Pancreatic cancer with liver metastases in a pregnant patient: case report and review of the literature

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Summary

In this case report, the authors discuss clinical presentation, surgical procedure and early results of chemotherapy of pancreatic carcinoma with liver metastases diagnosed a few days after delivery. Pancreatic adenocarcinoma occurs infrequently in pregnant and childbearing women: only ten cases have been reported in the literature. The early diagnosis of pancreatic cancer is difficult because symptoms appear when cancer is about to reach an advanced stage. In pregnancy, it is even more difficult because symptoms like dyspepsia, vomiting and epigastric pain may result confusing. The authors outline the difficulties in diagnosis and treatment of this kind of disease during pregnancy.

Key words: Pregnancy; Pancreatic adenocarcinoma; Surgical palliation; Chemotherapy; Liver metastases.

Introduction

Each year, more than 29,000 new cases of pancreatic adenocarcinoma are diagnosed in the USA (2% of the tumors detected every year) and about 25,000 patients die within 12 months of diagnosis. Radical surgery is reserved only to 10-20% of patients and this sort of cancer is the fifth most common cause of cancer-related death [1, 2]. This cancer is a common disease in men of advanced age, but is rare in childbearing and pregnant women.

We report a case of pancreatic adenocarcinoma in a pregnant patient focusing on diagnosis and therapy difficulties.

Pregnancy brings to some significant physiological and anatomical changes in the abdominal cavity. The diagnosis of certain gastrointestinal tract disorders may then be impaired, leading to a difficult pathology analysis in case of a vague symptomatic presentation.

Furthermore, optimizing both maternal and fetal outcomes is particulary challenging when a surgical procedure can be accomplished with the intention to cure.

Case Report

A 36-year-old Italian woman at 35 weeks of gestation was admitted to the Gynecologic and Obstetrics Department in February 2010. The patient's medical history revealed hepatitis C infection (diagnosed 5 years before and treated with interferon), cigarette smoking addiction (40/day before pregnancy, 4-5/day during pregnancy) and past cocaine use.

Her obstetric history was positive for five previous spontaneous abortions and one ectopic pregnancy treated by methotrexate.

The patient had been hospitalized at our clinic after 20 days of epigastric abdominal pain, vomiting and weight loss. At admittance she showed a recent abdominal ultrasound (US) analysis report (performed in a different hospital). The exam result was negative for any sort of lesion. We repeated abdominal US and the exam was still negative for any sort of lesion.

The hematologic exams revealed increased hepatic and pancreatic enzymes, impaired renal function, anemia and hypokalemia. Obstetric US scan showed a single fetus with normal biometry, Doppler velocimetry and amniotic fluid index. Significant laboratory data were: Alanine transaminase (ALT: 593 U/l), lactate dehydrogenase (LDH: 608 U/l), total bilirubin (1.92 mg/dl), glycemia (149 mg/dl), azotemia (56 mg/dl), creatinine (2.19 mg/dl), uric acid (18.3 mg/dl) and electrolytes (sodium, Na+: 133 mEq/l; potassium, K+: 2.5 mEq/l; chlorine, Cl-: 77 mEq/l). The patient was treated with rehydratation (Ringer's lactate solution and potassium chloride solution, KCl), furosemide and metoclopramide.

The patient's condition dramatically worsened and as well acute renal failure occurred (due to hypovolemia). It was therefore necessary to carry out a cesarean delivery, deferring the hepatic and pancreatic dysfunction diagnosis to the postpartum.

We administered two 12 mg doses of betametasone in a 12-hour interval to prevent neonatal respiratory disease and we planned the cesarean section (CS) after its completion. The patient underwent a low transverse CS via a Pfannenstiel incision under general anesthesia and she delivered a 2,520 g female with Apgar scores of 8 and 9 at 1 and 5 min. After delivery, clinical condition and laboratory values were improving: total bilirubin 0.87 mg/dl, ALT 395 U/l, LDH 438 U/l, creatinine 1.03 mg/dl; nevertheless hypokalemia, hyponatremia and hypochloremia persisted.

Four days after CS, the patient's condition worsened: vomiting, retrosternal pyrosis and epigastric pain radiating to the back. Moreover, no relief was achieved with the proper therapy (lansoprazole, magnesium hydroxide, metoclopramide and ketorolac).

