CASE REPORT

Extraosseous Ewing Sarcoma of Pancreas: A Rare Entity

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ABSTRACT

Ewing sarcoma is a rare type of cancer that typically arises in the bones or soft tissues of children and young adults. However, Ewing sarcoma can also occur in other body parts, including the pancreas. Ewing sarcoma of the pancreas is rare and often affects children or young adults. We reported a 33-year-old male with no medical illness who presented with worsening epigastric pain and vomiting for one-week duration. CT scan of the abdomen showed an obstructive duodenal mass complicated with perforation. The biopsy of the duodenal mass showed sheets of small round blue cells with immunohistochemical features favouring Ewing sarcoma. Pancreatoduodenectomy procedure (Whipple resection) was performed, which revealed an ill-defined whitish solid tumour at the head of the pancreas measuring 80x50x65mm. Histologically, the tumour is composed of sheets of malignant cells displaying uniform small round to oval nuclei containing fine chromatin, inconspicuous nucleoli, scanty cytoplasm, and indistinct cell membrane. A few mitoses are seen (4/10HPF). Areas of tumour necrosis are observed. Scattered lymphovascular invasion is also present. The malignant cells are infiltrating into the duodenal mucosa. The malignant cells are diffuse and strongly positive towards CD99, FLI-1 and NK2.2 (Figure 3). A diagnosis of primary pancreatic Ewing sarcoma was made.
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INTRODUCTION

The primitive neuroectodermal tumour (PNET), which was formerly known as the Ewing family of sarcomas, is a rare type of malignant tumour that can have varied degrees of differentiation (1). They are described as small round blue cell tumours that arise in soft tissue. The incidence of Ewing sarcoma in the United States is one per million for persons of all ages. It is possible for Ewing sarcoma to originate from solid organs that contain neuroendocrine cells. Some examples of these organs are the pancreas, heart, lungs, kidney, bladder and parotid glands (2). There is a slight male prevalence, and the majority of instances manifest within the second decade of life. Ewing sarcoma/PNET is an aggressive pancreatic tumour, has a poor prognosis and a high recurrence rate. This entity needs to be taken into consideration, particularly in situations where a pancreatic tumour has been found in persons who are younger than 35 years old.

CASE REPORT

We present a case of a 33-year-old guy who presented with increasing epigastric pain and vomiting for one-week duration. The CT scan of the abdomen revealed an obstructive duodenal tumour with perforation. The biopsy of the duodenal mass revealed sheets of small round blue cells with immunohistochemical characteristics consistent with Ewing sarcoma (1). No molecular studies were performed. The tumour was resected without chemotherapy. A pancreatoduodenectomy specimen (Whipple resection) revealed an ill-defined white solid tumor at the head of pancreas and uncinate process extending into the duodenum (Figure 1) measuring 80x50x65mm. Histologically, it consists of malignant cells invading the pancreatic parenchyma and duodenal mucosa in solid sheets separated by fibrous bands (2). The malignant cells have uniform small, round to oval nuclei with fine chromatin, inconspicuous nucleoli, and scanty cytoplasm (Figure 2). A few mitoses are present (4/10 HPF). Tumour necrosis and lymphovascular invasions are evident. The tumour infiltrates the duodenum with surgical margin involvement. The malignant cells are diffuse and strongly positive for

Vimentin, CD 99, NKX2.2, and *FLI 1* (Figure 3). They are negative for *CK AE1/AE3, EMA, LCA, CD3, CD20, S100, CD56, Melan A, HMB-45, WT1, Synaptophysin*, and *Chromogranin A*. *Ki-67* proliferation index is around 40-50%. The histomorphological features and immune profile (surrogate marker) are compatible with Ewing sarcoma. The patient was discharged well and referred to an oncologist for further treatment.

