

**Case report:**

**Bone metastases as the initial presentation of pancreatic cancer**

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**ABSTRACT:**

The diagnosis of pancreatic cancer in early stages is fraught with difficulty because of non specific and subtle symptoms. At the time of diagnosis, majority of patients present in an advanced stage. Pancreatic cancer spreads first to the regional lymph nodes, then to the liver and less commonly to the lungs. It can also invade adjacent structures. It can spread to any site in the abdominal cavity via peritoneal spread. Bone metastases as the initial presentation of pancreatic cancer is unknown. Here we report an interesting case of metastatic cancer to the bone which on evaluation was found to be from pancreatic cancer.

key words: bone metastases, pancreatic cancer

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**INTRODUCTION**

Pancreatic cancer is the fourth most common cause of cancer related death across the globe [1] It is difficult to diagnose pancreatic cancer in its early stages because of absence of specific signs and symptoms. The later signs and symptoms are non specific and varied. Hence, at the time of diagnosis, majority of patients present in an advanced stage. Only 7% of cases are diagnosed at an early stage [2]

Patients commonly present with pain, weight loss and jaundice.[3].Pain is present in majority of patients with locally advanced or metastatic disease. Patients experience intermittent dull aching pain in the upper abdomen which radiates straight through to the back and is made worse by eating. Significant weight loss may be present. Anorexia, early satiety, diarrhea and steatorrhea also can occur. Jaundice is often accompanied by pruritus and dark urine. Painful jaundice is present in approximately one-half of patients with locally unresectable disease, while painless jaundice is present in approximately one-half of patients with a potentially resectable and curable lesion.[3] The initial presentation depends on the location of the tumor. Malignancies in the pancreatic body or tail usually present with pain and weight

loss, while those in the head of the gland typically present with obstructive jaundice. Patients may give history of previous attack of pancreatitis. The recent onset of atypical diabetes mellitus, a history of recent but unexplained thrombophlebitis (Trousseau sign),should raise suspicion of pancreatic cancer. Presence of jaundice and palpable gall bladder (Courvoisier sign) is strongly indicative of pancreatic cancer, and may be used to distinguish pancreatic cancer from gallstones. Tiredness, irritability and difficulty eating because of pain also exist. Pancreatic cancer is often discovered during the course of the evaluation of aforementioned symptoms.

Pancreatic cancer spreads first to the regional lymph nodes, then to the liver and less commonly to the lungs. It can also invade adjacent structures. It can spread to any site in the abdominal cavity via peritoneal spread. Bone and brain are rare sites of metastases [2]. The prognosis for pancreatic cancer remains dismal. For all stages combined, the 1- and 5-year relative survival rates are 25% and 6%, respectively[2]; for local disease the 5-year survival is approximately 20%[2,4] while the median survival for locally

advanced and for metastatic disease, which collectively represent is about 10 and 6 months respectively[5]

Determining the site of primary cancer in patients with bone metastases of unknown origin is imperative because the treatment and prognosis depends on the site of the primary. The most commonly identified primaries in skeletal metastases of unknown origin include lung, prostate, breast, thyroid and renal cell carcinoma. Bone metastases as initial presentation of pancreatic cancer is unknown. Here we report an interesting case of pancreatic adenocarcinoma who presented with a left iliac bone lesion as the initial presentation.

#### **CASE REPORT**

42 year old male patient was evaluated for complaints of soft tissue swelling associated with pain in the region of left iliac bone for 10 days duration. He was a non smoker and there was no history of alcohol consumption. Patient was otherwise asymptomatic. So, the patient was evaluated with X ray pelvis which showed a large bony erosion of left iliac wing with adjacent soft tissue component. In order to know the true extent of the lesion, he was further evaluated with MRI of pelvis which revealed a large bony erosion with associated soft tissue mass measuring 9cm in left iliac wing just inferior to anterior superior iliac spine.[figure 1] Bony erosion with 6cm soft tissue mass was visualized in posterior aspect of trochanteric region of right femur.[figure 2]. Osteolytic lesions were found at S2 and left acetabulum. Large tumor deposits with bony erosion were found in L1 and L4 vertebral body. Whole body screening was done during MRI which revealed an irregular mass in periampullary region and uncinate process of pancreas. The lesion in the pancreas was incidentally picked up during whole body screening MRI. Histopathological documentation was done from soft tissue lesion in the region of left iliac bone which was reported as clusters of acinar configuration of malignant epithelial cells with moderate nuclear pleomorphism in a hemorrhagic

background suggestive of metastatic adenocarcinomatous deposit.

