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Large Mucinous Cystadenoma of the Pancreas During Pregnancy: Report of a Case

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Abstract
A 33-year-old woman, gravida 2, para 1, was diagnosed to have a benign mucinous cystic neoplasm of the pancreas 5 months before delivery. The tumor measured 12 cm in diameter at the time of diagnosis. The antenatal course was uneventful, and a vaginal delivery produced a normal infant. By 2 months after delivery, the tumor reached 18 cm. At surgery, a huge cyst was found to originate from the pancreas, and a distal pancreatectomy with splenectomy was performed. The cystic mass was multilocular 18 × 17 × 12 cm, 2450 g, and red to yellowish-gray. The histologic diagnosis was benign mucinous cystadenoma. The postoperative course was uneventful, and the patient remains free of recurrence at 7 months after surgery. To our knowledge, this is only the fifth reported case of pancreatic mucinous cystadenoma in association with pregnancy. This is the first reported case of a successful resection of such a tumor after delivery.

Key words Mucinous cystadenoma · Mucinous cystic neoplasm · Pancreas · Pregnancy

Introduction

Mucinous cystic neoplasm (MCN) of the pancreas is rare and it occurs predominantly in middle-aged women. Mucinous cystic neoplasms possess two distinct components: an inner mucinous epithelial layer and an outer dense cellular ovarian-like stromal layer.[1,2] Mucinous cystic neoplasm stromal cells have been shown by immunohistochemistry to be positive for estrogen receptor and progesterone receptor, thus suggesting regulation by sex hormones.[1,2] Although pregnancy can be complicated by pancreatic neoplasms, MCN associated with pregnancy is extremely rare; only four cases of pancreatic mucinous cystadenoma and two cases of pancreatic mucinous cystadenocarcinoma have been previously reported.[3–8]

The management of MCN of the pancreas, particularly during pregnancy, is not standardized. The decision whether to observe or to operate can be difficult and complicated. There are few data available concerning the conservative management of pancreatic MCN during pregnancy. We herein report a case of MCN of the pancreas that was incidentally found in a pregnant patient and was resected 3 months after normal delivery.

Case Report

A nontender epigastric mass of the upper abdomen was detected by palpation in a 33-year-old woman, gravida 2, para 1, during the 17th week of gestation. She was referred to our institution for further evaluation. The patient had complained of discomfort in the left hypochondrium for 1 year. Her previous pregnancy had been uncomplicated and resulted in a vaginal birth, and her family and medical histories were unremarkable. The blood and serum biochemistry values were within normal limits. Abdominal ultrasound showed a large multilocular hypoechoic mass with septa in the left upper abdomen. Magnetic resonance imaging showed a 12-cm diameter multilocular cystic lesion without any solid components in the body and tail of the pancreas. Mucinous cystic neoplasm of the pancreas was diagnosed. The patient was informed of the possibilities of malignancy, rapid growth and rupture of the tumor, and fetal intrauterine growth restriction. However, the decision was made to simply observe the mass because of the desire of the patient and few signs of malignant MCN on imaging modalities in the second trimester.

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The patient was followed up at a public clinic during the rest of her pregnancy. The antenatal course was uneventful and vaginal delivery produced a normal infant. Two months after delivery, the patient's abdomen remained abnormally distended and she continued to suffer upper abdominal discomfort. Abdominal computed tomography showed an 18-cm diameter multilocular cystic lesion of the pancreas without any solid components (Fig. 1).

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, mesocolon, and retroperitoneum (Fig. 2A). A distal pancreatectomy with a splenectomy was performed. The specimen obtained at surgery was multilocular, 18 × 17 × 12 cm, 2450 g, and red to yellowish-gray. The cystic mass had a smooth external surface and it was filled with thin, dark yellowish-green fluid, which had a carcinoembryonic antigen (CEA) concentration of 36800 ng/ml and a carbohydrate antigen (CA) 19-9 level of >10000 U/ml (Fig. 2B,C). Microscopically, the cyst wall was lined by a columnar epithelium supported by an ovarian-like stroma. The histologic diagnosis was benign mucinous cystadenoma with tumor-free tissue margins (Fig. 3A). Immunohistochemical studies showed positive staining for α-smooth muscle actin (SMA; Fig. 3B), and no staining for either progesterone receptor or estrogen receptor in the stromal component. The postoperative course was uneventful, and the patient remains free of recurrence at 7 months after surgery.

