Multidisciplinary diagnosis and treatment of severe acute pancreatitis associated with hypertriglyceridemia in pregnancy: a case report

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Background: Hypertriglyceridemia (HTG) is an important cause of acute pancreatitis (AP) in pregnant women. Due to the variable clinical features of acute pancreatitis, it is difficult to make a differential diagnosis when abdominal pain occurs in late pregnancy. Severe HTG induced acute pancreatitis during pregnancy is rare, but may be a fatal threat to both mothers and fetuses during the peripartum period, and can increase maternal and fetal mortality. If emotional disorder combined, difficulty of treatment increased. So, multidisciplinary diagnosis combination of psychiatric treatment could improve the diagnosis rate and cure rate of acute pancreatitis during pregnancy.

Case Description: We present the case of a 27-year-old Chinese woman in her first pregnancy, who was admitted to the hospital in the planned delivery period, but then developed progressive abdominal pain and whose biochemistry parameters were high enough to underwent a cesarean section as a result of AP a few hours after admission. The patient developed organ failure after a successful labor, which rapidly evolved to multi-organ failure, accompanied by depressive symptoms. Afterwards She appeared such as agitated, uneasy, and sad, and did not comply with the treatment, according to the classification of symptoms and course of disease, postpartum depression (PPD) was highly suspected. The patient benefited from multidisciplinary treatments that combined and integrated traditional Chinese medicine (TCM) with Western medicine therapies. The patient was discharged 35 days after her admission.

Conclusions: This case highlights the importance of monitoring and managing excess dyslipidemia during pregnancy. A proactive strategy should be encouraged in the management of the patients with high risk of pancreatitis to improve the outcomes of patients. Our case report elucidates the possible long-term effects of HTG and reminds us of the need for long-term management of those affected.

Keywords: Acute pancreatitis (AP); multiple organ dysfunction syndrome; hypertriglyceridemia (HTG); depression; case report

Submitted Jun 08, 2022. Accepted for publication Jul 29, 2022.
doi: 10.21037/atm-22-3313
View this article at: https://dx.doi.org/10.21037/atm-22-3313

Introduction

Acute pancreatitis (AP) during pregnancy is a rare but life-threatening disease of the mother and fetus, with an estimated incidence of approximately 3–10/10,000 (1,2). Previous study has shown that 60% of AP occurs in the 3rd trimester of pregnancy, and gallstones are the most frequent etiology, followed by alcohol abuse, hypertriglyceridemia (HTG), and unknown causes (3).

Recent studies have shown that HTG is the cause of AP in approximately 50% of pregnant patients in China (4,5). Compared to other causes, HTG-induced AP during pregnancy is more likely to develop into severe

AP, is associated with a poor outcome, and increases the maternal and infant mortality (6,7). The major causes of HTG-induced AP include hereditary diseases (e.g., familial chylous microparticles) and secondary lipid metabolic diseases (e.g., diabetes, hypothyroidism, and pregnancy). Pregnancy aggravates the illness. The short-term impact of HTG-induced AP is predictable, meanwhile, the long-term psychological impact on the mother is rare, and even the long-term impact on children is unclear. Therefore, regular follow-up of patients and children is necessary.

To diagnose acute pancreatitis, the revised Atlanta classification (RAC) combined with venous chylous blood or serum triglycerides >11.30 mmol/L, HTG-induced AP diagnosed, and acute pancreatitis can be diagnosed in about 80% of patients based on the presence of abdominal pain and elevated pancreatic enzymes only. However, the clinical diagnosis and subsequent treatment of AP is challenging in late pregnancy due to the changes in the physiological and anatomical structures. Due to the lack of specific guidelines on the management and treatment of hyperlipidemia during pregnancy, appropriate medical decision making depends on experienced clinicians implementing individualized treatments. When postpartum patients with HTG-induced AP have multiple systemic functional recoveries during pregnancy, the risk of secondary emotional disorders increases because of the fluctuations in hormone levels. A multidisciplinary team is urgently needed throughout the whole perinatal period to ensure the safety of treatment.

We described a case of HTG-induced AP during pregnancy that was successfully treated by a multidisciplinary diagnosis and treatment, which included the use of traditional Chinese medicine (TCM). We present the following article in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3313/rc).

