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Case Report

Mucinous cystic neoplasm of the pancreas with severe dysplasia during pregnancy: Case report and review of the literature

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Abstract

Objective: Mucinous cystic neoplasm (MCN) of the pancreas occurs mainly in women aged 40–60 years, so it is extremely rare in pregnant woman.
Case Report: A 28-year-old woman in the ninth week of pregnancy was referred to our hospital due to a tumor of the abdominal cavity. Abdominal ultrasound demonstrated a huge multicystic lesion in the left upper abdomen. There are mural nodules and hypertrophic septa partially with the presence of blood flow inside the tumor. Endoscopic ultrasonography was performed and a diagnosis of possible pancreatic MCN was made. At the second trimester, distal pancreatectomy with splenectomy was performed. Histopathological analysis of the specimen revealed a pancreatic MCN with severe dysplasia. Immunohistochemically, the tumor was positive for both progesterone and estrogen receptors in the stromal cell nuclei; moreover, MIB-1 stained positive in 10–20% of the nuclei in the epithelium with severe dysplasia.
Conclusion: MCN carries malignant potential, therefore, early detection and complete surgery is recommended. MCN in pregnancy is rare and the abdomen is distended during pregnancy, so clinicians can easily miss the presence of the tumor. We should recognize the presence of MCN in pregnant woman. We speculate that the presence of blood flow within the tumor and MIB-1-positive cells can be a predictor for premalignant or malignant MCN.

Keywords: dysplasia; MIB-1; mucinous cystic neoplasm; pancreas; pregnancy

Introduction

Mucinous cystic neoplasm (MCN) of the pancreas is an uncommon tumor characterized by mucin-producing columnar epithelium and a dense ovarian-type stroma [1,2]. MCN occurs almost exclusively in women aged 40–60 years, so it is extremely rare in pregnant woman. Pancreatic MCNs have been reported as potentially sex-hormone-sensitive, such as estrogen and progesterone, and therefore have rapid growth during pregnancy [2]. Pancreatic MCN presents a clinical problem in that it always carries malignant potential [3]. Cyst diameter and presence of mural nodule have been reported as predictive findings of malignant MCN [4].

In this report, we describe a 28-year-old woman with a large pancreatic MCN with severe dysplasia during pregnancy and also discuss some interesting findings regarding prediction of premalignant or malignant MCN.

Case report

A 28-year-old gravida 2, para 1 woman in the ninth week of pregnancy was referred to our hospital due to a tumor of the abdominal cavity. She had noticed a tumor over the past several years, but had taken no action. She had no previous history and no medication before pregnancy. Physical

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examination suggested the presence of an elastic hard mass, approximately 15 cm in diameter, in the left upper quadrant. Abdominal ultrasound demonstrated a huge multicystic lesion in the left upper abdomen. There are mural nodules and hypertrophic septa partially with the presence of blood flow inside the tumor (Fig. 1). Further evaluation by magnetic resonance imaging showed a multiloculated cystic tumor, measuring 14 cm × 12 cm, with a thick capsule probably originating from the distal pancreas. Thereafter, endoscopic ultrasonography was performed and a diagnosis of possible pancreatic MCN was made. Laboratory tests showed slight anemia with normal levels of amylase and liver enzymes. Cancer antigen (CA) 19-9 level was normal (10 U/mL; normal range: <37 U/mL), but CA125 level was high (76.3 U/mL; normal range: <35 U/mL). She was advised about possible prognoses such as fetal intrauterine growth restriction by the tumor, malignant potential of the tumor, and rupture of the tumor. A decision was made to resect the tumor at the second trimester. An operation was performed at 18 + 3 weeks of gestation. A laparotomy was performed, and a huge, smooth cystic tumor was found arising from the body and tail of the pancreas and adhering to the spleen and retroperitoneum. Distal pancreatectomy with splenectomy was performed.

The specimen obtained at surgery was multilocular, 15 cm × 14 cm, 1110 g. The cystic mass had a smooth external surface and it was filled with dark yellowish fluid. Histopathological analysis showed a mucin-producing tall columnar epithelium lining the inner wall of the cyst, with ovarian-type stromal tissue (Fig. 2A). The epithelium had a focal papillary architecture with severe atypia, giving a diagnosis of pancreatic MCN with severe dysplasia (Fig. 2B). Immunohistochemical studies showed positive staining for both progesterone and estrogen receptors in the stromal cell nuclei (Fig. 2C and D). Moreover, we further performed immunohistochemical studies using a proliferation marker, MIB-1, which stained positive in about 10–20% of the nuclei in the epithelium with severe dysplasia (Fig. 3B).

She was discharged on postoperative day 16. After that, she suffered from mild glucose intolerance (hemoglobin A1c level: 6.0%; normal range: 4.3–5.8%; fasting blood glucose level: 127 mg/dL) at 32 weeks of gestation, but she avoided any insulin requirement during pregnancy. Otherwise, she had an uneventful postoperative course, and at 39 + 4 weeks of gestation, she gave birth by normal vaginal delivery to a 2980 g healthy baby girl. The placenta weighed 610 g and gross examination displayed a hypertwisted cord with velamentous insertion. After delivery, she remained disease-free until the writing of this article, 8 months after surgery.

