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Metastatic adult granulosa cell tumor mimicking a benign pancreatic cyst

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Abstract We report an unusual case of metastatic adult granulosa cell tumor in the head of pancreas mimicking a benign pancreatic cyst in a 43-year-old female. Clinically, it was considered a benign cyst of the pancreas based on its appearance by imaging and that repeated fine-needle aspiration and cytologic examination of cystic fluid failed to identify malignant cells. The cyst in her pancreas grew slowly during the 15 months of close follow-up. Subsequent drainage and open biopsy of the cyst wall established the diagnosis of metastatic adult granulosa cell tumor that was confirmed in pancreaticoduodenectomy specimen. Immunohistochemical study and clinical history were critical to make the correct diagnosis and to differentiate this tumor from other more commonly encountered cystic neoplasms of the pancreas.

Keywords: Adult granulosa cell tumor; Pancreas; Pancreatic cyst; Cystic neoplasm of the pancreas

1. Introduction

Metastatic cancer in the pancreas is a rare event with the reported incidences ranging from 1.6% to 10.1% [1,2]. Metastatic cancer in the pancreas was found in 261 (10.1%) of 2587 consecutive autopsies performed between 1973 and 1978 at Memorial Hospital in New York with the most common primary tumors being breast cancer (20%), lung cancer (19%), and melanoma (9%) [2]. However, metastasis in the pancreas was only identified in 81 cases (1.6%) in another study of 4955 autopsies performed between 1977 and 1997, and the most common primary tumors were lung cancer, tumors of the gastrointestinal tract, and kidney tumors [1]. Because most patients had metastasis to multiple other sites at the time of diagnosis of metastasis in pancreas, resections of pancreatic metastases were rare [1]. Renal cell carcinoma is the most frequent metastatic cancer in pancreatectomy specimens followed by lung cancer, breast cancer, colon cancer, sarcoma, and melanoma [3-6]. Favorable outcomes have been achieved in patients who have selected metastatic cancer, most notably those with renal cell carcinoma. Metastases from gynecologic tract malignancies in pancreas are extremely rare. Only a few cases of metastatic uterine cervical cancer [7] and rare cases of metastatic endometrial carcinoma [6,8,9] have been also reported. To our knowledge, there are no reports of metastatic sex cord tumors in pancreas, including granulosa cell tumor. Here, we report a metastatic adult granulosa cell tumor (AGCT) in the pancreas presenting as a slow-growing simple cyst in the head of pancreas clinically mimicking a benign pancreatic cyst. Antibody titers and sources used for the immunohistochemical studies were the following: CD10 (1:70) and synaptophysin (1:600) from Leica/Vision BioSystem (St. Louis, MO, USA), chromogranin (Millipore, Billerica, MA, USA; 1:4000), inhibin (1:50; AbD Serotec, Raleigh, NC, USA), β-catenin (1:500; BD Biosciences, San Jose, CA, USA), CD56 (1:50; Invitrogen, Carlsbad, CA, USA), and CD117 (1:100; Dako, Carpinteria, CA, USA).

2. Case report

A 43-year-old G4P2 abortus 2 woman underwent right salpingo-oophorectomy in 1995 for an ovarian cyst. On gross examination, right ovary measured 14.0 cm in maximal