Case presentation

A 27-year-old woman at 40 weeks of gestation in her first pregnancy (G1P0Ab0) presented at the West China Hospital of Sichuan University. A few hours after her admission, she had a planned delivery, but then developed progressive severe epigastric pain accompanied by nausea and vomiting, whose biochemistry parameters show that serum amylase was 202 mmol/L, lipase was 346 mmol/L, triglyceride was 52.63 mmol/L. The significant laboratory findings indicated that she had HTG-induced AP. The patient's past medical and family history was unremarkable (there was no known chronic disease or drug use in the patient's history, such as diabetes mellitus, alcohol intake, psychiatric disease and pancreatitis). An cesarean section was performed immediately, as there was a risk that the patient's condition might rapidly deteriorate. Her condition progressively worsened after the emergency cesarean section. Her manifestations were confusion of consciousness, a fever (38 ℃), tachycardia (165/minute), and tachypnea (32–40/minute), but she had normal blood pressure of 118/78 mmHg. Soon afterward, she was referred to the intensive care unit.

A physical examination revealed upper abdominal tenderness and vaginal bleeding. Laboratory tests revealed pyemia, renal impairment, respiratory failure, severe HTG, and metabolic acidosis. Subsequently, her clinical condition deteriorated as her abdominal pressure peaked to 25 mmHg and her APACHE II (Acute Physiology and Chronic Health Evaluation II score) achieved 30 points. She received tracheal intubation with mechanical ventilation due to shock and respiratory distress, and echocardiography monitoring was started. She received hemoperfusion and continuous renal replacement therapy to decrease her blood lipid levels and to remove endotoxin.

On day 2, she had a nasointestinal tube and an anal tube placed, and she was treated with an enema, tube feeding and an external application of Chinese herbal medicines, in addition to acupuncture and moxibustion. The initial diagnosis included severe acute pancreatitis (SAP), multiple organ dysfunction syndrome (MODS), pyemia, acute respiratory distress, acute kidney injury, HTG, postpartum hemorrhage, and HTG-induced AP.

On day 4, her laboratory tests showed a gradual reduction in the inflammatory indicators and HTG, but she still had a persistent fever. Her routine blood examination showed that she had significantly increased band neutrophils. Her 2 central venous catheters had to be removed. The patient's condition remained complex and critical because she had hypoproteinemia, thrombocytopenia, anemia, coagulation dysfunction, venous thrombosis, and bacterial pneumonia. To ensure her hemodynamics remained stable, ventilators were used intermittently to assist the patient with her breathing, and her renal and respiratory parameters showed an obvious improvement. Her endotracheal tube was removed on day 8.

Next, she undertook restoring exercises under the guidance of a rehabilitation therapist, and nutritional, and endocrinology physicians gave her an individualized enteral nutrition allocation. On day 15, she gradually transitioned

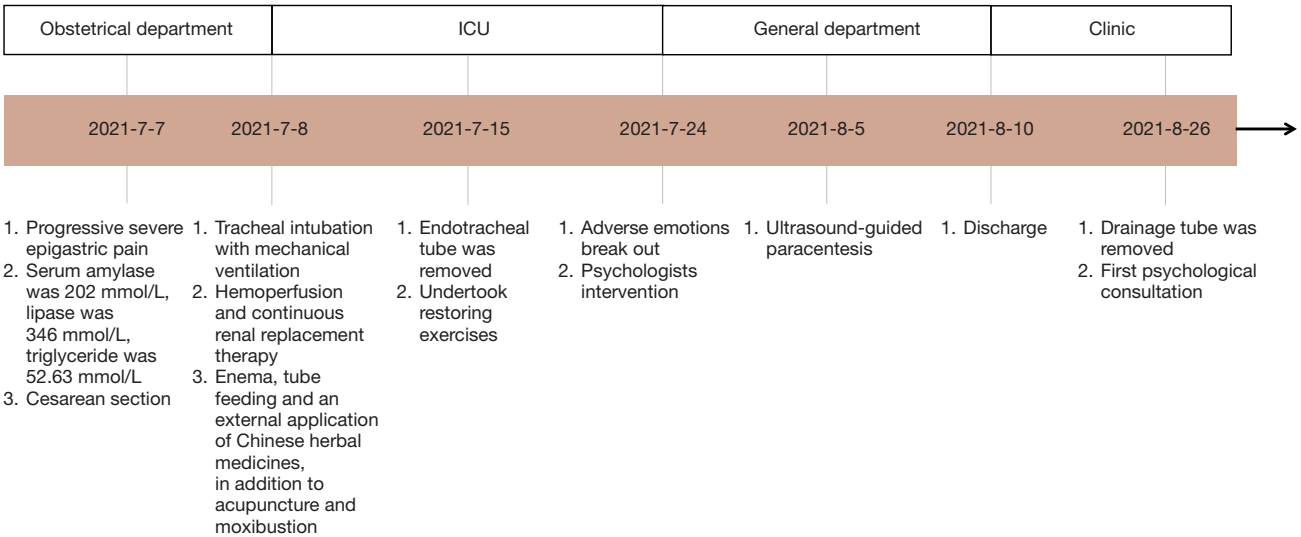

Figure 1 Timeline of the clinical course.

to walking beside the bed with assistance but had to fast temporally due to abdominal pain because of an intestinal obstruction.