A new abdominal US showed a solid mass of 4 cm in the pancreatic uncinate process, compressing the duodenum and causing fluid retention in the head of the pancreatic duct; a hyperechogenic angiomatous-like lesion was found in the right hepatic lobe.

Computed tomography (CT) of the abdomen revealed a

Revised manuscript accepted for publication August 4, 2011

Fig. 1

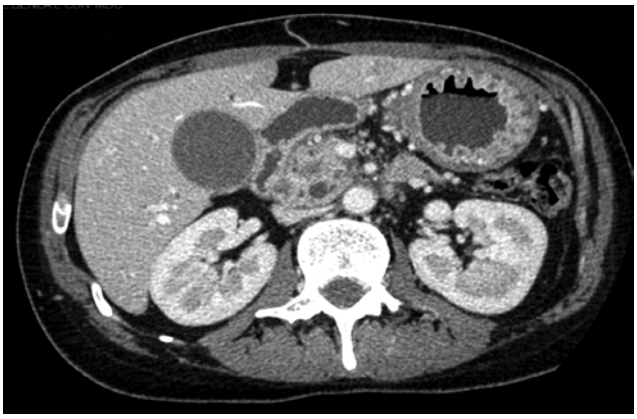

Fig. 2

Figure 1. — CT image before surgery: pancreatic mass compressing the duodenum.
Figure 2. — CT image showing the persistence of the pancreatic lesion after chemotherapy.

hypodense pancreatic mass with fringed borders, leaning toward the mesenteric vessels and to the inferior vena cava. Moreover, CT revealed three hepatic masses of uncertain significance; gastrohepatic ligament lymph nodes were not significantly enlarged (< 1 cm) (Figure 1).

Esophagogastroduodenoscopy (EGD) did not reveal gastric involvement despite a duodenal obstruction due to edema and external compression.

The patient underwent surgery in order to heal the gastric obstruction and the jaundice, reducing the tumor burden and bearing out the hypothesis of metastatic liver disease. After a midline incision was made, no ascites were found entering the peritoneal cavity.

Inspection and palpation of the liver showed metastatic lesion in segment 3 and another nodule was present deep between segments 4 and 5.

Palpating the pancreas, a firm mass (about 5 cm in diameter) was identified on its head, extending to the uncinate process.

The tumor partially infiltrated the superior mesenteric vein. The veins of the greater omentum and mesentery of the transverse colon were dilated. Enlarged lymph nodes around the hepatoduodenal ligament and close to the celiac vessels were present; due to a possible upward extention of the tumor, it was impossible to free and expose the right hepatic artery.

The duodenum compression was caused by two factors: the direct tumor growth into the third portion of the intestinal wall and mechanical obstruction of the duodenum itself due to the pancreatic mass.

After this staging evaluation was made during surgery, no attempt at pancreatic resection for optimal palliation was made. The decision was a selection of surgical procedures for palliative treatment and preparation for postoperative understaging chemotherapy with or without radiation regimens.

Several biopsies of pancreatic, peripancreatic tissue and from mesenteric lymph nodes were obtained. The gallbladder was removed and the patient received both a retrocolic gastrojejunostomy and a biliary bypass (double bypass).

The surgical procedure was completed resecting the two metastatic lesions on the liver. Postoperative histology showed sclerosis and chronic inflammation in the pancreatic and peripancreatic specimens, while the resected liver and lymph node revealed moderately differentiated metastatic lesions of likely pancreatic origin.

After the surgery the patient began palliative systemic chemotherapy with gemcitabine (1000 mg/m^2) and oxaliplatin (100 mg/m^2) every two weeks, along with nutritional support. A restaging CT scan obtained after three cycles of treatment (June 2010) revealed stable disease (SD) (Figure 2). After a collegial discussion, we decided to keep on administering gemcitabine (1000 mg/m^2) every two weeks. The decision was based on some considerations: the absence of indication for radiotherapy (non favorable cost/effectiveness approach related to colic dilatation and consequent iatrogenic risk of perforation), the hypersensitivity reaction to the last oxaliplatin including pruritus and erythema (rapid resolution with the suspension of therapy and use of steroids) and SD at CT scan.

Twelve months after the diagnosis, the clinical conditions were stable and the CT scan performed in December 2010 confirmed SD.

