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Case Report

Autoimmune pancreatitis with IgG-4 cholangiopathy in a pregnant woman: A case report ☆,☆☆

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ABSTRACT

Diagnosis and management of autoimmune pancreatitis during pregnancy. Autoimmune pancreatitis is a rare and life-threatening condition with increased maternal and fetal morbidity and mortality. Autoimmune pancreatitis may result in a mass-forming lesion in the pancreas resembling pancreatic cancer; therefore, meticulous and careful investigations must be done to avoid misdiagnosing autoimmune pancreatitis as pancreatic cancer. Since autoimmune pancreatitis improves dramatically to steroid therapy, accurate diagnosis of autoimmune pancreatitis can avoid unnecessary procedures, surgeries, and pancreatic resection. A case of a pregnant lady in her third trimester was presented with abdominal pain, nausea, and vomiting. On examination, there was tenderness in both epigastric and right hypochondrium associated with elevated serum amylase, liver transaminases, alkaline phosphatase, gamma-glutamyl transpeptidase, and immunoglobulin G4. Both abdominal ultrasound and magnetic resonance cholangiopancreatography showed a pancreatic head lesion with dilation in both pancreatic duct and common bile duct. Steroid was initiated that resulted in rapid and dramatic responsiveness. Acute pancreatitis is uncommon during pregnancy, and autoimmune pancreatitis is a very rare form of acute pancreatitis; therefore, a clear and rapid assessment, diagnosis, and management plan are necessary to avoid maternal and fetal morbidity and mortality.

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Introduction

Acute pancreatitis during pregnancy is a very uncommon condition, with an estimated incidence of 1 occurrence per 1000-10,000 pregnancies [1,2]. Acute pancreatitis is rare during the first 2 trimesters of pregnancy, occurring more frequently in the third trimester and early postpartum period, with an incidence rate of 50% and 38%, respectively [2]. Autoimmune pancreatitis is a rare form of the disease that is considered as a pancreatic manifestation of a newly suggested disease condition, immunoglobulin G4 (IgG4)-related disease [3].

Autoimmune pancreatitis on radiographs could show a pancreatic mass lesion that may resemble pancreatic cancer, possibly resulting in unnecessary surgeries [4]; therefore, it is important to have clear guidelines and protocols to diagnose and manage patient with such conditions to improve the fetal and maternal outcomes for such patients.

In this report, we present a challenging case of a 23-year-old female at 33 weeks of pregnancy, complaining of mild abdominal pain radiating to the back that was difficult to diagnose as either autoimmune pancreatitis or pancreatic cancer.

Case presentation

A previously healthy 23-year-old nulliparous woman at 33 weeks of pregnancy with no known comorbidities presented to our emergency department at An-Najah National University Hospital complaining of mild upper quadrant pain radiating to the back, nausea, and vomiting. According to her past history, she was medically and surgically free. There was no family history of autoimmune diseases. There had been no previous history of fever, diarrhea, constipation, dark color urine, vaginal bleeding, or discharge.

On regular exam, the patient and the fetus were in good health till the onset of symptoms. Her vitals at presentation were as follows: pulse rate of 75/min, blood pressure of 100/60 mmHg, body temperature of 37.0°C, and a respiratory rate of 20/min. On physical exam, she was not jaundiced. There was mild tenderness in both epigastric and right hypochondrium, slightly decreased bowel sounds and a gravid uterus.

Her initial lab tests were as follows: normal complete blood count, C-reactive protein 48 mg/L (negative < 6), serum amylase 106 U/L (31-107 U/L), lipase 14 U/L (13-60 U/L), aspartate aminotransferase 66 U/L (8-40 U/L), alanine aminotransferase 80U/L (4-34 U/L), alkaline phosphatase (ALP) 730 U/L (<240 U/L), gamma-glutamyl transpeptidase (GGT) 191 U/L (6-42 U/L), and total bilirubin 0.6 mg/dL (0.25-1.2 mg/dL). Moreover, an elevated level of a subclass of serum circulating immunoglobulins (IgG4) 165 mg/dL (8-140 mg/dL) which raised the suspension for acute pancreatitis.