On day 17, she suddenly developed agitation, was uneasy, and did not comply with the treatment recommendations. She started crying, as she said she was worried about her high medical expenses, missed her babies and was afraid that she had a poor prognosis, postpartum depression (PPD) was diagnosed. Given the patient's physical condition, psychotropic drugs were not recommended. She underwent multiple psychological interventions and had consultations with psychotherapists during her treatment. The patient's emotional disorder improved after 1 week, and she was transferred out of her single room. On day 29, a total of 820 mL dark-colored liquid was drained by an ultrasound-guided paracentesis.

On day 35 of her admission, the patient was discharged home in good clinical condition with an indwelling abdominal drainage tube to continue peritoneal drainage. It was recommended that she continue her diet following the nutritionist and endocrine doctors' advice to treat HTG according to the laboratory tests. The pathogenesis of HTG could not be determined due to the absence of genetic testing.

The diagnosis of PPD was considered by psychologists according to the American Diagnostic Statistical Manual of Mental Disorders—5th Edition and the Edinburgh Postnatal Depression Scale. And we exclude organic mood disorders and depression due to general medical conditions. While PPD is a typical manifestation of postpartum emotional disorder, it is not an independent disease. There may be comorbidities between PPD and other subtypes of postpartum emotional disorder.

The patient needed regular medication and psychotherapy. A clinical timeline is presented in *Figure 1*.

Finally, the drainage tube was removed 16 days after discharge, and the patient returned to our hospital 4 months later with almost normal laboratory tests (see *Table 1*), but dyspepsia persisted. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

HTG is the 3rd most common cause of AP. The rates of local complications and organ failure increase significantly and dose-dependently with the level of triglycerides (8). The trend of HTG-induced AP has been observed to increase with the gestational age and number of pregnancies (9). This disease constitutes a systemic inflammatory process accompanied by thrombosis, and bleeding disorders result in multiple organ dysfunction and disseminated intravascular coagulation (9). Yang *et al.* showed that HTG-

Table 1 Laboratory results during the patient's hospital stay

Laboratory results	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 9	Day 22	Day 31	Day 47	4 months
HGB (g/L)	199	144	127	112	93	81	78	82	69	79	111	–
Platelets ($\times10^9$/L)	232	29	26	26	43	72	192	567	481	489	449	–
WBC ($\times10^9$/L)	19.45	15.81	18.61	27.31	14.05	13.5	26.11	24.9	16.69	8.12	6.28	–
Serum AST (U/L)	13	401	622	219	221	96	61	40	7	21	15	35
Serum ALT (U/L)	26	292	510	200	90	43	34	31	16	21	22	25
ALB (g/L)	24.6	34.4	28.6	28.8	26.7	40.3	41.7	46.5	30.3	44.4	47.7	47.1
Serum glucose (mmol/L)	15.5	12.3	12.3	8.2	10.9	9.95	9.97	10.4	8.39	4.79	5.1	4.95
BUN (mmol/L)	2.8	3.4	8.6	8.2	7.1	10.8	14.2	27	7	4.3	3.3	4.2
Serum creatinine (mmol/L)	109	49	135	113	117	145	143	153	47	43	50	49
Serum TG (mmol/L)	141.41	37.25	27.14	4.42	5.03	6.96	6.32	6.93	3.31	2.76	1.34	2.12
Serum TC (mmol/L)	24.74	20.4	10.56	3.64	3.13	3.8	4.34	4.73	3.52	2.96	4.18	4.74
Serum amylase (U/L)	1,132	–	335	169	148	–	121	–	39	24	38	–
Serum lipase (U/L)	1,875	–	414	195	124	–	104	–	55	31	21	–
Serum calcium (mmol/L)	1.33	1.64	1.37	2.55	1.72	2.17	2.26	2.4	2.04	2.37	–	–
PT (seconds)	11.6	12.3	12.6	13.5	10.5	11.1	11.9	13.1	30.7	12.3	11.7	–
APTT (seconds)	35.8	41.9	37	30.8	29.3	26.5	26.2	26.8	49	36.7	27.1	–
PCT (ng/mL)	2.92	54.5	65.9	34	14.5	–	4.68	1.91	0.09	0.06	–	–
CRP (ng/mL)	397	355	232	191	187	–	307.7	87.4	99.9	82.2	–	–

HGB, hemoglobin; WBC, white blood cell; AST, aspartate transaminase; ALT, alanine transaminase; ALB, albumin; BUN, blood urea nitrogen; TG, triglyceride; TC, total cholesterol; PT, prothrombin time; APTT, activated partial thromboplastin time; PCT, procalcitonin; CRP, C-reactive protein.

induced AP along with a delayed diagnosis was related to a 66.7% fetal loss (10).