Discussion

To the best of our knowledge, 17 cases of pancreatic MCN associated with pregnancy have been reported since the first report in 1986 [5]. Eight cases were histologically diagnosed as benign mucinous cystadenoma, whereas six cases were diagnosed as mucinous cystadenocarcinoma and three as MCN with dysplasia (also referred to as "borderline tumor") [3,6,7]. Our case might be the fourth case of pancreatic MCN with dysplasia in association with pregnancy (Table 1). Pancreatic MCNs usually grow slowly, but they sometimes show rapid growth during pregnancy. It has been reported that pancreatic MCNs may be responsive to sex hormones, accounting for their tendency to grow to enormous size especially during pregnancy [6].

Pancreatic MCNs pose a clinical problem in that they always carry malignant potential [3]. Also, pregnancy with a large MCN can be a risk for fetal growth restriction [8]. Therefore, prompt and complete surgery is recommended as the treatment for MCN [1]. The prognosis for MCNs treated with complete surgical resection without any additional treatment is excellent, with a 5-year survival rate of 94% [2]. Generally, the second trimester is believed to be relatively safe for surgery during pregnancy [3,6]. In fact, our case was MCN with severe dysplasia, in other words, a premalignant condition, so we could prevent the progression to malignancy by performing complete resection during pregnancy.

We reviewed factors believed to predict the malignancy of MCN. Patients with carcinoma had a significantly larger size of cyst and higher frequency of mural nodules than those with adenoma [4]. CA19-9 concentration >37 U/mL has a positive predictive value of 95.7% for potentially malignant lesions but a sensitivity of only 35.8% [9]. Carcinoembryonic antigen concentration >800 ng/mL is a moderately sensitive (48%) but highly specific (98%) marker for mucinous cystadenoma or mucinous cystadenocarcinoma [10]. Progesterone stimulation of the stroma in MCNs may actually suppress malignant

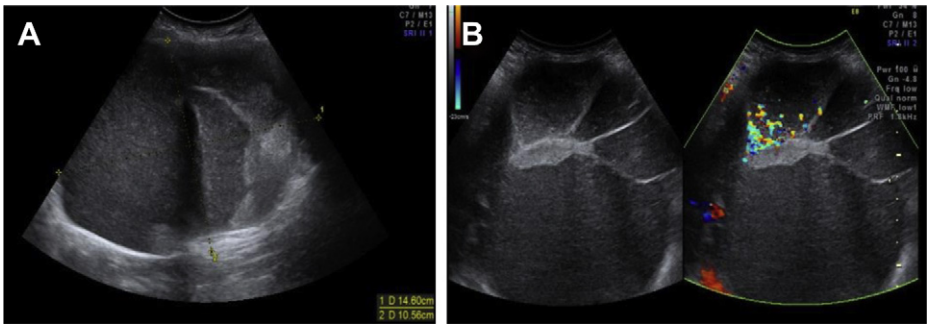

Fig. 1. Ultrasound of pancreatic mucinous cystic neoplasm (MCN) performed in the ninth week of gestation. (A) Abdominal ultrasound demonstrating a large cystic mass (14 cm × 11 cm) with septations and mural nodules. (B) Blood flow was present around the mural nodule and a hypertrophic septum in the tumor.

