

Skeletal Muscle Metastases from Pancreatic Carcinoma—A Case Report and Review of Literature

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Abstract With an overall mortality approaching nearly 100 %, pancreatic cancer is still a challenging disease. A major proportion of pancreatic cancers are still diagnosed at the locally advanced or metastatic stage. Tumors originating from tail region present very late due to the absence of specific symptoms and signs. The usual sites of metastases are the liver, peritoneum and lungs, with occasional reports of metastases in other sites. There are very few documented cases of gastrointestinal cancers manifesting as metastases to muscle. This is a report on a case of pancreatic cancer presenting as metastases to skeletal muscle and multiple other viscera and review of literature for pancreatic cancer metastases.

Keywords Pancreatic carcinoma · Skeletal muscles · Metastases · Tail of pancreas · Pelvic deposit

Introduction

Pancreatic carcinoma is an extremely lethal tumor with overall mortality rates approaching 100 % [1]. Due to its anatomic location deep within the abdomen, diagnosis and treatment of this cancer also presents to be a difficult problem. Up to 80–90 % of pancreatic tumors are already locally advanced or metastatic at the time of diagnosis [2]. The commonest sites of metastases are the liver, the peritoneal lining, and the lungs [3]. Less common sites include skin and soft tissues. Medical literature review reveals a very few reports of skeletal muscles being the metastatic site from gastrointestinal cancers. We

present a case of a patient who presented with multiple skeletal muscle swellings and was detected to have metastases in multiple organs from distal pancreatic cancer.

Case Report

A 55-year-old male patient presented to the surgical outpatient department with complaints of multiple swellings in the right thigh, left shoulder, and both calves of 2 months' duration. Except for mild pain along these swellings, he had no other significant complaints. Medical history was insignificant except for history of chronic tobacco abuse. Clinical examination revealed multiple swellings at these sites, the largest measuring about 3 cm×3 cm. On further examination, the swellings were found to be located within the regional muscles, namely the peroneal muscles in calf and the anterior compartment muscles in thigh and shoulder (Fig. 1). Abdominal examination was normal. Digital rectal examination revealed deposits in the pelvic peritoneum.

Fine-needle aspiration cytology (FNAC) from the calf swelling came inconclusive, being reported as spindle cell lesions with atypical cells. Trucut biopsy revealed malignant cells amid normal muscle tissue, and the diagnosis was given as a malignant neoplasm from adenocarcinoma, the possible primaries being suggested as gastrointestinal tract and prostate (Fig. 2). Laboratory investigations revealed a CA 19.9 value of more than 1,000 IU. Upper and lower gastrointestinal endoscopies were normal. A contrast-enhanced CT scan of the abdomen revealed a tumor arising from the tail of pancreas with infiltration to left adrenal, upper pole of left kidney, spleen, and splenic vessels. CT also revealed multiple small metastases in liver, lung, peritoneum, and abdominal lymph nodes (Fig. 3). On the basis of the very high CA 19.9 values and CT findings, a diagnosis of disseminated pancreatic cancer was made and the patient was offered palliative chemoradiation after discussion with the radiotherapy department.

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Fig. 1 Skeletal muscle metastasis in thigh

Discussion

Pancreatic cancer is a major cause of death all round the world. It comprises about 2.5 % of all newly diagnosed tumors and 5 % of all cancers [4]. The majority of pancreatic cancers (85 %) are adenocarcinoma of the ductal origin. Early diagnosis and treatment options are still limited for this condition. A major factor behind the high level of morbidity and mortality is the high percentage of metastases at the time of diagnosis. Tumors of the head region present comparatively earlier due to the early onset of jaundice and gastrointestinal obstruction. On the other hand, body and tail region tumors present in an advanced stage. Risk factors include smoking, familial cancer syndromes, and familial chronic pancreatitis.

