Abstract

The case is a 39-year-old parous female with a history of untreated hyperlipidemia. She presented at another hospital at 37 weeks gestation with the chief complaint of epigastralgia, and was diagnosed with acute pancreatitis due to elevated pancreatic enzymes. Complication with severe neonatal asphyxia led to her transferal to this hospital, where an emergency cesarean section was performed the same day. Severe acute pancreatitis was diagnosed based on three prognostic factors and CT Grade 3, and the patient was admitted to the ICU. Progress with conservative treatment was favorable, and she was discharged from hospital on the 20th day of admission after her symptoms receded.

While acute pancreatitis in pregnancy is rare, there are reports of approximately 100 cases in Japan. The rate of gestational pancreatitis due to hyperlipidemia in Japan is high, and swift diagnosis and treatment is required as the prognosis is often poor. In this case, familial type IV hyperlipidemia was suspected due to the patient’s history of hyperlipidemia and family history. Exacerbation of hyperlipidemia due to pregnancy is thought to have induced onset of pancreatitis.

Introduction

While acute pancreatitis as a complication of pregnancy is rare, it requires careful handling due to the limitations imposed on imaging and treatment by consideration of their effect on the fetus as well as the mother. In addition, the prognosis can be poor for both mother and child depending on the cause of the pancreatitis, making appropriate diagnosis and treatment essential. We encountered a case of acute pancreatitis onset in late gestation caused by exacerbation of hyperlipidemia during pregnancy in a patient with a background of familial hyperlipidemia. We have described it in this report along with a general discussion of the literature on pregnancy-related acute pancreatitis.

Case presentation

The patient in the case was a 39-year-old female (37 weeks gestation; gravida 3; para 1) with a history of untreated hyperlipidemia, time of onset unknown. Family history includes diabetes in her mother and father, and hyperlipidemia in her older
sister. The patient was a non-smoker with alcohol consumption of 100g/day of ethanol (abstaining during pregnancy). She conceived through clomiphene+hCG treatment at another hospital and was under observation. On the morning prior to admission at our institution, at 37 weeks gestation, she experienced sudden onset of epigastralgia and presented at another hospital for consultation. Fasting, fluid replacement, and administration of gabexate mesilate and antibiotics were commenced upon diagnosis of acute pancreatitis. The following day (the day of admission), a drop in the fetal heartbeat was observed and the patient was transferred to this hospital as an emergency admission. She was lucid at the time of admission. Her height was 159 cm and body weight 64.5 kg (56.5 kg before pregnancy: BMI 22.3). Her pulse was 108 beats/min, blood pressure 113/68 mmHg, respiratory rate 28 breaths/min, SpO2 97% (6L oxygen mask), and body temperature 37.4°C. Conjunctival anemia and jaundice were absent. Cardiac sounds were normal. Coarse crackles were heard across the lung area. Upper abdominal tenderness, muscular defense, and rebound tenderness were present. Pedal edema was absent. Examination findings showed elevated pancreatic enzymes, elevated inflammatory response, hypertriglyceridemia, and hypercholesterolemia (Table 1). Overt DIC score was 4 points. Chest x-ray showed a bilateral decrease in lung permeability. Despite suspected pancreatitis, CT was not performed prior to surgery in consideration of the fetus. Observation of uterine contractions due to pancreatitis and repeated late decelerations via a cardiotocogram non-stress test.
led to diagnosis of severe neonatal asphyxia at the time of arrival at the hospital. An emergency cesarian section was performed with the intention of treating the pancreatitis post-operatively. Surgical findings revealed moderate milky ascites. The patient was transferred to the ICU after surgery.

Plain abdominal CT (figure 1) directly after surgery showed inflammation extending beyond the inferior pole of kidney and pancreatic enlargement in more than two areas, as well as irregular shadows, and was assessed as CT Grade 3. At time of entry into ICU, the patient had three prognostic factors, a Ranson score of 5, a Glasgow score of 3, an APACHE II score of 1, and a SOFA score of 2. Large-volume fluid replacement and administration of 2000 mg/day of gabexate mesilate, 30000 units/day of ulinastatin, prophylactic antibiotics (doripenem 1.5 g/day), and selective intestinal decontamination (vancomycin 1.5 g/day, polymyxin B 1.5 million units/day) were commenced for severe acute pancreatitis. In addition, continuous hemodialysis and filtration was conducted until the third day of hospitalization in light of the risk of a further advance in severity. Pancreatic enzymes and inflammatory response improved rapidly, and on the fourth day of hospitalization the prognostic factors had improved to one. Triglycerides, which were elevated at the time of admission, decreased rapidly following delivery of the child. Abdominal contrast-enhanced CT on the seventh day of hospitalization showed an improvement to Grade 1, and the patient was discharged from the ICU on the eighth day having improved to P-AMY 47 IU/1, LIP 89 IU/1, TG 402 mg/dl, and Tcho 383 mg/dl. Tube feeding was commenced on the sixth day of hospitalization with ingestion commenced on the 13th day, after which the patient was discharged on the 20th day with abated symptoms. Choledocholithiasis, congenital abnormalities of the pancreaticobiliary duct, and pancreatic pseudocysts were absent on MRCP after discharge. While the infant suffered respiratory arrest for two minutes after birth and was admitted to the NICU, the respiratory condition gradually stabilized and the infant was transferred to the GCU at four days of age. The infant is currently attending outpatient care and is not afflicted by developmental problems.