The abdominal ultrasound (US) of the patient showed a dilation in the distal part of the pancreatic duct (up to 8 mm), also both of the pancreatic ducts are dilated (double duct sign) indicating a high likelihood of pancreatic head lesion which appears bulky on US, with a suspected 4 cm isoechoic lesion. The common bile duct is dilated measuring 10-12 mm in diameter; the gallbladder is markedly distended

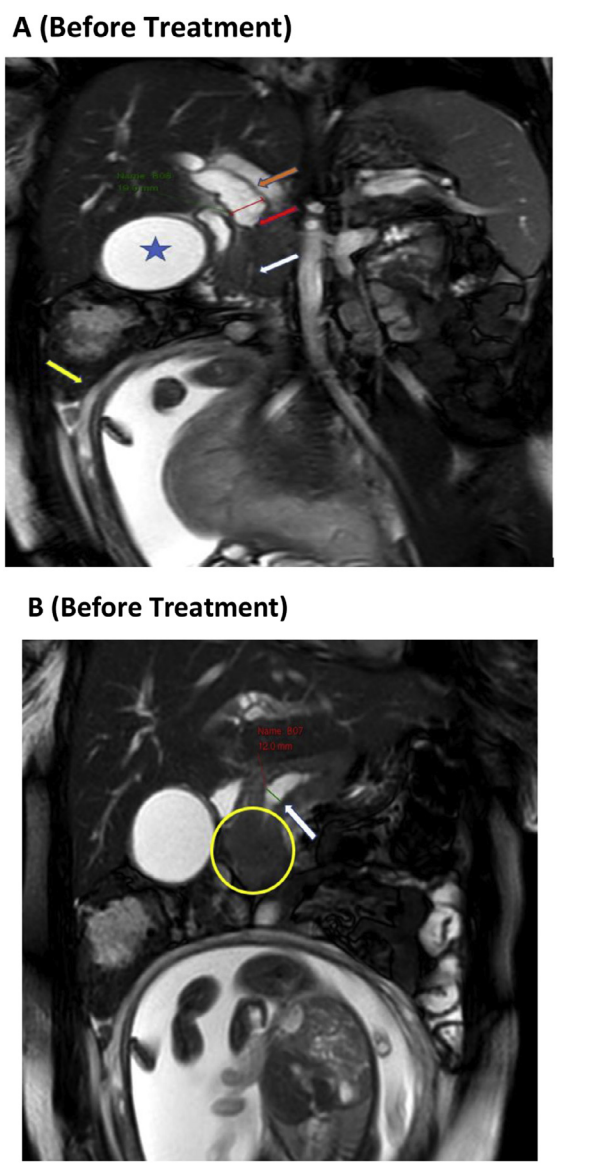

Fig. 1 – (A) Before treatment. The orange arrow denotes common bile duct dilation (19 mm). The red arrow denotes the cut-off sign. The white arrow denotes common bile duct tapering. The blue star denotes gallbladder distention. The yellow arrow denotes the pregnancy. (B) Before treatment. The white arrow denotes the pancreatic duct dilation (12 mm). The yellow circle denotes the head of the pancreas.

with no biliary stones or signs of cholecystitis. There was no intraperitoneal-free fluid. Liver, kidneys, and spleen were unremarkable. Also, it showed a single viable fetus with normal to-date biometric measurements. The magnetic resonance cholangiopancreatography (MRCP) was performed as it is the study of choice in pancreatobiliary diseases: it showed a bulky head of the pancreas with a smooth out line confirming the findings observed on the abdominal US, dilated pancreatic duct up to 12 mm, dilated common bile duct (CBD) up to 19 mm with an abrupt cutoff and tapering at the level of the pancreatic head, Intrahepatic biliary tree dilatation and significant distension of the gallbladder (Fig. 1). All the previous

findings were suggestive of pancreatic head inflammatory process like acute pancreatitis rather than mass lesion.

The diagnosis of acute pancreatitis was assumed and the patient was admitted and was managed with intravenous fluids, analgesics, nil per oral and was started on prednisone 40 mg, the mother and the fetus were monitored during treatment. The mother showed significant improvement within a few days and was started on a soft diet with no complaints. On the 10th day of hospital stay, her lab values were as follows: serum amylase 90 U/L (31-107 U/L), aspartate aminotransferase 33 U/L (8-40 U/L), alanine aminotransferase 42 U/L (4-34 U/L), ALP 214 U/L (<240 U/L), and GGT 70 U/L (6-42 U/L).