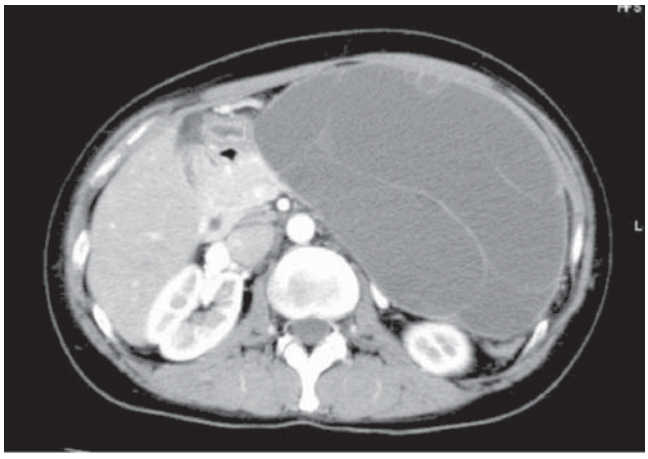


Fig. 1. Abdominal computed tomography scan shows a multilocular cystic lesion of the pancreas, 18 cm in diameter, without solid components

Discussion

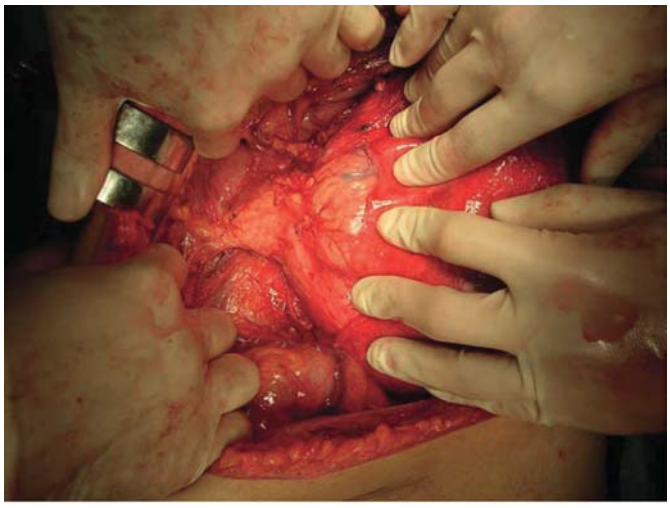
To our knowledge, there have only been five reported cases, including ours, of mucinous cystadenoma associated with pregnancy (Table 1).[3–6] All four previously reported cases were successfully treated by resection during pregnancy, thus resulting in the birth of healthy infants. A rapid tumor growth over the course of pregnancy has been reported.[3,4] As a result, tumor growth appears to be hormonally regulated. In addition, immunohistochemical staining revealed positivity for sex hormone receptors. In our case, the tumor grew from 12 to 18 cm in size over 8 months. This is the first reported case of successful tumor resection after delivery.

Current imaging modalities are not sufficiently accurate to allow for differentiation among multiple benign, premalignant, and malignant lesions.[9] Nevertheless, multilocularity and the presence of papillary projections or mural nodules as well as a large size (>15 cm in diameter) or increasing size have been reported as signs of malignant MCN.[1,2,9] In our patient, there were few signs of malignant MCN in the second trimester.

Several reports have addressed the diagnostic value of a cyst fluid analysis in differentiating cystic lesions of the pancreas.[10,11] Several tumor markers have been tested, and CEA has been shown to be a useful marker for differentiating mucinous tumors from nonmucinous ones. CA19-9 is a less discriminating marker in the diagnosis of such tumors. High levels of CEA (>400 ng/ml) and CA19-9 (>50,000 U/ml) in cyst fluid have a good specificity for differentiating pseudocysts from mucinous tumors but do not provide a reliable determination of malignant tumors.[10] Moreover, preoperative percutaneous aspiration of a cystic lesion is debatable because of the theoretical risk of tumor cell seeding. A cyst fluid analysis may help in the differential diagnosis, particularly in patients with unilocular or paucilocular lesions, thus precluding an unjustified resection in patients with benign cystic lesions of the pancreas.[10]

In ovarian neoplastic lesions such as MCN, smooth muscle differentiation of the stromal cells has been reported.[12–14] The phenotypic plasticity of ovarian stroma and its propensity for smooth muscle differentiation were the results of its response to the presence in the lesion of various stimuli, and these phenomena are characteristic of ovarian stroma. Izumo et al.[14] reported the similar nature of the ovarian stroma in MCN of the pancreas and the stromal cells in MCN of the ovary from the point of view of smooth muscle differentiation. Regarding SMA, both the ovarian stroma in MCN of the pancreas and the stromal cells in MCN of the ovary showed the same positivity rate (100%).