Discussion

Gestational-onset acute pancreatitis is a rare disease, with a reported frequency of one in every 1,000 to 10,000 births, averaged to a rate of around 0.03%. The single-facility, retrospective study conducted by Ramin et al. showed first trimester onset at 19%, second trimester at 26%, and third trimester at 53%, while Takii et al. in Japan reported 18% in the second trimester, 63% in the third trimester, and 6% in the puerperal period, showing a high rate of onset in the third
trimester. There was also a tendency towards a higher rate in parous women. While previous reports have described a maternal death rate of 20% and a fetal death rate of 50%, recent advances in diagnostic and treatment techniques have reduced the maternal death rate to less than 5% and the fetal death rate to 7%. Reports from Europe and America describe gallstones as contributing to the onset of pregnancy-related pancreatitis in 50~70% of cases, followed by alcohol and hyperlipidemia, with idiopathic onset in approximately 10% of cases. In contrast, reports from Japan list hyperlipidemia as being involved in 34% of cases, malfusion of pancreaticobiliary ducts in 9%, gallstones in 7%, and parathyroid dysfunction in 4% of cases. At the case report level, concomitance of HELLP syndrome or acute fatty liver of pregnancy, has been reported, with angiospasms thought to be the mechanism for these cases.

In cases of gallstone pancreatitis, increased intraluminal pressure due to pancreatempyphraxis causes activation of trypsin within pancreatic acinar cells, leading to inflammation of the pancreatic parenchyma through activation of pancreatic enzymes. Increases in cholesterol secretion due to pregnancy, cholestasis, and progesterone-induced gallbladder hypomotility accelerate the formation of gallstones.

Hyperlipidemia is known to occur as one of the physiological changes accompanying pregnancy. Triglycerides are about 3~4 times higher in late pregnancy than when not pregnant, and total cholesterol increases to about 1.5 times. The hyperlipidemia causing acute pancreatitis is a triglyceride-dominant form with high levels of chylomicrons and VLDL, and the generally accepted explanation of its onset mechanism is Havel’s theory. Namely, that as the free fatty acids occurring when triglycerides are hydrolyzed with lipase damage acinar cells and capillaries, the chylomicrons block capillaries causing ischemia and acidosis, and the free fatty acids activate trypsinogen under this acidosis environment to induce acute pancreatitis. Triglyceride levels of 1,000 mg/dl or more are held as being capable of causing onset of acute pancreatitis. Familial hyperlipidemia is reported in many cases of onset of pancreatitis, with V-type hyperlipidemia accounting for 90% of reported cases.

In this case, a TG-dominant increase in TG and Tcho levels was observed at the time of onset of acute pancreatitis indicated a V-type hyperlipidemia pattern, but in subsequent outpatient follow-up Tcho levels normalized showing an IV-type pattern with elevated TG levels only. Familial type-4 hyperlipidemia was suspected to be the underlying disease due to a family history of hyperlipidemia, with onset of acute pancreatitis in this case thought to be caused by pregnancy-induced exacerbation of hyperlipidemia.

In addition, pancreatic exocrine hyperfunction due to pregnancy, progesterone-induced hypertension of Oddi’s sphincter, and an increase in intraabdominal pressure caused by the expanding uterus in late pregnancy are other factors thought to contribute to the onset of pancreatitis.

Treatment methods for gestational pancreatitis are the same as those for non-gestational
pancreatitis\textsuperscript{11}. As the use of fibrate formulations and statins is difficult in pregnancy complicated with hyperlipidemia, we will investigate the use of an ultra low-fat diet (less than 40 g/day or 10~15\% of total calorie intake) with the objective of keeping triglycerides to 1,000mg/dl or less to prevent pancreatitis\textsuperscript{12}, and for difficult cases we will investigate nutritional management with TPN.

As a general rule, the pregnancy should be continued in mild to moderate cases of pancreatitis, but as the prognosis is poor in many severe cases or those complicated with hyperlipidemia, terminating the pregnancy will be investigated as an effective treatment method.

While continuous hemodialysis and filtration in pregnancy-related pancreatitis involves the risk of influence to the fetus during pregnancy and of hemorrhage after delivery, it has been reported to be effective as with other types of pancreatitis\textsuperscript{14}. Also, combined treatment with plasma exchange may be effective in cases with hyperlipidemia\textsuperscript{15}. While it requires due caution, hemocatharsis may also be an effective treatment option in pregnancy-related pancreatitis.

Conclusion

We encountered a case in which familial hyperlipidemia was exacerbated by pregnancy, leading to onset of acute pancreatitis in late pregnancy. Acute pancreatitis carries a high mortality rate for both the mother and the fetus, requiring appropriate diagnosis and treatment. In addition, anticipation and prevention of onset of pancreatitis through follow-up of serum lipids throughout the course of the pregnancy is important, particularly in expectant mothers with hyperlipidemia.

References


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