Gallstones, an increased maternal age, an increased pregnancy number, a high-fat diet, and a higher body mass index significantly increase the incidence of AP (11). Most patients with HTG do not have a recognizable genetic cause, and the elevated triglyceride levels result from a combination of multiple genetic variations and environmental influences (12).

Normal pregnancy is characterized by adaptive changes in lipid metabolism. Triglyceride levels gradually increase during pregnancy and peak at late pregnancy and are 2 to 4 times higher than early pregnancy levels; however, such concentrations are not sufficient to cause AP. The factors associated with HTG-induced AP include physiological changes in lipid metabolism, diet changes, including excess caloric consumption, high saturated fat intake, high refined sugar intake, excessive weight gain, and decreased exercise during pregnancy; these factors increase the prevalence of HTG-induced AP.

There is no consensus as to when and how to terminate a pregnancy in patients with HTG-induced AP. In this case, a cesarean section was performed based on the severity of the pancreatitis and the fetal maturity, and the cesarean section reduced the perinatal mortality. Luo *et al.* indicated that once 1 or more indications were met, a cesarean section is a safe and necessary option to stop the deterioration of the patient due to pancreatitis and can save both the mother and the baby (13).

Once the correct diagnosis is achieved, the management principles of pregnant patients follow the current guidelines for the general population, but these principles are complicated by the decision regarding the timing and route of delivery (14). Because the patient was in a critical condition and the fetus was full-term, we performed a cesarean section as soon as possible in this case.

Intensive medical support is required to treat persistent symptoms after the termination of a pregnancy. Due to postpartum conditions deterioration rapidly, accompanied by insufficient organ perfusion, excessive inflammatory mediators and endotoxin should be removed to reduce the autoimmune injury. So, we recommend an early consideration of continuous blood purification therapy.

After the patient was transferred to the intensive care unit, she immediately received treatment with hemoperfusion and renal replacement therapy and had a combination of antibiotics to control infection because of the steep increase in infection indicators, including a high fever and organ dysfunction. The patient's inflammatory indicators and total cholesterol (TG) decreased significantly 3 days later due to the treatment of her disease and the cautious medical decision making in the early stage. Her symptoms of infection were gradually controlled after 3 weeks of antibiotic therapy.

Timely clinical management, such as fasting, nutritional support, fluid therapy and antibiotics, is effective at improving the therapeutic outcomes of patients with AP (15-17). The patient achieved good results in the adjuvant use of various TCM therapies, including enemas, external applications, oral administrations, and acupuncture. Liuhedan is a well-known TCM prescription developed at our hospital, and its external application to the abdomen effectively relieves pancreatitis inflammation. Previous study has shown that its anti-inflammatory properties inhibit pancreatic secretion and reduce the inflammatory index, and it can improve the immune regulation (18).

Chaiqin Chengqi decoction (CQCQD), which is a Chinese herbal formula, has been used in the treatment of AP at the West China Hospital for more than 30 years. Recent studies have shown that excessive visceral adipose tissue lipolysis by pancreatic lipase can cause systemic injury, and the components in CQCQD can antagonize pancreatic triglyceride lipase (19,20).

Zhu *et al.* reported that electroacupuncture, another TCM treatment, significantly reduced the severity of AP by inducing anti-inflammatory effects and reducing the time to refeeding (21). The combined use of multiple supplementary TCM treatments had a significant effect on the whole hospitalization process. There is accumulating evidence that TCM reduces the levels of serum and urinary amylase, decreases the permeability of capillaries, decreases the production of inflammatory cytokines, inhibits neutrophilic granulocyte activation, and attenuates pancreatic injuries (22). However, patients need to adhere to the oral administration of TCM for 1 month after discharge.