Pathogenesis of Metastases

A vexing problem about pancreatic cancer is the rapid evolution of local infiltration as well as metastatic deposits very early in the disease. A complex interaction between the tumor and the host is supposed to contribute toward this phenomenon. The major factors which drive metastatic process in any cancer are self-sufficiency in growth signals, insensitivity to

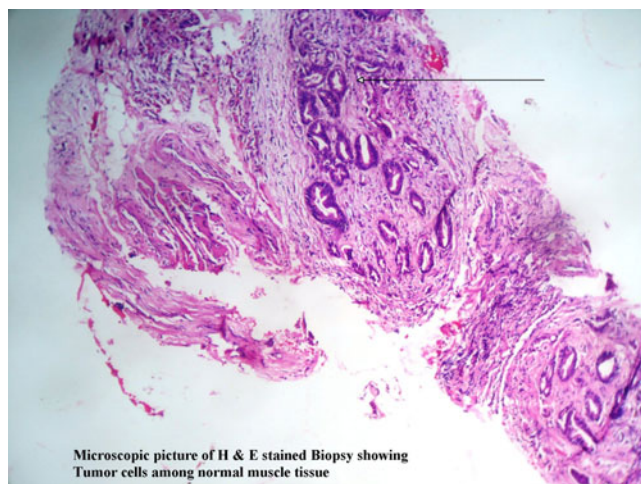


Fig. 2 Trucut biopsy microscopy

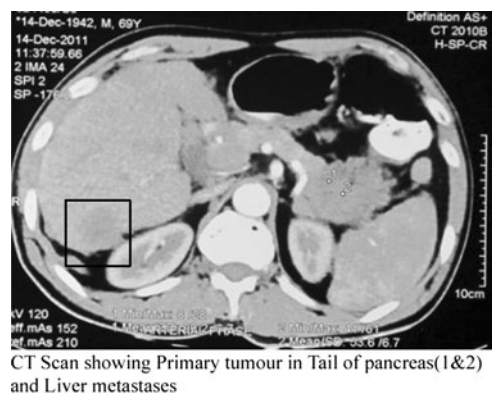


Fig. 3 CT scan abdomen

growth-inhibitory signals, evasion of programmed cell death, limitless replicating potential, sustained angiogenesis, and tissue invasion [5]. Although several discoveries have been made regarding the evolution of metastases, the exact mechanisms regulating their movement, survival in foreign tissues, and choice of residence have remained more or less elusive.

Several conflicting theories exist to explain the metastatic specificity. The homing theory suggests that organs distant to primary malignancy sites actively attract malignant cells via expression of adhesion receptors or by secretion of soluble chemotactic factors [6]. In contrast, the fertile soil theory proposes that different organ environments provide variable growth conditions for specific circulating cell types. Some distinct mechanisms might govern a malignant cell's journey to an ectopic tissue, separate from those regulating its growth and survival once its destination is achieved [5]. Loss of junctional contact between adjacent epithelial cells and cell–extracellular matrix association are essential prerequisites for tumor cell detachment from the primary tumor site [7]. Several genes including those coding for cell adhesion molecules, subtypes of the cadherin family, integrins, urokinase plasminogen activator and its receptor (uPA/uPAR) system, the matrix metalloproteinases, and the metastasis suppressor gene KAI1 are identified as the direct agents involved in this process [8]. Furthermore, an interaction between angiogenesis, lymphangiogenesis, and lymphangiogenesis aids in this by enabling the tumor to outgrow the host tissue [8].

Clinical Features

Pancreatic cancers of the head and uncinate process present comparatively early due to development of jaundice. In contrast, body and tail cancers present at an advanced stage due to absence of pointing symptoms. Very often, the common symptoms are highly nonspecific, including weight loss, malaise, and radiating pain [3]. In all forms of pancreatic cancer, apart from jaundice, physical examination may be grossly normal. A

distended, palpable but nontender gallbladder in a jaundiced patient (Courvoisier's sign) is a highly specific but very less sensitive indication for malignant jaundice [9]. It is difficult to distinguish between periampullary and pancreatic head carcinomas by physical examination alone.

The commonest organs to be involved by metastasis in pancreatic cancer appear to be lymph nodes, livers, and lungs. Less common sites include kidneys, adrenals, and bones [4]. There are a few case reports of cutaneous metastasis also, the umbilicus being the commonest site thus affected [10, 11]. There are some reported cases of metastases at previous incision sites [12]. Skeletal muscle metastases from all carcinomas are rare, the lung being the commonest primary site responsible. Skeletal muscle metastases from gastrointestinal origin malignancies are rarer still, with a very few anecdotal cases only being reported. In a series of 15 cases of skeletal muscle metastases, only 1 was found to be of gastrointestinal origin [12]. In another review of 12 cases, 2 were found to be of gastric origin [13]. Only 1 study directly reports on skeletal muscle metastases from pancreatic cancer [14]. Other findings associated with advanced pancreatic cancer include left supraclavicular lymphadenopathy (Virchow's node) and recurring superficial thrombophlebitis (Trousseau's sign).