Moreover, there was significant improvement regarding the dilatation of the CBD and the pancreatic duct which became 6 mm and 4 mm, respectively. With complete resolution of the pancreatic head lesion when demonstrated by MRCP (Fig. 2).

The plan was to gradually taper steroids over a period of 6 months, during that period, clinical, biochemical, and radiological follow-ups were carried out.

The patient delivered a viable female infant at 38 weeks + 4 days by spontaneous normal vaginal delivery. The newborn's physical exam was normal and the patient maintained good health.

After 5 months, the patient stopped taking steroids without counseling the medical team, and started to take bee propolis (propolis) as a part of natural home remedy; her symptoms recurred and she started to complain of abdominal pain, nausea, and vomiting; her abdominal US showed evidence of pancreatic head lesion recurrence with heterogeneous echotexture measuring 3 cm; and the CBD is mildly dilated measuring 7 mm, consistent with recurrence of autoimmune pancreatitis after stopping steroids.

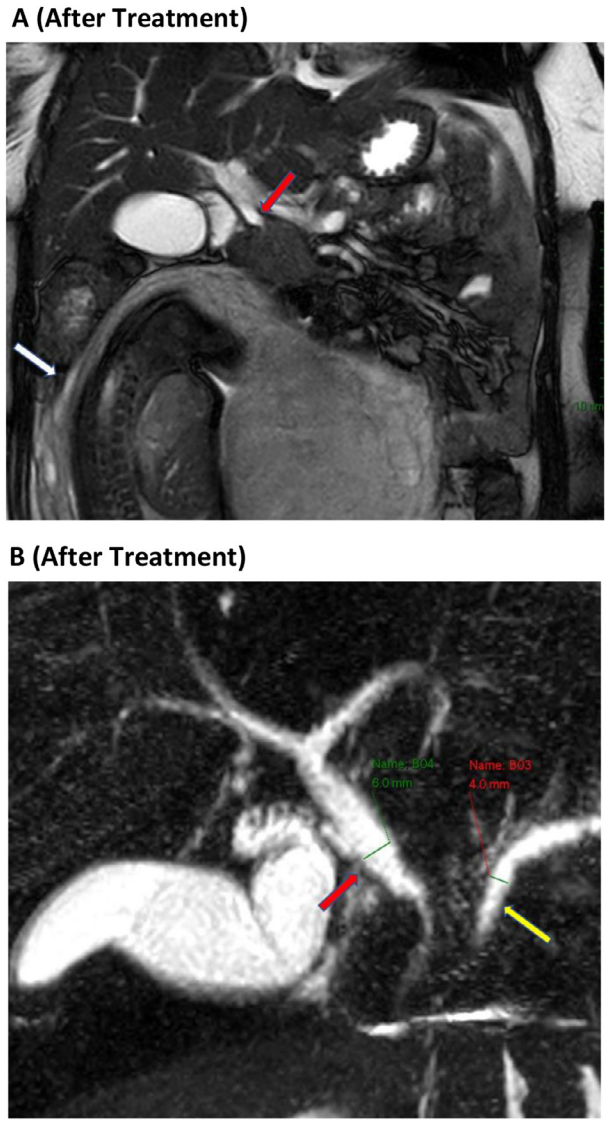

Fig. 2 – (A) After treatment. The red arrow denotes the common bile duct showing significant improvement. The white arrow denotes the pregnancy. (B) After treatment. The red arrow denotes the common bile duct (6 mm). The yellow arrow denotes the pancreatic duct (4mm).

Discussion

Acute pancreatitis in pregnancy is considered a serious disease that is associated with high rates of both maternal and perinatal mortality. Before the 1980s, the mortality rates for mothers and their babies ranged from (21 to 37)% and (20 to 34.6)%, respectively [5,6]. However, a number of reports since the 1990s suggest that there is a drop in both maternal and perinatal mortality [7–9].