The involvement of sex hormones in the genesis of MCN of the pancreas has been supported by the immunohistochemical demonstration of various hormonal receptor markers and hormone-associated markers.[4]



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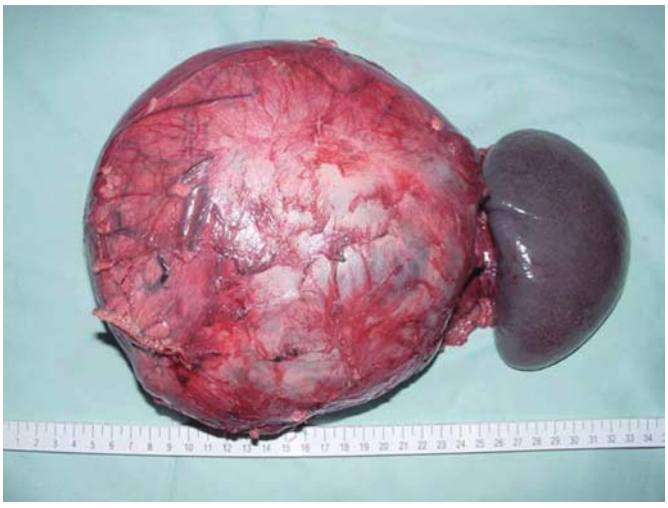

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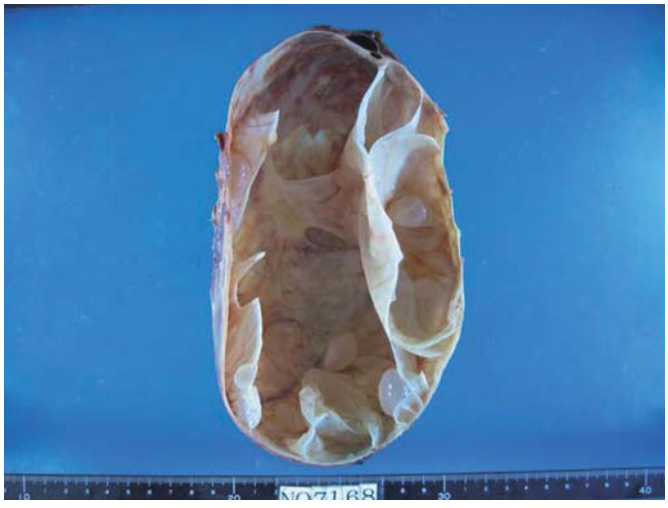
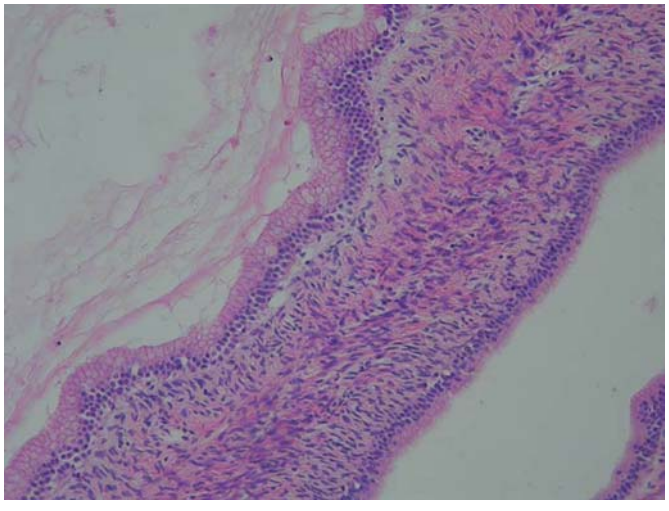


C

Fig. 2. A Intraoperative findings. A large cystic tumor was found arising from the body and tail of the pancreas. **B** Macroscopic observations showed a smooth external surface. **C** The cut surface of the tumor, showing a large cyst including multiple small cysts without solid components



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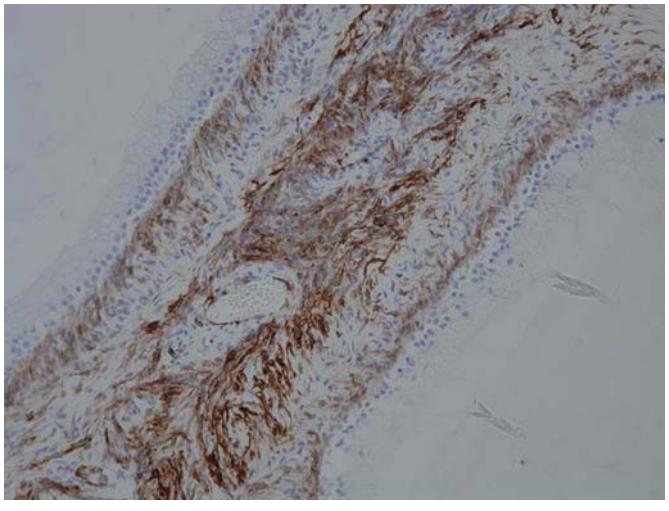