Discussion

Cancer during pregnancy is not a rare event: about one out of 1,000 pregnancies has tumoral complications [1].

Pancreatic adenocarcinoma occurs infrequently in pregnant and childbearing women: only ten cases have been reported in the literature (Table 1) [3-12].

Age of the patients ranged from 32 to 43 years old and gestational age from 16 to 30 weeks. Only a few had a cancer risk factor related to cigarette smoking, gastrointestinal tumor inheritance or use of oral contraceptives [3, 5, 8].

The patient presented in our study was 36 years old and in the 35th week of pregnancy. Her medical history revealed she had contracted hepatitis C five years earlier and was consequently treated with IFN for one year. It was reported that she had a past use of cocaine and a cigarette smoking addiction (40 cigarettes a day).

While traditional risk factors (advanced age, male gender, diabetes, obesity, chronic pancreatitis, smoking, hereditary factors) have been widely demonstrated, the association between use of cocaine and pancreatic adenocarcinoma has been suggested just in one study [15]. Our case report highlights the difficulties encountered diagnosing pancreatic adenocarcinoma during late pregnancy.

Table 1. — *Review of the literature on pancreatic adenocarcinoma in pregnant patients*.

Author	Patient age	Gestational age	Risk factors	Clinical features	Diagnosis	Management	Maternal outcome	Fetal outcome
Gamberdella 1984	37	24	–	Chondral burning, epigastric discomfort, weight loss	Made by ERCP and exploratory laparotomy before delivery	Cesarean section at 32 weeks and cholecystostomy (palliative)	Patient died 3 months after delivery	Healthy twins
Porcel *et al*. 1992	43	28	none	Epigastric pain, upper lumbar backache, nausea,vomiting, pre-eclampsia	Made by abdominal ultrasound and aspiration cytology of hepatic metastases after delivery	Cesarean section at 30 weeks	Patient died 35 days after delivery	Live newborn
Simchuk *et al*. 1996	39	16	–	Right upper quadrant pain and anorexia	Made during a Whipple procedure before delivery (at 20 weeks)	Choledocho-duodenostomy and jejunostomy (palliative bypass procedure) at 20 weeks. Cesarean section at 28 weeks	Patient months after surgery	Healthy male
Sciscione *et al*. 1996		20	–	Asymptomatic	Detected accidentally during a routine obstetric ultrasound	Pyloric-preserving pancreatico-duodenectomy. Cesarean section at 28 weeks	Good outcome postoperatively	The baby died
Blackbourne *et al*. 1997	32	17	2-year history of smoking cigarettes	Back pain, nausea, vomiting, dark urine, scleral icterus	Made by exploratory laparotomy and aspiration cytology of the mass before delivery	Pylorus-preserving pancreatico-duodenectomy (curative)	Patient outcome was good at 3 months after surgery (no other informations reported)	Normal fetl development at 3 months after surgery
Gojnic *et al*. 2005	37	Second trimester	Family history for digestive tract carcinoma	Abdominal pain and frequent fatty stools alternating with constipation		Cesarean section, hysterectomy and pancreatic resection	Patient alive at date of publication	Live female
Marinoni *et al*. 2006	38	27	Cigarette and combined oral contraceptives use for 10 years	Epigastric abdominal pain, right chondral burning pain, upper lumbar backache, nausea and vomiting	Made by abdominal ultrasound, ERCP with biopsy, magnetic resonance before delivery	Cesarean section at 30 weeks and intrabiliar stent (palliative)	Patient died 50 days after delivery	Live female
Su *et al*. 2006	37	22	–	Epigastric pain	Made by abdominal ultrasound and biopsy before delivery	Patient decided to terminate the pregnancy at 24 weeks and proceed with chemotherapy	Patient died 4 weeks after diagnosis	
Kakoza *et al*. 2009	40	24	none	Epigastric pain, nausea, vomiting, early satiety, anorexia, reflux and weight loss	Made by ERCP with biopsy and computed tomography before delivery	Cesarean section at 28 weeks. Pancreatico-duodenectomy 2 weeks after delivery followed by chemotherapy	Patient died 6 months after surgery	Healthy female
Onuma *et al*. 2010	32	30	none	Pain and tenderness in the upper right quadrant	Made by surgical exploration	Cesarean section and pancreatoduodenectomy at 34 weeks, followed by chemotherapy	Patient is disease-free at 2 years	Healthy male

Usually early diagnosis of pancreatic cancer is difficult because the symptoms appear when the cancer is about to reach an advanced stage; in pregnancy, it is even more difficult because some symptoms like dyspepsia, vomiting and epigastric pain may result confusing [5].