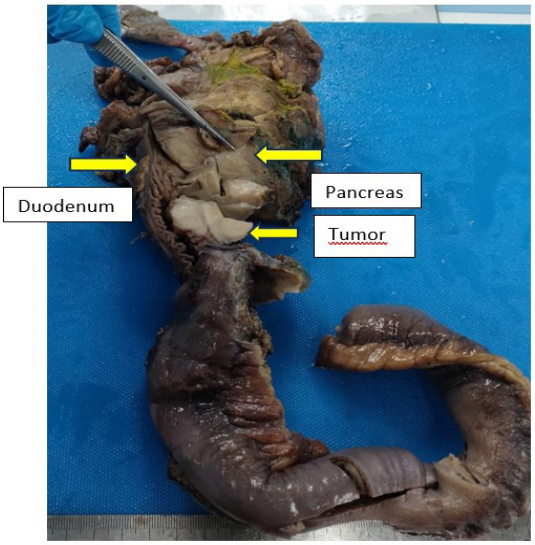

Figure 1: Gross picture ill-defined whitish solid tumour was noted at the head of the pancreas and uncinate process extending into the duodenum.

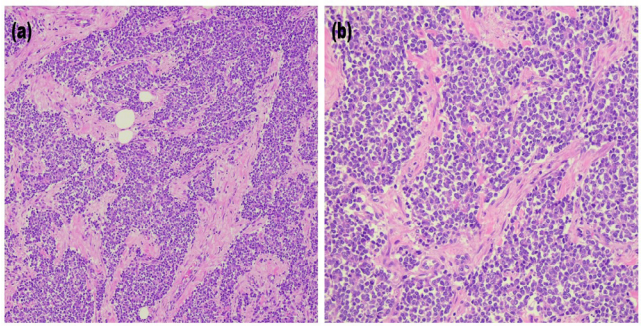

Figure 2: Hematoxylin and eosin (H&E) stain x 200 (a) showed solid sheets of tumour cells intersected by fibrous bands. Hematoxylin and eosin (H&E) stain x 400 (b) showed uniform small round to oval-shaped nuclei containing fine chromatin, inconspicuous nucleoli, scanty cytoplasm, and an indistinct cell membrane.

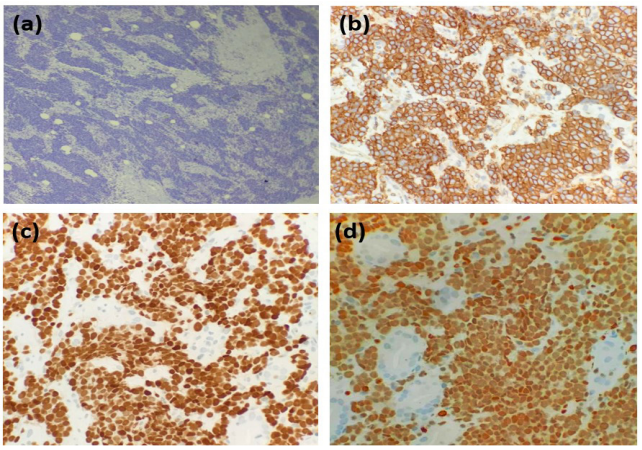

Figure 3: IHC stains x 400. CKAE1/AE3 (a) showed malignant cells are negative for epithelial marker (arrow). CD99 (b) showed malignant cells are strong membranous positivity for CD99. NKX2.2 (c) showed malignant cells are strong and diffuse positivity for NKX2.2. FLI1 (d) showed malignant cells are diffuse positivity for FLI1.

DISCUSSION

The vast majority of pancreatic neoplasms are classified as ductal adenocarcinomas, also called scirrhous carcinomas. This carcinoma is characterized by tubular glands and scattered clusters of neoplastic cells surrounded by desmoplastic stroma (3). Solid pseudopapillary tumours (SPTs), acinar cell carcinoma, pancreatoblastoma, pancreatic neuroendocrine tumour, small round blue cell tumours (EWS), and small cell carcinoma are rare types of neoplasm with high cellularity and stroma-poor neoplasia in this organ. Several distinct types of malignancies are the differential diagnoses that can account for these peculiar morphological characteristics.

The disease that is currently known as extraosseous Ewing sarcoma (EES) was previously referred to as the Ewing family of tumours (EFT) and primitive neuroectodermal tumour (PNET). A member of the ETS family of transcription factors, the *FLI1* protein is a structural component. Because of a reciprocal translocation of the *FLI1* and *EWSR1* genes at 22q12, also known as t(11;22)(q24;q12), the pathogenesis is brought about with this mutation. Through its influence on transcription and apoptosis, the fusion gene EWS-FLI1 contributes to

the formation of disease-causing tumours. MIC2 is a gene that encodes CD99, a glycoprotein found on the surface of cells and strongly expressed by the majority of EFT. Therefore, it is essential to conduct genetic and molecular investigations for confirmation. In this case, surrogate markers (Immunohistochemical stains) were performed to support the diagnosis. No molecular study was done.