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dimension with a smooth outer surface. By light microscopy, it was an AGCT with no significant nuclear atypia or necrosis. Scattered Call-Exner bodies were present. Up to 7 mitotic figures per 10 high-power fields were identified. The right fallopian tube was not involved by the tumor. In December 2001, she found a small mass at the site of the Pfannenstiel incision that was resected and showed recurrent AGCT. Further workup in January 2002 by computed tomographic (CT) scans revealed complex bilateral pelvic masses filling the anterior pelvis. There was no involvement of the uterus, liver, spleen, pancreas, or lungs. There was no pelvic or inguinal lymphadenopathy, and no ascites or problems with the bowel were noted. She underwent exploratory laparotomy, total abdominal hysterectomy, left salpingo-oophorectomy, removal of right ovarian remnant, omentectomy, bilateral pelvic lymph node dissection, and optimal tumor reductive surgery. Microscopically, recurrent/metastatic AGCT involved left ovary, omentum, space of Retzius, cul-de-sac, and serosal surface of sigmoid colon. Bilateral pelvic lymph nodes were negative for tumor. Cytologic examination of pelvic washing was positive for AGCT. The patient received 6 courses of Taxol and carboplatin chemotherapy. In October 2005, the patient was found to have a 4.2 × 4.1-cm cystic lesion in the head of the pancreas with an indeterminate 2.2 × 1.3-cm cystic area near the rectum at previous hysterectomy site, but no other lesions were identified by abdominal CT scan. The CT scan of the pancreatic cyst is shown in Fig. 1A. There was no evidence of pancreatic duct or common duct dilatation noted proximal to this lesion. Repeated fine-needle aspirations of pancreatic cyst wall had negative results, and the cystic fluid was negative for malignant cells. Clinically, it was considered that this most likely represent a benign cyst of the pancreas that just required follow-up and no surgical intervention. The patient was observed closely by CT scans. Because the cyst continued to enlarge and the patient developed metastatic AGCT in periaortic lymph nodes, the patient was taken to the operating room for drainage and underwent biopsy of the cyst wall of her pancreatic cyst with resection of periaortic lymph nodes in January 2007. A frozen section diagnosis of a malignant neoplasm, favor metastatic AGCT, was rendered on the biopsy of the cystic wall. A pancreaticoduodenectomy was then performed. The pancreaticoduodenectomy specimen showed a 3.8 × 3.8 × 3.8-cm cyst in the head of the pancreas with no connection with pancreatic duct (Fig. 1B). The cyst was filled with red-tan hemorrhagic fluid. On histologic examination, there was no lining of the cyst. The cyst wall was composed of sheets of small blue cells invading pancreatic parenchyma with fibrous septae that contained small pancreatic ductules. The cells were bland, with pink cytoplasm, ill-defined cell borders, oval nuclei with prominent grooves, fine chromatin, and with no prominent nucleoli (Fig. 2A and 2B). There was no necrosis, but rare mitoses were present. Immunohistochemistry was performed and showed that tumor cells were positive for inhibin and negative for CD10, pancytokeratin, chromogranin, synaptophysin, β-catenin, CD56, and CD117 (Fig. 2C-2F), which were consistent with the diagnosis of a metastatic AGCT. Currently, the patient is still alive 30 months after pancreaticoduodenectomy and has stable peritoneal disease.

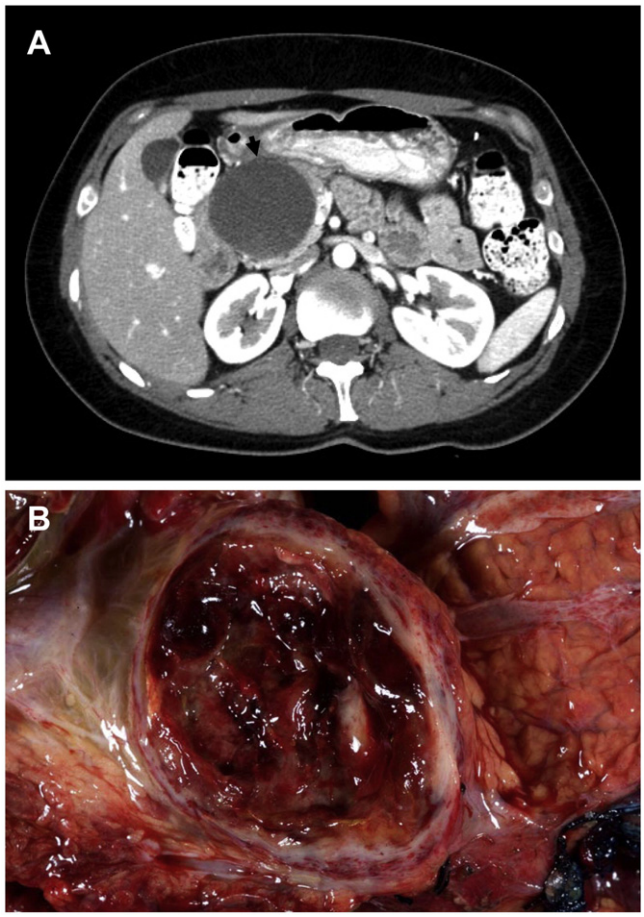

Fig. 1. (A) Axial CT image reveals a simple cyst in the head of pancreas (arrow). (B) The pancreaticoduodenectomy specimen shows a hemorrhagic cyst in the head of pancreas.

3. Discussion

Adult granuloma cell tumor is an uncommon sex cord stromal tumor of the ovary accounting for approximately 5% of all primary ovarian malignancies [10-12]. Usually, they are localized in the ovary and have an indolent clinical course with late relapses and long survival. Tumor stage, large tumor size, bilateral ovarian involvement, ovarian capsule rupture, and high mitotic counts have been reported to be associated with risk of recurrence in patients with AGCT [10-12]. Mitotic count of more than 5 mitoses in 10 high-power microscopic fields is typically regarded as the "cutoff" point for increased risk of more aggressive disease [13]. In our case, 7 mitoses per 10 high-power fields were identified in her primary AGCT of right ovary.