Physical examination, laboratory tests, tumoral markers (CEA, CA19-9) combined with abdominal US can help in most cases to recognize the presence of a gastrointestinal cancer. Along with a proper work-up and right timing, it can also succeed in detecting the cancer itself. Abdominal US is usually the front-line diagnostic exam because it is a simple and non-invasive procedure.

Although the literature reports high sensitivity (90%) of ultrasounds, in some cases this test is unable to detect a pancreatic mass. In such case there are some risks associated with the eventual more invasive methods and to diagnostic delay [3, 10, 12].

Indeed, in other cases the diagnosis was performed early in the pregnancy period, when the uterus had not yet reached considerable size.

In our patient, the US exam was negative and the pancreatic mass was detected only after the delivery; the gravid uterus probably caused some difficulties during the echography process, interfering with abdominal viscera visualization.

Nevertheless, the diagnostic difficulties in detecting pancreatic cancer have been early described by other authors: in the case described by Kakoza *et al*., the US showed only a biliary sludge and the condition was ascribed to cholecystitis and gallstone pancreatitis. The mass was discovered only with duodenal mucosal biopsy during endoscopic retrograde cholangiopancreatography (ERCP) and with CT scan [4].

In the case reported by Blackbourne *et al*. all the tech-

niques used (abdominal US, ERCP with cytology, CT scan, exploratory laparoscopy) did not show the pancreatic tumor, which was discovered only during an exploratory laparotomy [5].

Onuma *et al*. was unable to identify pancreatic cancer by transabdominal US because the large uterus surrounded by the intestine obscured the pancreas and intestinal and colon gas interfered with US. A retroperitoneal mass was detected by CT but was confused with an appendicitis or perforation of the stomach and retroperitoneal abscess. The correct diagnosis was achieved only by means of surgical exploration [12].

Another aspect to consider is the proper management of this pathology in pregnancy. The choice of correct management is a crucial decision requiring counseling with the patient and collaboration between surgeons and gynecologists. The only curative therapy is surgery, but only 15-20% of patients have, at time of diagnosis, lesions that can be surgically treated. Those that can be treated do not present any metastatic disease, distant lymphatic involvement (i.e., celiac, aortocaval, iliac), superior mesenteric-portal venous confluence nor superior mesenteric artery or celiac axis involvement.

Since the patient in our study was at a gestational age of 35 weeks – which allowed the completion of delivery without particular risks for the newborn – we decided to perform a cesarean section and postpone the diagnosis until after the birth.

However, even if the diagnosis had been made before the birth, it would not have altered the prognosis of the patient nor the management itself.

In others cases early gestational age during diagnosis (16-28 weeks) presented many problems related to the correct patient management.

Wherever it was possible to resort to surgery, the mother and the clinicians could choose among three options:

1. Immediate surgical resection with pregnancy termination risk in case of a too early gestation;

2. Delay the surgery until the maximum fetal outcome with disease progression risk for the mother;

3. Perform surgical resection at the gestational age (starting from 28 weeks) with good fetal survival chances.

In most cases the patients decided to postpone the surgery to a later gestational age in order to reach a good survival probability for the newborn [3, 4, 6, 7, 10, 11]. Unfortunately the prognosis for patients was poor: five patients died within four months after delivery.

These reports show how difficult the management of these cases can be during pregnancy, suggesting a greater aggressiveness of pancreatic cancer in pregnant women. This may be caused by the suppression of the immune system, typical of pregnancy. Some authors support the hypothesis that pancreatic cancer may be, in part, an estrogen-dependent disease, but in the literature there is no agreement on this issue [14].

Finally, even though pancreatic adenocarcinoma is rare during pregnancy, in a woman with symptoms like abdominal pain, vomiting, jaundice and impaired liver and pancreas function the presence of pancreatic adenocarcinoma should be excluded although the diagnosis may be difficult and require more than one diagnostic procedure.

Once the tumor is diagnosed, it is necessary to pay great attention to the therapeutic choice in order to ensure the best outcome for both mother and fetus.

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