Pancreatic Ewing sarcoma is an uncommon, aggressive malignant tumour. The most common symptoms are abdominal discomfort, followed by jaundice, vomiting, and dyspepsia. Ewing sarcoma of the pancreas has an expansile growth pattern, as opposed to the infiltrative growth pattern of pancreatic adenocarcinoma, which usually appears later in the disease progress. The pancreatic head is the most common site, and it is characterized by histological features such as sheets of small round blue cells with hyperchromatic nuclei and scanty cytoplasm. On the basis of the histomorphology of small round blue cells, the differential diagnoses include pancreatoblastoma, Ewing sarcoma (ES)/ PNET, desmoplastic small round cell tumour (DSRCT), and small cell neuroendocrine carcinoma (SNSC). According to the findings of immunohistochemical studies, malignant cells express a number of proteins, including CD99, FLI-1, NKX-2, O13, HBA71, 12E7, and RFB1. The neural marker Neuron Specific Enolase (NSE) and the neuroendocrine markers Chromogranin A and Synaptophysin are also expressed. A few studies have shown that the presence of neuronal secretory granules, neurofilaments, and pyknotic nuclear granules in the cytoplasm of a cell is a significant diagnostic characteristic for Ewing sarcoma (2). For the purpose of diagnosing peripheral PNETs, no recognized diagnostic criteria exist. As a result, the diagnosis of Ewing sarcoma of the pancreas was made on the basis of clinical symptoms, imaging investigations, and a biopsy, with confirmation coming from immunohistochemistry stains (surrogate markers) and molecular studies.

The most widely used treatment methods for localized Ewing sarcoma are primary induction chemotherapy, local therapy, and adjuvant chemotherapy. Surgical intervention is frequently preferred over alternative treatment options in the context of local therapy. Due to the risk of radiation-induced sarcomas, radiation therapy (RT) is often not suggested for patients who are undergoing complete resection. However, there is a case study that has been published in which the patient had a remarkable response to radiation therapy but was refractory to chemotherapy in a one-of-a-kind instance with ES that had spread to the pancreas (3). Modern adjuvant chemotherapy has significantly contributed to an increase in overall survival. Doxorubicin, Cyclophosphamide, Vincristine, Actinomycin-D, Ifosfamide, and Etoposide are medications that are commonly used in chemotherapy and have improved overall survival.

Pancreatic Ewing sarcoma frequently has a poor prognosis, with a five-year survival rate of less than 20%. The prognosis may be improved, however, with the use of extensive multimodality treatment, which may include surgical procedures, chemotherapy, and radiation therapy. Early detection and surgical treatment have resulted in a significant improvement in these patient's survival rates (4). There is a correlation between poor outcomes and factors such as increasing age, advanced stages of cancer, tumours that are not functioning, and tumours that are rapidly growing.

Ultimately, although molecular testing is typically necessary to establish a certain diagnosis of Ewing sarcoma, the presence of specific histological characteristics, immunohistochemical staining patterns (surrogate marker), clinical symptoms, and response to therapy strongly indicate the probability of Ewing sarcoma in this particular instance (5). To guide treatment decisions and improve results, the argument highlights the need to include Ewing sarcoma in the differential diagnosis of pancreatic masses, particularly in younger patients. This is important in order to improve outcomes (5).

CONCLUSION

The Ewing sarcoma of the pancreas is a malignant tumour that is aggressive and has a high probability of recurrence. In spite of the fact that Ewing sarcoma of the pancreas is a very rare entity, it is important to take it into consideration when developing a differential diagnosis of pancreatic masses, particularly in younger people. It is important to emphasize the importance of taking pancreatic Ewing sarcoma into account early in the differential diagnosis process when dealing with pancreatic tumours. This will allow for a better prognosis and a longer survival time. The survival percentage of these individuals has been considerably influenced by the advancements that have been made in the diagnosis and early surgical excision of the tumour.

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