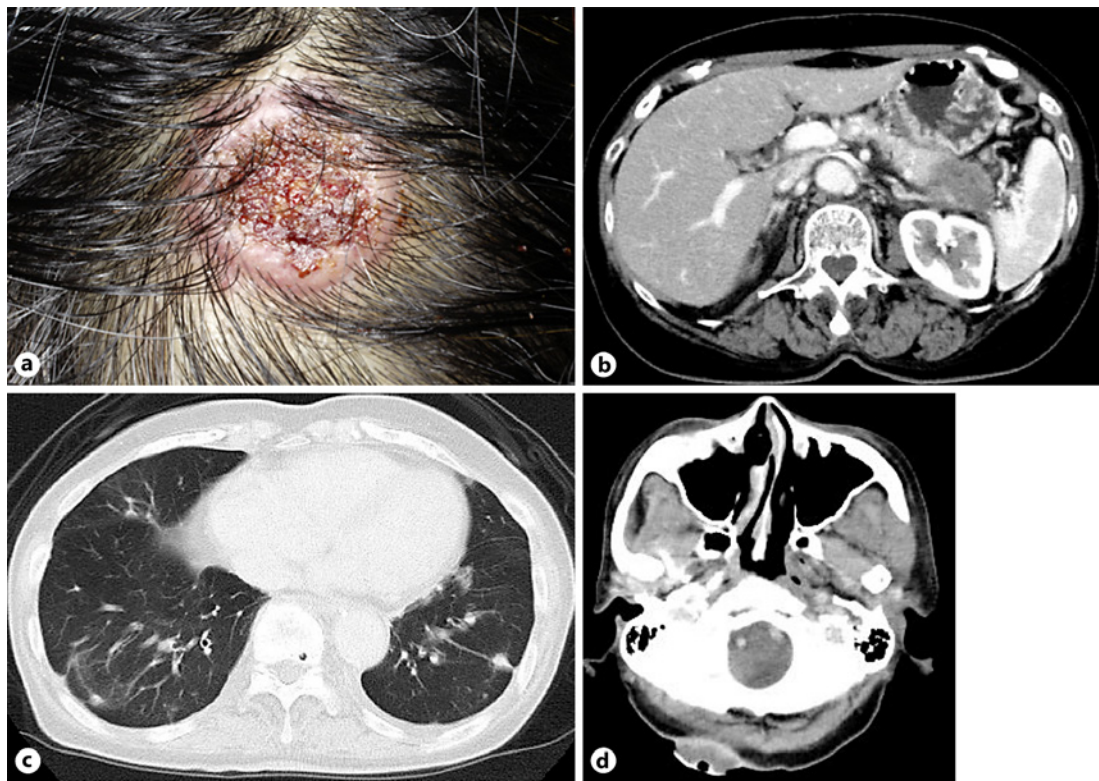


Fig. 1. **a** A fragile ulcer lesion measuring 2.5 cm in diameter in the occipital region. **b** Abdominal computed tomography (CT) image showing a tumor measuring 30 mm in diameter with an unclear margin and poor contrast effect in the pancreatic tail; invasion of the surrounding adipose tissue was suspected. **c** Chest CT image revealing small nodular lesions sized 1 cm or less in both lungs, indicative of multiple lung metastases. **d** Head CT image revealing a bulging mass with contrast enhancement in the occipital ulcerated region without skull infiltration.

Case Report

A 71-year-old woman presented to a nearby hospital with an occipital scalp ulcer with exudate. Thoracoabdominal enhanced computed tomography (CT) was performed due to suspected cancer. The imaging results showed tumors in the pancreatic tail and at multiple sites in the lung, whereupon she was referred to our hospital for further investigation.

A fragile occipital scalp ulcer lesion measuring 2.5 cm in diameter was noted (Fig. 1a), but no other skin lesion was observed upon examination. Her consciousness was clear; no jaundice or anemia was observed, and both lungs were clear on auscultation. The abdomen was flat and soft, and the mass was not palpable.

The blood test results for routine parameters were within the normal range: white blood cells, 8,000 cells/ μ L; hemoglobin, 14.2 g/dL; platelets, 23.1 cells/ μ L; glutamic oxaloacetic transaminase, 19 U/L; glutamic pyruvic transaminase, 16 U/L; lactate dehydrogenase, 190 U/L; alkaline phosphatase, 190 U/L; γ -glutamyltranspeptidase, 21 U/L; amylase, 54 U/L; lipase, 45 U/L; elastase-1, 263 U/L; BS, 117 mg/dL; HbA_{1c}, 5.8%; total bilirubin, 0.9 mg/dL; international normalized ratio, 1.00; and C-reactive protein, 0.01 mg/dL. However, tumor markers were elevated: carcinoembryonic antigen, 3.0 ng/mL; carbohydrate antigen 19-9, 1,720.9 U/mL; DUPAN-2, 1,400 U/mL; and SPAN-1, 880 U/mL.