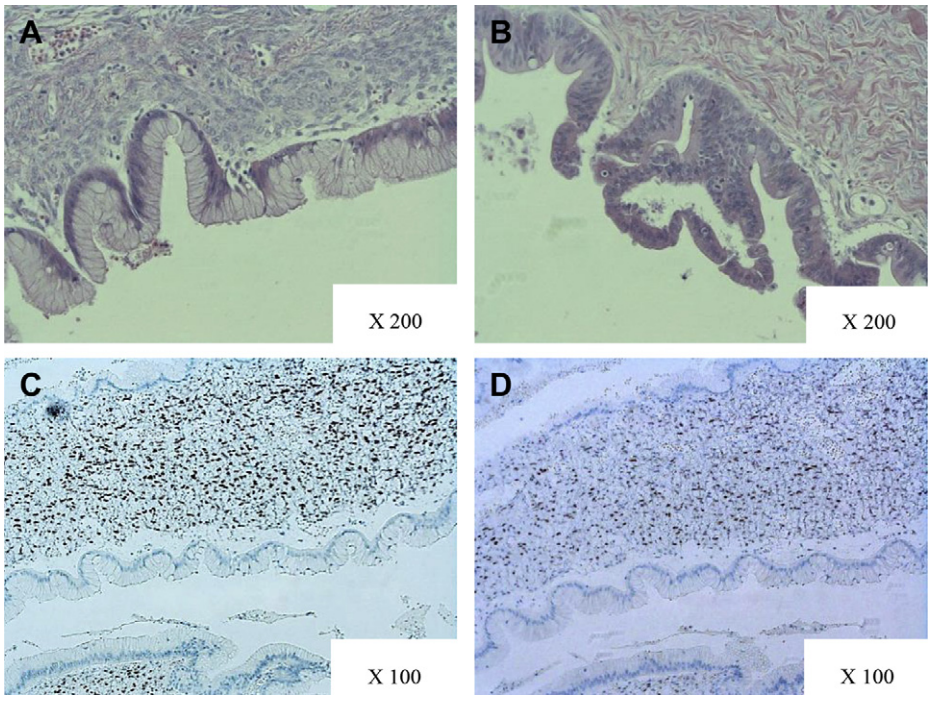

Fig. 2. Microscopic pathological features of the resected pancreatic cystic neoplasm. (A) Histopathological examination revealed a pancreatic cyst lined with mucin-producing columnar epithelium and wall with ovarian-type stroma (hematoxylin–eosin, 200×). (B) Nuclei of the epithelium were swollen and the polarity of the nuclei was disturbed. These findings led to the diagnosis of mucinous cystic neoplasm (MCN) with focal severe dysplasia (hematoxylin–eosin, 200×). (C, D) Immunohistochemical examination revealed ovarian-type stromal cells expressing progesterone receptor (C), and estrogen receptor (D) (original magnification, 100×).

proliferation of epithelial cells and an absence of progesterone receptors has been correlated with worse outcomes [2]. There are mural nodules and hypertrophic septa partially with the presence of blood flow inside the tumor. Generally, blood flow within the tumor alerts us to the possibility of malignancy. There are no reports regarding the blood flow in MCNs, but this finding can indicate the possibility of premalignant or malignant MCNs. Next, in our case, MIB-1 immunohistochemical staining was positive in the nuclei in the epithelium with severe dysplasia. This is believed to be the first report to examine the expression of MIB-1 in MCNs. MIB-1 can respond to the dividing cells and reflect the aggressiveness of cellular proliferation in human neoplasms. Therefore, the presence of MIB-1 positive cells can be a predictor for premalignant or malignant MCNs.

In our case, the patient was suffering from mild glucose intolerance after resection of the pancreatic body and tail, but it was transient with spontaneous remission. Herring et al [8] have reported that a patient with mucinous cystadenocarcinoma developed gestational diabetes after resection of the pancreatic tail. It is not clear whether resection of the pancreas can be the etiology of gestational diabetes, but we should be on guard not only for recurrence of the tumor but also for the occurrence of gestational diabetes after surgery for MCN.

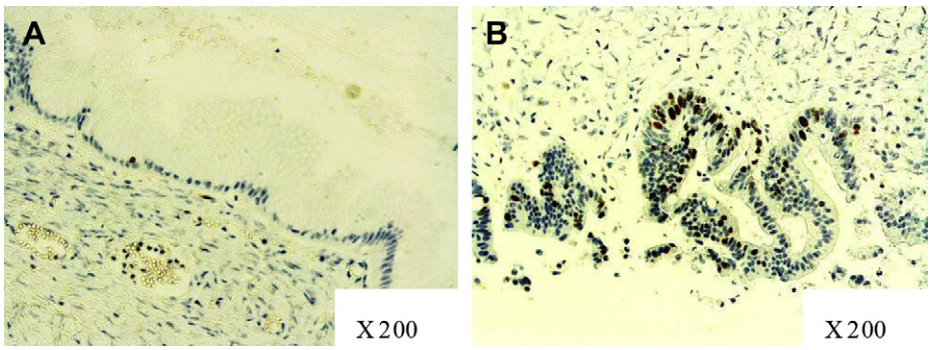

Fig. 3. Immunohistochemical examination of MIB-1 staining of the epithelium of mucinous cystic neoplasm (MCN). (A) Few MIB-1-positive cells were revealed at the columnar epithelium without dysplasia (original magnification, 200×). (B) MIB-1 staining was positive in 10–20% of the nuclei in the epithelium with focal severe dysplasia (original magnification, 200×).

Table 1
Summary of pancreatic mucinous cystic neoplasms (MCNs) with dysplasia in association with pregnancy reported in the literature.

Ref.	Age (y)	Operation (wk)	Size (cm)	Pathological diagnosis	HR	
					ER	PgR
[3]	30	10	18 × 14	Moderate dysplasia	+	+
[6]	32	15	15 × 13	Low grade dysplasia	+	+
[7]	38	2nd trimester	14 × 14	Borderline	ND	+
Our case	28	18	14 × 12	Severe dysplasia	+	+

ER = estrogen receptor; HR = hormone receptor; ND = not described; PgR = progesterone receptor.

In conclusion, we report a case of MCN with severe dysplasia during pregnancy. MCN in pregnancy is rare and the abdomen is distended during pregnancy, so the patient and medical staff can easily miss the presence of the tumor. MCNs carry malignant potential, so complete surgery, if possible during the second trimester, is recommended. We hope that many obstetricians can keep the clinical features of MCN in mind. The presence of blood flow within the tumor and of MIB-1-positive cells can be a predictor for premalignant or malignant MCN.

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