ABCDDV/928

ABCD Arq Bras Cir Dig
2013;26(2):159-161

Letter to the Editor

PANCREATIC PRIMITIVE NEUROECTODERMAL TUMOR: CASE REPORT

Tumor primitivo ectodérmico pancreático: relato de caso

Andre Roncon **DIAS**, Thatyana **ARANTES**, Renato Catojo **SAMPAIO**,
Ricardo **JUREIDINI**, Jose Eduardo Monteiro da **CUNHA**, Ivan **CECCONELLO**

From the Pancreatic Surgery Division, Department of Gastroenterology, University of São Paulo, São Paulo, SP, Brazil..

Correspondence:
André Roncon Dias
Email: roncon86@hotmail.com

Financial source: none
Conflicts of interest: none

Received for publication: 19/07/2011
Accepted for publication: 13/11/2012

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[1]. 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[2, 3]. Pancreatic PNETs (PPNET) are extremely rare and need to be distinguished from neuroendocrine carcinomas, small cell undifferentiated carcinoma, other childhood small round cell tumors, pancreatoblastomas, 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 carcioembryonic 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.

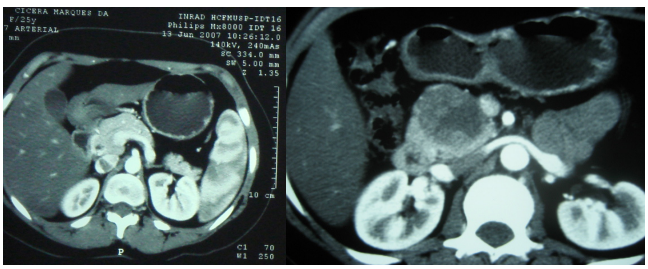


FIGURE 1 - CT scan showing a 4.2 x 4.0 cm heterogeneous solid–cystic mass in the pancreatic head

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.

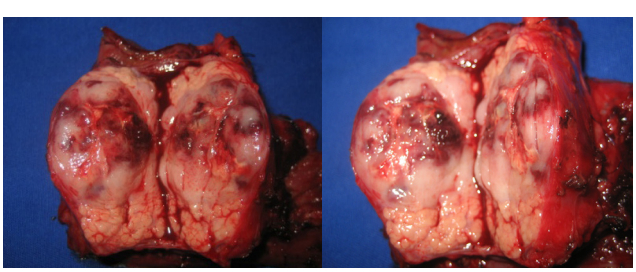
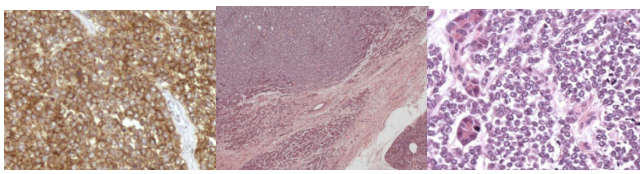


FIGURE 2 - Macroscopic aspect of the specimen



A B C

FIGURE 3 - A: Immunohistochemistry with strong cytoplasmic membrane positivity to MIC2 (Glycoprotein CD99); B: the tumors were composed of atypical small round cells with scant cytoplasm (H&E, ×4); C: tumor cells with round nucleus and scant cytoplasm (H&E, ×40)

Postoperatively, a urinary tract infection was treated with intravenous antibiotics. No major surgical complications occurred. After discharge, patient received three cycles of chemotherapy, first one consisted of vincristine (1.5mg/m^2), dactinomicine (1.25mg/m^2) and ifosfamide (1.8g/m^2), followed by two cycles of vincristine (1.5mg/m^2), doxorrubicin (40mg/m^2) and cyclofosfamide (1.2g/m^2).

The patient remained disease free for six months and after this period she abandoned the follow-up and returned to her hometown in a remote countryside 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[2]. 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[2]. Additionally, immunohistochemistry can be 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 [4]. 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 [5,6]. 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[7]; postoperatively, Perek et al[2] reported one men 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 Ciclofosfamide alone, having no evidence of disease after 43 months[3]. 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%[5, 6].

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, recomedations 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 paraneoplasic 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[13].

REFERENCES

1. Schutte WP, Knight PJ. Precocious puberty because of a pancreatic neuroectodermal tumor. J Pediatr Surg. 2006 Nov;41(11):1916-8.
2. Perek S, Perek A, Sarman K, Tuzun H, Buyukunal E. Primitive neuroectodermal tumor of the pancreas. A case report of an extremely rare tumor. Pancreatology. 2003;3(4):352-6.
3. Movahedi-Lankarani S, Hruban RH, Westra WH, Klimstra DS. Primitive neuroectodermal tumors of the pancreas; a report of seven cases of a rare neoplasm. Am J Surg Pathol. 2002 Aug;26(8):1040-7.
4. Delattre O, Zucman J, Melot T, et al. The Ewing family of tumors -- a subgroup of small-round-cell tumors defined by specific chimeric transcripts. N Engl J Med. 1994 Aug 4;331(5):294-9.

5. de Alava E, Gerald WL. Molecular biology of the Ewing's sarcoma/primitive neuroectodermal tumor family. J Clin Oncol. 2000 Jan;18(1):204-13.
6. Terrier P, Llombart-Bosch A, Contesso G. Small round blue cell tumors in bone: prognostic factors correlated to Ewing's sarcoma and neuroectodermal tumors. Semin Diagn Pathol. 1996 Aug;13(3):250-7.
7. Haq MM, Legha SS, Choksi J, et al. Doxorubicin-Induced Congestive Heart Failure in Adults. Cancer 56:1361-5. 1985.
8. Luttges J, Pierre E, Zamboni G, et al. [Malignant non-epithelial tumors of the pancreas]. Pathologe. 1997 May;18(3):233-7. [Article in German]
9. Shorter NA, Glick RD, Klimstra DS, Brennan MF, Laquaglia MP. Malignant pancreatic tumors in childhood and adolescence: The Memorial Sloan-Kettering experience, 1967 to present. J Pediatr Surg. 2002 Jun;37(6):887-92.
10. Bulchmann G, Schuster T, Haas RJ, Joppich I. Primitive neuroectodermal tumor of the pancreas. An extremely rare tumor. Case report and review of the literature. Klin Padiatr. 2000 Jul-Aug;212(4):185-8.
11. Takeuchi M, Kuwae Y, Hamana K, et al. Primitive neuroectodermal tumor of the pancreas. Arch Histopathol D D. 2003 10: 23-26.
12. Welsch T, Mechtersheimer G, Aulmann S, et al. Huge primitive neuroectodermal tumor of the pancreas: report of a case and review of the literature. World J Gastroenterol. 2006 Oct 7;12(37):6070-3.
13. Doi H, Ichikawa S, Hiraoka A, et al. Primitive neuroectodermal tumor of the pancreas. Intern Med. 2009;48(5):329-33.
14. Bristow M R, Mason J W, Billingham M E, Daniels J R. Dose effect and structure function relationships in doxorubicin cardiomyopathy. Am Heart J. 1981; 102(4): 709-18.