PANCREATIC PRIMITIVE NEUROECTODERMAL TUMOR: CASE REPORT

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INTRODUCTION

Primitive neuroectodermal tumors (PNETs) are small round cell malignant tumors classified as part of the Ewing’s sarcoma family of neoplasms, which represents approximately 1% of all sarcomas. Predominantly occurring in soft tissues along the extremities, they have also been reported in a variety of organs such as kidney, urinary bladder, testis, ovary, uterus, heart and lung. Pancreatic PNETs (PPNET) are extremely rare and need to be distinguished from neuroendocrine carcinomas, small cell undifferentiated carcinoma, other childhood small round cell tumors, pancreaticoblastomas, and pancreatic tumors. Knowledge about PPNET is scarce; only 17 reports can be found in the literature. Here is reported the case of a 25 year old woman with a solid-cystic mass at the pancreatic head that later revealed to be a PPNET.

CASE REPORT

A 25 year old white woman, epileptic in use of fenobarbital for a year, was admitted presenting upper abdominal pain during the last 12 months. There was no other complaint and physical examination was unremarkable. Laboratory tests were within normal range except for a carcinoembryonic antigen (CEA) of 64.1 ηg/ml. Computed tomography scan of the abdomen revealed a solid-cystic mass in the cephalic portion of the pancreas, with normal remaining parenchyma (Figure 1). Main pancreatic duct was not dilated. The mass measured 4.2 x 4.0 cm and slightly dislocated the superior mesenteric artery anteriorly. Main hypothesis was a solid-cystic pseudopapillary tumor of the pancreas (Frantz’s tumor) and the patient was then submitted to a pancreaticoduodenectomy.

Gross analysis of the specimen showed a pancreatic segment of 5.0 x 5.0 x 3.0 cm infiltrated by a nodular and firm grey mass with foci of semi-solid yellowish material without macroscopic cystic areas (Figure 2). Lesion measured 4.0 x 3.0 x 2.5 cm. Adjacent pancreatic tissue was preserved. Margins were free. Tumor was composed of uniform small round cells with fine chromatin and scant cytoplasm. Some of the cells showed small nucleoli. The yellowish areas were identified as necrotic tissue being predominantly located away from the blood vessels. There was no evidence of disease in 10 lymph nodes dissected. Vascular and neural invasion were absent. Immunohistochemical profile was compatible with a primitive neuroectodermal tumor of the pancreas, been strongly positive for CD99 and negative for either neuroendocrine markers (synaptophysin and chromogranin) and lymphoid markers (CD20, CD3 and TDT). Lesion also expressed cytokeratin 8 (35BH1) and was negative for desmin (Figure 3). In situ hybridization (FISH) confirmed a t (11;22) (q24;q12) translocation.
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(21,22) rearrangement, which are associated with
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with round or oval nuclei without any distinctive
little or no stroma, cells are poorly differentiated,
neuroectodermal differentiation. Generally, there is
spectrum of appearances, reflecting the degree of
histological analysis, these lesions have a varied
area in Brazil. She died two months later from a sudden
cardiac event. Pancreatic insufficiency was not present
during the follow-up.

DISCUSSION

Primitive neuroectodermal tumors are poorly
differentiated, small round cell neoplasms that arise
from primitive neuroepithelial stem cells, showing
morphologic, histological, immunohistochemical
and ultrastructural evidence of neuroectodermal
differentiation. The ES/PNET family includes several
neoplastic entities, such as malignant small-cell tumor
of the thoracopulmonary region (Askin's tumor),
paravertebral small-cell tumor, atypical ES, PNET of the
bone and extra osseous Ewing sarcoma. PNETs occur in
the pediatric, adolescent and young adult population,
and although they may develop in almost any bone or
soft tissue, they are usually peripheral.

Diagnosis is commonly troublesome to achieve
since pain and swelling are the most common
symptoms and there is no specific radiologic image.
At histological analysis, these lesions have a varied
spectrum of appearances, reflecting the degree of
neuroectodermal differentiation. Generally, there is
little or no stroma, cells are poorly differentiated,
with round or oval nuclei without any distinctive
cytoplasm. Additionally, immunohistochemistry
is a helpful diagnostic tool revealing a high
expression of CD99. When doubt persists in situ
hybridization (FISH) or RT-PCR analysis can be
performed showing a t(11;22) translocation or a
(21,22) rearrangement, which are associated with
hybrid transcripts of the EWS gene with the FLI1 or ERG
gene. The balanced t (11;22)(q24;q12) chromosome
translocation occurs in about 83% of the cases of
Ewing's sarcoma and is a genotypic marker. At
diagnosis, approximately 25% of the patients with
ES/PNET have detectable metastatic disease to bone,
lung or bone marrow, and nearly all patients have
undetected micrometastases, so local therapy alone
should not be encouraged. Based on this, standard
care is surgery or radiotherapy for local control
combined with systemic chemotherapy. There is
also no concrete evidence about the best moment
for the systemic therapy. For instance, chemotherapy
has been used for pancreatic PNETs preoperatively
allowing an unresectable mass to regress and have
a salvage R0 resection; postoperatively, Perek et al.
reported one man who underwent three surgical
procedures associated with first, second and third
lines chemotherapy for a metastatic PPNET, having
one of the longest known overall survival (50 months);
and there is even one patient successfully treated with
Vincristine, Doxorubicin and Cyclofosfamide alone,
having no evidence of disease after 43 months. The
best chemotherapy regimen is also yet to be defined
and despite all advances in the disease's knowledge
and treatment, 5-year survival rates still range around
50%.

Pancreatic PNETs are particularly rare. Only 17
reports can be found in the literature. These lesions
should be differentiated from poorly differentiated
small round cell tumors of the pancreas, pancreatic
endocrine tumors and Frantz's tumor. Due to their
rarity the best therapeutic strategy for pancreatic
PNETs is yet to be defined. At this time, recomendations
are based on the ones for the Ewing's sarcoma
family. A major drawback in this case is the fact that
she abandoned the follow-up. An autopsy was not
performed and her death from a sudden cardiac
arrest remains a mystery. Her last exams (two months
earlier) showed no signs of pancreatic insufficiency
or paraneoplastic ectopic hormonal production. It
is also unlikely that a severe doxorubicin-induced
cardiotoxicity occurred, since the cumulative dose
was low and there was no evidence of pre-existing
heart disease.

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