Case Report

A 37 year-old pregnant woman with pancreatic adenocarcinoma treated with surgery and adjuvant chemotherapy: A case report and literature review

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Case report

A 37 year old G3P1011 pregnant female presented to her primary care physician with 10 days of nausea, vomiting, back pain, acholia, and dark colored urine. Her symptoms worsened as the day progressed. She initially thought the symptoms were related to her pregnancy, which was 16 weeks at the time of presentation. She had only minimal symptoms during the first trimester, and prenatal evaluations/ultrasounds had all been normal, demonstrating a single intrauterine pregnancy with appropriate growth for dates. No familial cancer syndromes were identified, and there were no known toxic exposures. On initial examination, she was afebrile, and not in acute distress. Murphy's sign was present. No guarding or rebound was demonstrated. She had a serum bilirubin of 2.8 mg/dL (direct 1.5 mg/dL), and an alkaline phosphatase of 261 u/L. Hepatitis serologies were negative. Abdominal ultrasound demonstrated gallstones, no evidence for cholecystitis, with mild dilation of the intrahepatic and extrahepatic biliary ductal systems. ERCP was performed the following day which found a distal common bile duct stricture (Figure 1). A plastic biliary stent was placed for relief of the obstruction. A CA19-9 was elevated at 200 U/mL. Cytology from the ERCP was not revealing, so EUS (endoscopic ultrasound) with FNA (fine needle aspiration) was performed two days later (Figure 2). This returned cells positive for poorly differentiated adenocarcinoma.

Given her pregnancy, consultation with radiology regarding the most appropriate staging workup was pursued. CT was inadvisable given the radiation dose, and gadolinium contrast enhanced MRI was not advised by ACR guidelines (1,2). Non-contrast MRI was performed, which confirmed the presence of a 2.7 x 3.2 cm mass within the pancreatic head which abutted, but did not clearly invade the superior mesenteric vein (Figure 3&4).

Staging laparoscopy with intraoperative ultrasound was performed. A 2mm lesion was seen and biopsied in segment 2 of the liver, and a single nodule on the surface of the uterus was biopsied. Both biopsies were negative for malignancy, and peritoneal washings were negative for malignancy as well. Fetal heart tones remained normal throughout the case.

With the staging evaluation complete, multidisciplinary consultation including oncologic surgery, medical oncology, anesthesiology, and obstetrics was undertaken. Our institutional preference for neoadjuvant therapy (chemo+radiotherapy) was not utilized due to the known teratogenic risk of radiation. After thorough preoperative discussion of risks and benefits to her and the fetus, she agreed to undergo pancreaticoduodenectomy. She proceeded to pancreaticoduodenectomy and cholecystectomy approximately two weeks after initial presentation. Pathologic frozen sections of the inferior margin were positive for tumor; thus, an extended pancreatic resection was performed. A second frozen specimen was performed of the pancreas showed no evidence of cancer. Fetal heart tones were normal

No potential conflict of interest.

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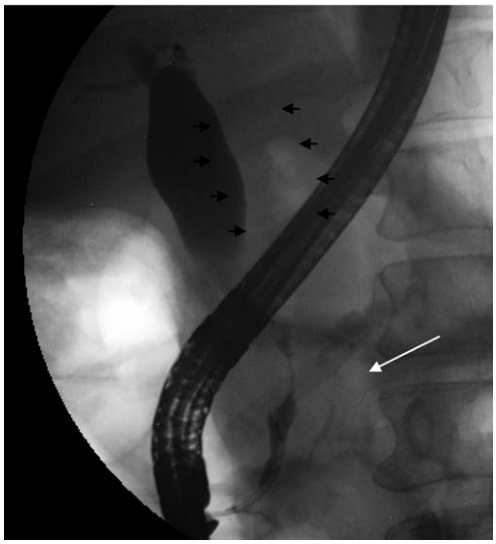

Figure 1 ERCP image demonstrating common bile duct stricture (white arrow) in the area of the pancreatic head with upstream biliary ductal dilation (black arrowheads)