Investigations

The initial workup for a patient with suspected pancreatic cancer would include an abdominal ultrasonography and CA 19.9 estimation. CA 19.9 may help confirm the diagnosis and help predict prognosis and recurrence after resection. However, CA 19.9 lacks sufficient sensitivity and specificity to effectively screen asymptomatic patients [15]. Whenever a pancreatic tumor is detected by USS and no definite signs of unresectability are found, the next is CT scan. CT should be done before endoscopic retrograde cholangiopancreatography (ERCP) and insertion of an endoprosthesis, because artifacts and post-ERCP pancreatitis may hamper the diagnostic accuracy. Contrast-enhanced multidetector CT scan (preferably 64-slice MD CT scan) using pancreatic protocol with a power injector can be used to evaluate local extension, invasion of adjacent vascular structures, and surgical resectability with an accuracy of 80–90 % and should be done before planning surgery [16]. Endoscopic ultrasound is the most sensitive imaging test for the detection of small pancreatic head tumors, particularly when smaller than 2 cm as these tumors can be missed even on a technically excellent CT [17].

An FNAC guided by endoscopic ultrasonography may provide tissue diagnosis in patients who are not surgical candidates [18]. Patients with resectable disease can undergo definitive surgery without preoperative histologic confirmation. Although ERCP has a high sensitivity for detecting pancreatic head tumors, it is no longer indicated because it

offers no useful tumor staging information and because preoperative bile duct drainage may not be truly beneficial for the patient [19]. Laparoscopy is much more sensitive than any other technique for the detection of peritoneal implants and superficial liver metastases, and it permits local staging by adding laparoscopic ultrasound. However, the yield of laparoscopy after CT is not high and may be useful in selected cases where there is doubt about resectability or when metastatic disease is suspected [20].

Treatment

The only curative treatment option is surgical resection. Only 20 % of diagnosed cases are found to be fit for laparotomy. The resection consists of a classical partial pancreaticoduodenectomy–Whipple's procedure, or its Traverso–Longmuire variant, the “pylorus-preserving” pancreaticoduodenectomy. Unresectable disease is defined by distant metastasis (e.g., hepatic, extra-abdominal, peritoneal, omental, and distant lymph nodes); invasion of superior mesenteric artery, inferior vena cava, aorta, or celiac axis; or encasement or occlusion of the superior mesenteric–portal venous complex. For patients with unresectable disease at laparotomy, a “double bypass” (gastroenterostomy and hepaticojejunostomy) is performed as palliation. When curative resection is not considered, based on a preoperative decision, palliation consists of endoscopic or percutaneous stenting.

Five-year survival for resection of body or tail lesions is similar to that of resection for pancreatic head lesions and range from 10 to 30 % [21]. Negative prognostic factors include poorly differentiated histology, positive resection margins, lymph node involvement, and a tumor larger than 2 cm [22]. Unlike colorectal cancer, liver resection in metastatic pancreatic cancer has not met with significant survival though there are some multimodality approaches for such cases [23]. Pain from pancreatic cancer can be managed with opioid analgesics, radiation therapy, chemotherapy, or celiac plexus neurolysis. Celiac plexus neurolysis with alcohol eases pain without the side effects of opioids and can be administered intraoperatively, percutaneously or by endoscopic ultrasonography. Adjuvant chemotherapy with leucovorin and fluorouracil or gemcitabine may increase survival to some extent [24].

Conclusion

Carcinoma of the pancreas has remained an academic curiosity from both pathophysiological and therapeutic points of view. The overzealous pattern of local and distant spread adds to the enigma of the disease. Among the sites of metastases, nonvisceral sites are very rare. Various genetic and cellular factors are implicated in the development of

metastases from pancreatic cancers. The treatment options, though offering limited survival benefits, revolve around surgical resection and adjuvant chemotherapy. Extensive literature review reveals that a very few patients have been reported with skeletal muscle metastasis leading to a diagnosis of pancreatic carcinoma. Hence, we have presented this particularly interesting case.

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