PPD is highly comorbid with anxiety disorders, and 40.1% of women suffer from at least 1 episode of PPD (23). Recent studies have suggested that mental health issues may be more prevalent in postpartum women than previously thought (24). As the patient's serious physical condition may have led to or even aggravated her PPD, we took a series of positive measures for preventive interventions (25), such as rehabilitative exercises, allowing the patient to listen to soothing music, starting a social support system, including fundraising, and reducing her economic pressure. However, she still appeared depressed, irritable, self-accusatory, and even refused further treatment.

The mental state of a patient may be ignored in perinatal women with severe diseases due to the excessive attention directed to the physical health of the mother and fetus. The American College of Obstetricians and Gynecologists recommends that care providers screen patients at least once during the perinatal period for depression and anxiety symptoms using a standardized, validated tool (26). An early identification and intervention, including professional psychological support, may alleviate clinical symptoms and reduce the duration of symptoms.

Severe HTG is usually asymptomatic, and the exposure to predisposing factors can cause a series of fatal maternal complications. Due to the lack of guidelines for the management and treatment of HTG-APP (HTG-induced AP during pregnancy), the treatment options are also less effective. Several studies have found that pregnancy with dyslipidemia may cause oxidative stress in the fetal vessels, exposing the newborn to greater fatty streak formation and a higher risk of atherosclerosis (27). It should be noted that dyslipidemia during pregnancy should be carefully assessed not only for its acute complications but also to determine the long-term disease risk and risk of death of the fetus. Previously, the application of Beite drugs, heparin, and plasma exchange was reported to rapidly reduce blood lipids in pregnant women (28,29). However, few studies have addressed the management of HTG during pregnancy through medical nutrition therapy (30,31).

Changes in hormone levels in pregnant women lead to the occurrence of individual anatomical and physiological transient changes, which become the conditions for pancreatitis. With the increase in the number of pregnant women adjusted by the national family planning policy, as well as the improvement of living standards, changes in dietary patterns and working and rest rules during

pregnancy, unhealthy lifestyles lead to obesity and increased body mass index, which further increases the risk of occurrence and recurrence of acute pancreatitis. The importance of regular physical examinations should be highlighted, and also the patient should have their blood lipid levels monitored, should maintain a healthy lifestyle, and should avoid excessive weight gain during pregnancy. Dyslipidemia during pregnancy is closely related to the high risk of gestational diabetes mellitus, which can easily increase the incidence of adverse pregnancy outcomes, such as premature delivery, cesarean section, macrosomia, and fetal distress (32,33), and even have a long-term effect on the metabolic status of postpartum mothers (34). Thus, we should pay attention to the changes in blood lipid levels throughout pregnancy, strengthen interventions to address the unhealthy lifestyles of pregnant women, and implement medical interventions if necessary to reduce the incidence of adverse pregnancy outcomes and a long-term adverse prognosis.

Depression is common in the acute phase of acute pancreatitis. Most patients will relieve or disappear with the improvement of the disease. However, when pregnancy is complicated with acute pancreatitis, the duration of depression may be prolonged. Considering the development of the fetus or the health status of the mother, the treatment will be limited, and comprehensive individualized benefit and risk assessment should be carried out before drug treatment. The combination of scientific hierarchical management, self-management, family management, community and hospital management may have a good effect on the recurrence and occurrence of PPD.

Conclusions

AP is a potentially life-threatening complication of hyperlipidemia in pregnant women. Due to the possibility of obstetric emergency episodes, the early identification and diagnosis of AP are needed to reduce the complications under limited conditions. Once AP has been confirmed or is highly suspected, the pregnant patient should receive multidisciplinary integrated support. TCM has a powerful auxiliary role in this condition. Patients, who suffer from AP during pregnancy, experience severe physical and mental stress throughout the rehabilitation period, and require more psychological support and even professional psychological interventions. However, in this case, gene detection was not conducted, and we failed to identify whether the patient had any genetic defects. We implemented a positive psychological intervention; however, while our patient eventually received a psychotropic drug treatment, she has not yet fully recovered.

In the absence of guidelines on the management and treatment of hyperlipidemia during pregnancy, high-risk patients must engage in preventive measures during pregnancy, including the regular monitoring of their blood lipids, and early diet therapy can be considered to control excessive increases in blood lipids to minimize maternal and fetal harm. After the acute-stage treatment, lifestyle changes, including diet adjustment and drug treatment, are essential for the long-term management and to prevent the recurrence of HTG-induced AP.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3313/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3313/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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Cite this article as: Zheng L, Wang D, Li G, Zhao X, Yang R. Multidisciplinary diagnosis and treatment of severe acute pancreatitis associated with hypertriglyceridemia in pregnancy: a case report. Ann Transl Med 2022;10(16):911. doi: 10.21037/atm-22-3313