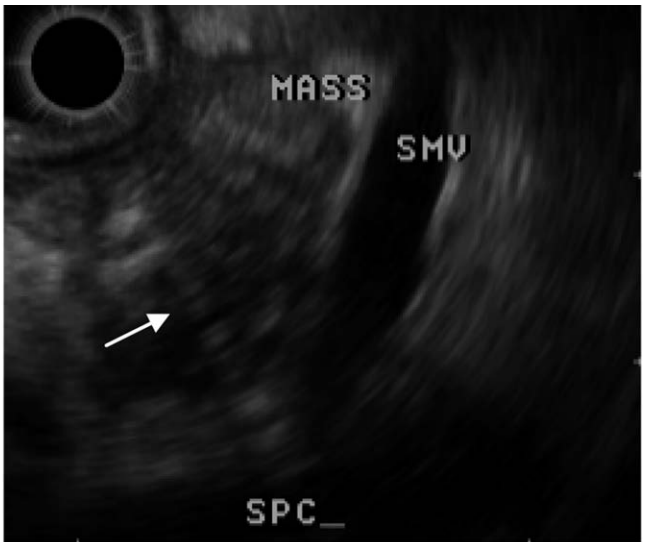

Figure 2 Endoscopic ultrasound image showing mass abutting SMV. Mass and SMV labeled; suggestion of abutment labeled with white arrow

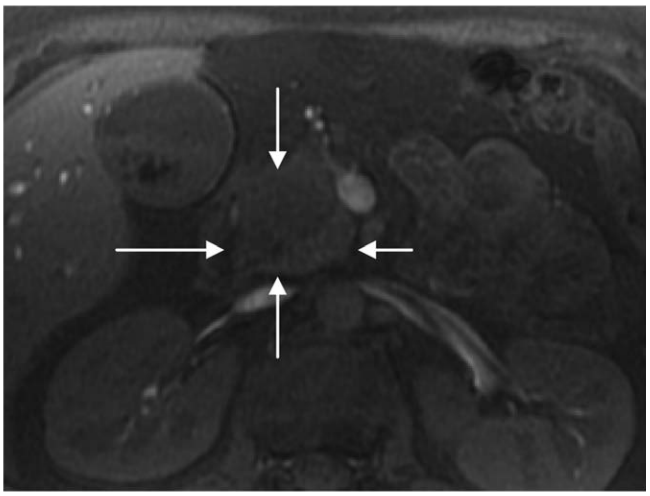

Figure 3 Noncontrast MRI T1spgrFAT axial section showing 32x27 mm pancreatic head mass (arrows)

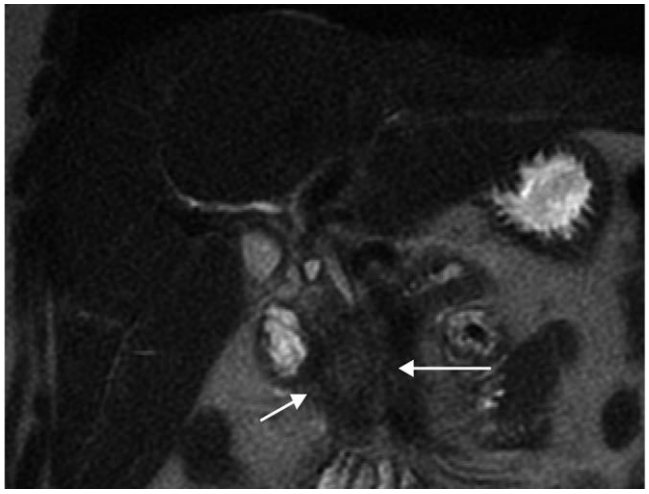

Figure 4 T2 sagittal section of noncontrast MRI demonstrating mass surrounding biliary tree (arrows)

throughout the case, and the uterus was undisturbed during the procedure. Postoperative evaluation of fetal heart tones was normal.

Pathology from the specimen demonstrated poorly differentiated (grade 3) adenocarcinoma of the pancreas. The tumor was > 5cm in greatest dimension with extension beyond the pancreas and perineural invasion, but no involvement of the celiac axis (pT3). Eighteen of 33 lymph nodes were positive for tumor, and there was extensive invasion of the tumor within associated lymphatic channels with extranodal extension (pN1). All surgical margins were negative for carcinoma. The patient recovered well from the procedure and was discharged to home on postoperative day six.