B

Fig. 3A,B. Microscopic findings. **A** The cyst wall was lined by columnar epithelium supported by ovarian-like stroma (H&E stain, ×200). **B** An immunohistochemical analysis showed positive staining for α-smooth muscle actin (×200)

Table 1. Pancreatic mucinous cystadenoma during pregnancy: reported cases (*continued on next page*)

First author[Ref.]	Age (years)	Gestational age at diagnosis (weeks)	Gestational age at surgery (weeks)	Tumor diameter at diagnosis	Tumor diameter at surgery	Tumor location in pancreas	Surgical procedure	Pregnancy outcome
Olsen[5]	25	5.5	18	5 cm	5 cm	Tail	Tumor resection	SVD at term after surgery
Ganepola[4]	37	4	23	5.5 cm	12 cm	Tail	DP	SVD at term after surgery
Kato[3]	33	15	23	2619 ml	4950 ml	ND	DP	SVD at term after surgery
Fernandez[6]	26	20	ND (in the second trimester)	15 cm	15 cm	Tail	DP with splenic preservation	ND (4 years after the intervention, mother and child are in good health)
Present case	33	17	3 months after delivery	12 cm	18 cm	Body and tail	DP	SVD at term before surgery

OS, ovarian-type stroma; ER, estrogen receptor; PgR, progesterone receptor, α-SMA, α-smooth muscle actin; IUGR, intrauterine growth restriction; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; SVD, spontaneous vaginal delivery; ND, not described; DP, distal pancreatectomy

For most of the duration of pregnancy, high levels of sex hormones are considered to be associated with a rapid growth. As shown in Table 1, the cases of rapid tumor growth over the course of pregnancy have been reported since immunohistochemical staining revealed positivity for sex hormone receptors.[3,4] In our case, no immunopositivity for estrogen receptors or and progesterone receptors was observed, but the tumor grew rapidly, thus suggesting that the tumor was sensitive to other sex hormones associated with pregnancy.

A pancreatic mass detected during pregnancy requires special consideration for management because of its tendency to demonstrate rapid growth. There are several issues, the first being the timing of surgery. There are no data available concerning conservative management of pancreatic masses during pregnancy. Olsen et al.[5] suggested that the management of ovarian masses during pregnancy would be an appropriate model. Agarwal et al.[15] suggested that the best time for surgery would be early in the second trimester when the time for spontaneous resolution as well as the risk of abortion has passed and surgery is easier. A mass in the third trimester that is not a clinically suspicious malignancy is best managed by waiting until delivery. All cases of MCN during pregnancy require careful monitoring. All four previously reported cases were treated by resection in the second trimester of pregnancy because of the malignant potential, rapid growth, and large size of the tumor, the possibility of fetal intrauterine growth restriction, and the presence of symptoms.[3–6] The second issue is that of fetal intrauterine growth restriction. In the case reported by Kato et al.,[3] the tumor increased in volume over 46 days and appeared to compress the fetus in the abdomen. The third issue is the risk of a tumor rupture due to the high estrogen level during pregnancy.[8] The possibility that the tumor might rupture during labor is also another important consideration.[5] In this regard, a complete resection of the tumor is the principle of treatment; recurrence is extremely rare. Spilling of the tumor contents during the surgical procedure should be avoided because of possible complications such as pseudomyxoma peritonei.

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Table 1. (*continued from previous page*)

OS	ER	PgR	α-SMA	Malignant signs on imagings	IUGR	CEA (ng/ml) of cyst fluid	CA19-9 (U/ml) of cyst fluid	Reason for surgery
ND	ND	ND	ND	No	ND	ND	ND	Malignant potential
ND	Negative	Positive	ND	ND	ND	ND	ND	Rapid growth, malignant potential
Yes	Positive	Positive	Positive	No	Suspected	2470	450000	Possibility of IUGR
Yes	ND	ND	ND	Yes (1.5 cm solid component, minor irregularities inside the cyst mass)	ND	ND	ND	Large size of the tumor, presence of symptoms, malignant potential
Yes	Negative	Negative	Positive	No	No	36800	>10000	Large size of the tumor, presence of symptoms, malignant potential

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