Yoshida et al. [10] introduced the term "autoimmune pancreatitis" in 1995 describing an entity of chronic pancreatitis with autoimmune manifestations evident in laboratory, histological, and clinical testing.

There is still an unknown cause for autoimmune pancreatitis, but current evidence strongly suggests this disease has an autoimmune basis [11]. According to Kawa et al. [12], it is a distinctive disease entity characterized by high serum IgG4 concentrations.

Clinical manifestations of acute pancreatitis are similar in pregnant and nonpregnant women. Symptoms include nausea, vomiting, anorexia, abdominal pain, dyspepsia, and intolerance to fatty diet. The most common signs are low-grade fever and tachycardia [13].

It can be challenging to diagnose acute pancreatitis during pregnancy due to pregnancy-associated hematological and biochemical changes associated with normal pregnancy that may have an influence on the interpretation of the diagnostic tests (serum amylase and lipase levels) and the assessment of the acute pancreatitis' severity (physiologic leukocytosis of pregnancy, increase in ALP up to 3 times its normal range in normal pregnancy) [14]. In pregnancy, high serum amylase and/or a lipase level that exceeds 3 times the normal range has a good positive predictive value for the diagnosis of acute pancreatitis. For diagnosing acute pancreatitis, the serum lipase level is more sensitive (94% vs 83%) and specific (96% vs 88%) than the serum amylase level [15]. Additional laboratory tests that are essential for diagnosing acute pancreatitis and determining the possible cause can include complete blood count, blood glucose, serum triglycerides, lactate dehydrogenase, cal-

cium, bilirubin, GGT, and liver function tests [16–18]. Regarding autoimmune pancreatitis in particular a set of diagnostic criteria have been suggested to be "gold standard" including histopathology and IgG4 subclass staining [19]; therefore, determining the level of IgG4 in the case of autoimmune pancreatitis is critical for both diagnosis and treatment response monitoring [18–20].

Most radiological investigations that utilize ionizing radiation are usually contra-indicated in pregnancy due to the potential risks to the fetus [21]. US is the primary diagnostic tool used to evaluate pregnant women with abdominal and pelvic pain, as it is safe, inexpensive, and accurate [22]. Computed tomography (CT) is well-established noninvasive method for biliary tree and pancreas evaluation, but it is only of limited use to pregnant women due to fears about radiation-induced teratogenicity [21–23]. MRCP allows an accurate assessment of the entire biliary system and allows diagnosis of various illnesses that cause acute pancreaticobiliary disease in pregnant women. MRCP allows the identification of patients who require immediate intervention, as well as avoiding unnecessary endoscopic retrograde cholangiopancreatography by excluding a biliary abnormality when US findings are inconclusive. The use of MRCP as a complement to US can improve the management of pregnant patients with a suspected pancreaticobiliary condition [24].

According to Kamisawa et al. [25,26], steroid is a cornerstone in treating autoimmune pancreatitis patients, due the dramatic improvement clinically, serologically, and radiologically. Steroid therapy is indicated when there is a symptom such as abdominal pain, obstructive jaundice, diffuse pancreatic enlargement and hydronephrosis. Initially, oral prednisolone (0.6 mg/kg/d) is administered for 2-4 weeks, and then is tapered by 5 mg every 1-2 weeks while the patient is monitored carefully clinically, serologically, and radiographically, to reach a maintenance dose, a process usually requiring a period of 3-6 months. A poor response to the treatment protocol with steroids should raise the suspicion of pancreatic cancer and the need for re-evaluation. To reduce the possibility of relapse, it is recommended to maintain steroid therapy (2.5-5 mg/d) for at least 6 months.

Conclusion

The diagnosis and management of pancreatitis in pregnancy is a complicated issue for gastroenterologists and obstetricians worldwide. A delay in diagnosis and treatment can result in maternal and fetal morbidity and mortality. A treatment option must be selected based on clinical risk and benefit, as well as local expertise and technology availability.

Authors' contributions

YA and BM: wrote the manuscript; AA: performed the radiological examination; QA: diagnosis, management, and follow-up of the case. All authors read and approved the final manuscript the final manuscript.

Ethical approval and consent to participate

The University IRB has approved conducting and publishing the manuscript.

Availability of data and materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Patient consent

The authors have written informed consent for publication.

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