Due to the positive margin and tumor stage, adjuvant gemcitabine was considered (3). After a literature review of available case reports, the risks of teratogenicity and preterm labor while receiving gemcitabine were approached with

the patient and her family. She was willing to proceed. She received two cycles of gemcitabine (1000 mg/m^2) beginning her 24th week of pregnancy, until her 31st week. She tolerated chemotherapy well without significant myelosuppression. Chemotherapy was administered on an inpatient basis to facilitate fetal monitoring; no adverse fetal effects were seen during the pregnancy. After a period of washout from her chemotherapy to minimize the risk of thrombocytopenia in the infant and mother, labor was induced at 35 weeks and delivered a male infant (4 pounds 9 ounces) with APGAR scores of 8 and 9 and blood counts that were within normal limits. The patient and her baby were monitored in the hospital and discharged home 6 days after delivery.

Given the prolonged period of time off of chemotherapy, restaging was performed prior to reinitiating chemotherapy in an adjuvant strategy. Two weeks after delivery, and 6 weeks off chemotherapy, CT scans demonstrated multiple low attenuation lesions within the liver (largest 1.4 cm), as well as enlarged mesenteric, aortocaval, and peripancreatic lymph nodes. With the evidence of recurrence, she was started on a salvage regimen including capecitabine 1000 mg/m^2 po BID days 1-14, gemcitabine 750 mg/m^2 days 4 and 11, and docetaxel 30 mg/m^2 day 1 and 14. She enrolled on a series of clinical trials and subsequently received many different chemotherapy regimens but never achieved a durable response. She died 12 months after diagnosis.

The patient's child has met all appropriate developmental milestones in terms of growth, cognitive development, language development, and socialization. He has a functionally intact immune system. He is now nearly two years old.

Discussion

Other case reports of administration of chemotherapy in pregnancy have been reported, as have cases of pancreatic cancer treated surgically in pregnant patients (described below). We report this case of pancreatic cancer in a pregnant woman who underwent surgical exploration and adjuvant chemotherapy, which we believe to be the first case in the literature.

For her staging, the patient underwent a non-contrast MRI given theoretical concerns for fetal exposure to gadolinium based contrast agents. Based on pre-clinical data, animal data, as well as incidental administration to pregnant patients, the ACR recommends against the use of gadolinium contrast agents in pregnancy, and recommends written informed consent disclosing risks and benefits (1).

Approaching her surgical procedure, pancreaticoduodenectomy has been described in the setting of an ampullary tumor in a pregnant woman at 25 weeks' gestation (4), and in pancreatic adenocarcinoma in at 17 weeks' gestation (5). In another pregnant patient with pancreatic cancer, labor was induced at 28 weeks and the patient then proceeded to the operating room for pancreaticoduodenectomy two weeks later (6). In each of the described cases, no significant adverse fetal outcomes have been described from the surgical procedures alone. In all but one of these cases, the maternal outcome was reported to be uniformly poor.

The use of gemcitabine in pregnancy has been described in non-small cell lung cancer and choriocarcinoma, with little to no teratogeneic effect when administered after the first trimester (7-9). A single patient received multi-agent chemotherapy including docetaxel, cisplatin, and gemcitabine during the first trimester of an unrecognized pregnancy without significant teratogenesis. Experience in breast cancer, lymphoma and leukemia suggest that chemotherapy can be considered in the second and third trimesters after a full disclosure of the potential risks (10,11). The case described in this report is the first described in the literature for adjuvant chemotherapy for pancreatic cancer given while the patient is still pregnant. No adverse outcome has been seen in the child, nearly 24 months post delivery. Even with these case reports, the potential teratogenic effects in the first trimester or during fetal organogenesis have not been systematically described in the literature, and this discussion in no way endorses their use during that phase.

This case demonstrates many of the medical and interpersonal issues that complicate treating pregnant patients with cancer. In this case, the patient's primary goal was to bring a healthy infant to term, understanding the risks of the proposed treatments to herself and her fetus during the treatments. With no data to guide in this specific instance, the treatment team extrapolated data from other tumor types regarding safety and efficacy of the chosen treatments. The patient, and all involved physicians (surgeon, obstetrician, perinatologist, oncologists) were willing to accept an uncertain degree of risk to help achieve the patient's objective of bringing the fetus to term. In spite of aggressive anticancer therapy, the patient manifest progressive disease rapidly, and eventually succumbed to her cancer. There is debate in the oncology community about the efficacy of neoadjuvant chemotherapy with or without radiation, and studies are ongoing (12,13). Her case demonstrates that both locoregional recurrence and distant recurrence need to be addressed in perioperative treatment. Her case also highlights the relatively limited effective treatment options for patients with pancreatic adenocarcinoma, and underscores the need for research in the treatment of this disease.

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