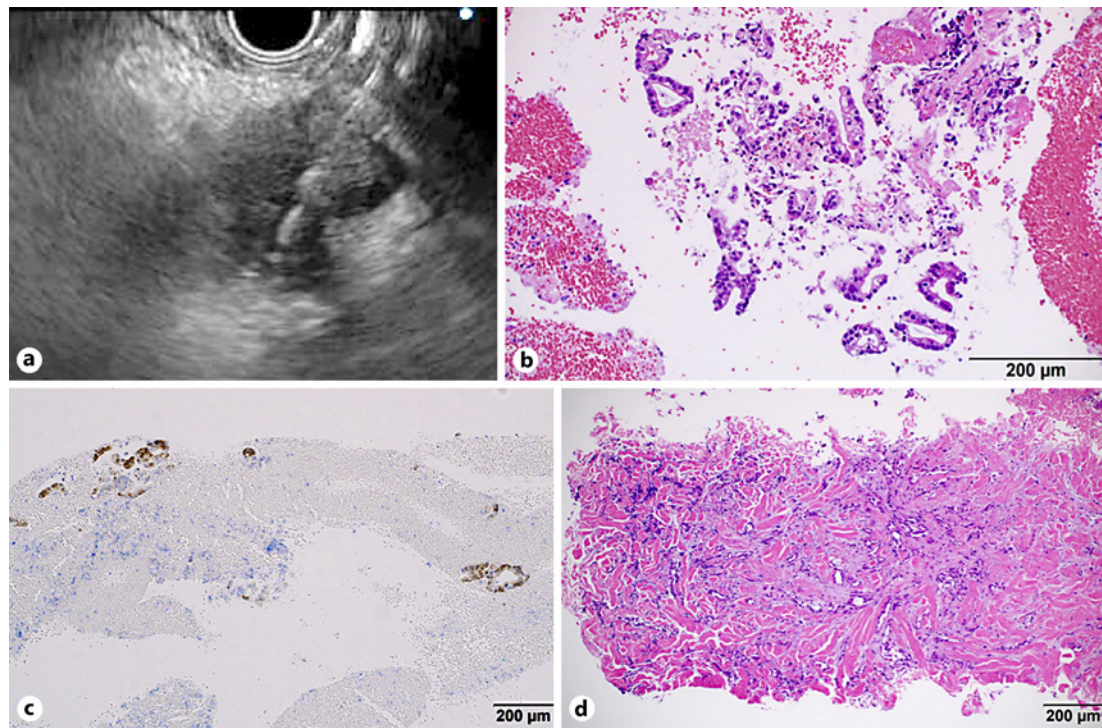


Fig. 2. **a** An irregular and heterogeneous mass measuring 33 × 35 mm in the pancreatic tail, and infiltration into the splenic artery and vein are observed. **b** Histologically, the tumor tissue showed proliferation of small atypical gland ducts with a clear cytoplasm, indicating adenocarcinoma. **c** Immunohistochemically, the tumor tissue expressed IMP3. **d** Histological tissue collected from the occipital ulcer showed almost the same morphology as that from the pancreatic tail.

Abdominal CT showed a tumor measuring 30 mm in diameter with an unclear margin and poor contrast effect in the pancreatic tail, which had possibly invaded the surrounding adipose tissue (Fig. 1b). Chest CT revealed small nodules sized 1 cm or less in both lungs, possibly indicating multiple lung metastases (Fig. 1c). Head CT revealed a bulging mass with contrast enhancement in the occipital region which had not infiltrated the skull (Fig. 1d).

Next, endoscopic ultrasound-guided fine needle aspiration was performed for histological diagnosis. An irregular and heterogeneous mass measuring 33 × 35 mm was observed in the pancreatic tail. Infiltration of the splenic artery and vein was also observed (Fig. 2a). Histochemical staining showed proliferation of small atypical gland ducts, and immunostaining revealed that the tumor was p53 negative and IMP3 positive (Fig. 2b, c). These findings indicate that the primary cancer was pancreatic ductal adenocarcinoma with a clear cytoplasm. Tissue obtained from the occipital ulcer showed almost the same morphology as the primary tumor (Fig. 2d), and therefore, we diagnosed a metastatic cutaneous tumor derived from the pancreatic cancer (Fig. 2d).