Subsequently patient was evaluated with CT abdomen which showed a hypodense lesion in the pancreas which showed no enhancement. Multiple hypodense lesions were found in right lobe of liver suggestive of carcinoma pancreas with liver metastases[figure 3]. His liver parameters were normal except for raised alkaline phosphatase. Patient was taken up for palliative radiotherapy to bone secondaries and bisphosphonates and palliative chemotherapy was planned.

#### **DISCUSSION**

Bone metastases are most commonly associated with tumors of the breast, prostate, lung, and kidney and thyroid cancers. Bone metastases can also occur in association with other solid tumors. The spread of any cancer to bone can cause significant morbidity, including severe pain, hypercalcemia, pathologic fracture, and spinal cord and/or nerve root compression.. Bone metastases in pancreatic cancers is very uncommon and bone metastases as the initial presentation of pancreatic cancer is an infrequent occurrence.

The estimated prevalence of bone metastases in pancreatic cancers ranges from 5 – 20% [6,7] The first case of pancreatic cancer with bone metastases was found in Russian literature in 1963[8]. Usually patients with bone metastases had liver as the most common extra skeletal site of metastases [9]. Bone as the only site of metastases is also reported [10]. Osteolytic metastases are more common in pancreatic cancers. However osteoblastic metastases are also reported [11,12]. The most common site of bone metastases is the vertebra [9].

The pathogenesis of metastases in pancreatic cancer is not known. Recently a multistage carcinogenesis model similar to that of colorectal cancers has been proposed for pancreatic cancers.[13]. Sooner or later during the development of pancreatic cancer the primary tumor mass spawns pioneer cells that move out, invade adjacent tissues, and circulate to distant organs where they may form new colonies.[14]. The theories which exist to explain the metastatic specificity

include the homing theory and fertile soil theory. In addition, disruption of adhesive connections between cells may lead to detachment of tumor cells from the primary lesion. One widely observed alteration in cell-to-environment interaction in pancreatic cancer involves E-cadherin, which couples adjacent cells by E-cadherin bridges[14]. Alteration of cell adhesion molecule expression namely NCAM, ICAM - 1 and VCAM -1 also appear to play a role in invasion and metastases[14]

Extracellular proteases, namely urokinase expression is induced in stromal cells by pancreatic cancer cells which bind to urokinase receptor expressed on cancer cells[15]. High expression of matrix metalloproteases was found in pancreatic cancers[16]. Lymph node and distant metastases in pancreatic cancers was associated with loss of KAI1 expression which is a potential suppressor gene of metastases[17]. Various cytokines like IL-6[18], VEGF, and PTHrP [19] have been implicated in the osseous progression of pancreatic cancers. The fundamental hypothesis of the development of bone metastases is that an interaction between tumor and bone cells leads to an increase in bone destruction and proliferation of tumor cells within the bony compartment. Local production of osteolytic factors by cancer cells in bone stimulates osteoclast-

mediated bone resorption, which induces the production of numerous growth factors and stimulates secretion of osteolytic cytokines, resulting in local foci of osteolysis [20]

Our patient presented with both liver and skeletal metastases but the primary site and the liver metastases did not produce any symptoms. His main symptomatology was confined to the site of skeletal metastases. Though skeletal metastases is uncommon in pancreatic cancers, it can contribute to significant morbidity. The overall prognosis of metastatic pancreatic cancer is dismal. However, it is imperative that the skeletal metastases is identified and treated early to improve the quality of life of patients.

In conclusion, the uniqueness of this case lies in the way of presentation. In a patient presenting with skeletal metastases of unknown origin, the histology of primary lesion provides information that is valuable in the selection of treatment. Pancreatic cancer is not normally considered in the differential diagnosis of a skeletal metastases of unknown origin. The purpose of reporting this case is to make clinicians aware of the variations in the presentation of pancreatic cancer and to emphasize the fact that in the investigation of an unknown primary, pancreatic cancer as the cause of bone lesion should not be overlooked.

Figure 1 : large bony erosion with adjacent soft tissue mass in left iliac wing

Figure 2 : Bony erosion with soft tissue mass is visualized in posterior aspect of trochanteric region of right femur

Figure 3 : CT Abdomen showing hypodense lesion in head of pancreas with multiple hypodense lesion in the liver

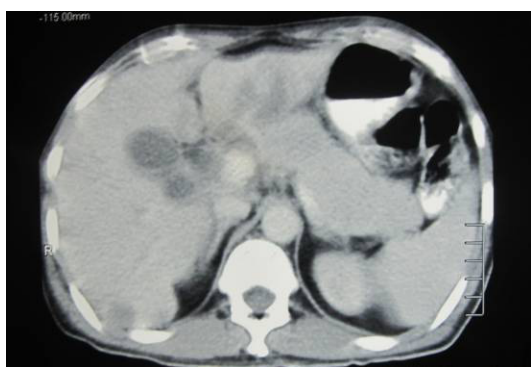
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