Combination chemotherapy (gemcitabine and nab-paclitaxel) was started for advanced pancreatic cancer with distant metastasis. About 4 months later, the patient developed right lower back pain. Conditional abdominal CT imaging showed partial sclerosis of the right iliac bone and multiple spinal lesions, indicating multiple bone metastases (Fig. 3a, b). Narcotic analgesics were started. Imaging also revealed further growth of the pancreatic tumor and the multiple lung tumors. Therefore, second-line combination chemotherapy (FOLFIRINOX,



Fig. 3. **a** Computed tomography image showing partial sclerosis of the right iliac bone. **b** Computed tomography image showing multiple spinal sclerotic lesions and other bone metastases.

i.e., leucovorin, fluorouracil, irinotecan, and oxaliplatin) was started. Chemotherapy is ongoing, as there have been no special adverse events or worsening of the patient's general condition since the diagnosis was made 10 months ago.

Discussion

Pancreatic cancer has a high malignant potential and is considered to have one of the worst prognoses. Since the pancreas is located in the retroperitoneum and is a long, slender organ with a thin film, local symptoms are not well defined [1]. Tumors grow on the outer surface of the pancreas, and hence can easily cause peritoneal dissemination and lymph node metastasis when their diameter exceeds 2 cm [2]. Pancreatic cancer cells are highly proliferative and have low adhesiveness, thereby contributing to the highly metastatic nature of the cancer. Cancer cells metastasize first to major organs, such as the liver and lung, and then to relatively slow-growing tissues such as skin, muscle, and bone [3]. It is thought that, initially, distant dissemination and major organ metastases occur and the general condition of the patient becomes poor, followed by metastases to the skin, muscle, and bone [4]. In recent years, improvements in treatment have extended survival, possibly increasing the detection rate of atypical symptoms due to distant organ metastasis as seen in this case.

Regarding the incidence of cutaneous metastasis among patients with pancreatic cancer, Lookingbill et al. [5] reported that cutaneous metastasis was noted in only 2 of 420 autopsies of pancreatic cancer patients (0.5%), while Cubilla and Fitzgerald [6] observed this finding in 7.6% of their autopsies of pancreatic cancer patients (9 out of 119). The frequency of cutaneous metastasis varies between reports. Macroscopically, primary cutaneous adenocarcinomas often present as a wart, erosion, or ulcer. They usually arise either from the sebaceous or the sweat gland system. Brownstein and Helwig [7] classified metastatic cutaneous tumors into three types: nodular, inflammatory, and sclerodermoid; the most common is the nodular type. Additionally, cutaneous tumors deriving from hematogenous metastatic pancreatic cancer and those originating from lymphatic metastatic pancreatic cancer are macroscopically different. While hematogenous metastatic cutaneous tumors have papule induration with fusion of nodules, lymphatic metastatic cutaneous tumors are considered to be painful lesions with redness and swelling [8]. Metastatic cutaneous tumors derived from pancreatic

cancer are usually considered to be hematogenous and painless, consistent with the findings of the present case [9].

Although the abdomen is the most common site for cutaneous metastasis from pancreatic cancer, head, chest, and scalp metastases have been reported. Abdominal cutaneous metastases are common because the tumor cells disseminated in the peritoneum metastasize to the umbilicus, close to the epidermis, and form a nodule, named Sister Mary Joseph nodule [10]. About 44% of the cutaneous metastases from pancreatic cancer are Sister Mary Joseph nodules.

Bone metastases in the context of pancreatic cancer arise when the tumor is primarily situated in the organ's tail region. The most common site for bone metastasis is the spine. Metastases to the ribs, scapulae, and cheekbones have also been reported [3]. The blood flow from the pancreatic body and tail passes through the vertebral venous plexus via the portal vein, and therefore a transvenous route for metastasis is possible. According to Garcia [11], bone metastasis is usually osteolytic, and osteogenic metastasis, as noted in this case, is rare.

Bone metastasis is treated using pharmacotherapy and radiation therapy, to relieve pain and reduce neurological symptoms. As pharmacotherapy, in addition to an analgesic agent, a bone resorption inhibitor (having an osteoclast-inhibitory effect) is used for the osteolytic type [12]. In this case, bone resorption inhibitor treatment was not indicated because the metastases were osteogenic. Furthermore, radiotherapy was not indicated because it was difficult to identify the exact site responsible for the pain, as there were multiple pelvic and spinal metastases.

Recently, the overall survival rate of pancreatic cancer patients has increased due to advances in treatment such as chemotherapy, but distant metastases, which are considered rare, are expected to become a new problem [13, 14]. Therefore, when treating patients with pancreatic cancer, it is necessary to consider the possibility of distant metastases, such as cutaneous and bone metastases.

Statement of Ethics

This paper does not contain any studies with human participants performed by any of the authors. Written informed consent was obtained from the patient using the hospital default informed consent form.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All the authors contributed to the paper, including writing and revising it. All authors read and approved the final manuscript.

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