



Acute Pancreatitis in a Pregnant Woman Complicated by Hypovolemic Shock: A Case Report and Literature Review

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Abstract

This case reviews a unique course of a 39-year-old pregnant woman presenting on second trimester with an uncommon combination of vomiting, hypovolemic shock, pancreatitis and thyrotoxicosis. In this case report, we discuss a few possible explanations of presenting illness, including pregnancy-related and unrelated causes, with a possibility that a combination of some of these causes could have led the complete picture. We hope this study will contribute to the understanding of the causes and possible outcomes of acute and severe illnesses presenting during pregnancy.

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Background

Acute pancreatitis is a leading gastrointestinal cause of hospitalization in the United States [1]. Etiologies include gallstones and alcohol consumption (that account for the majority of cases), as well as hypertriglyceridemia, specific medications, iatrogenic (especially post ERCP) and trauma. Less common causes include vasculitis, hypercalcemia, anatomic anomalies, and hereditary pancreatitis. The diagnosis of acute pancreatitis requires the presence of at least two of the following: 1. typical abdominal pain; 2. serum lipase or amylase levels over 3 times the upper limit of normal; and 3. characteristic findings on cross-sectional abdominal imaging [2]. Disease severity cor-

relates with mortality, and is estimated by the presence of organ failure including shock, respiratory and/or renal failure, and local or systemic complications [3].

Thyrotoxicosis is defined as an excess of thyroid hormone in the circulation. The diagnosis is based on the elevation of serum free thyroxine [T4] and/or triiodothyronine [T3] and, in primary hyperthyroidism, low TSH levels. Disorders causing thyrotoxicosis can be divided according to mechanism and radioiodine uptake pattern: 1. Thyrotoxicosis with hyperthyroidism (normal or high uptake) – including Grave's disease, toxic multinodular goiter, toxic adenoma, TSH-secreting pituitary adenoma, gestational thyrotoxicosis amongst others; 2. Thyrotoxicosis without



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hyperthyroidism (low uptake) – including destructive inflammatory processes of thyroid tissue such as subacute and silent thyroiditis, and extrathyroidal sources of hormone [4].

We describe a patient who presented at the emergency room during her second trimester of pregnancy with hypovolemic shock due to acute pancreatitis, with at first unexplained thyrotoxicosis and with a poor pregnancy outcome post-hospitalization.

Case Report

A 39-year-old Bedouin woman, 17 weeks pregnant (G7P6), was referred to the Emergency Room (ER) of Soroka medical center on November 2020 due to recurrent vomiting.

Her medical history included obesity, hypertension not previously treated, factor V Leiden heterozygosity with provoked massive Deep Vein Thrombosis (DVT) following her 6th delivery in 2017, and a history of mild acalculous pancreatitis that required hospitalization in 2010. She was prescribed Rivaroxaban that was changed to Enoxaparin and Aspirin during the pregnancy. Her obstetric history included six normal deliveries with no adverse events except for peripartum DVT as noted. Current pregnancy was with poor prenatal care, including a single visit to the gynecology ER due to first trimester vaginal bleeding.

The patient reported multiple and recurrent vomiting throughout her current pregnancy similar to previous pregnancies, only this time it did not resolve by the end of the first trimester. Her complaints worsened during the two weeks before her hospitalization, with poor oral intake during this time. The patient denied fever, respiratory, genitourinary and other gastrointestinal complaints, as well as alcohol or drug use or recent medication changes.

At the ER the patient presented with shock with low blood pressure and extreme weakness. On physical examination heart sounds were regular and rapid without additional sounds or murmurs, lung examination was normal, abdominal examination revealed a large soft and non-tender abdomen, extremities were without edema or DVT signs.

Laboratory tests on arrival: Normal coagulation functions with high fibrinogen levels (903 mg/dL). Normal hemoglobin (13.0 gr/dL) with low hematocrit (35.4%), Leukocytes $11.15 \times 10^3/\mu\text{l}$ with normal differential except for mild monocytosis ($1.18 \times 10^3/\mu\text{l}$), and mild thrombocytosis ($412 \times 10^3/\mu\text{l}$). Marked elevation of creatinine (4.14 mg/dL) and urea (176.7 mg/dL). Low sodium (128 mEq/L), potassium (3.1 mEq/L) and chloride (73 mEq/L), and high calcium (11.1 mEq/L), phosphorus (6.2 mEq/L) and magnesium (3.18 mEq/L) levels. Bilirubin levels were elevated (total 2.89, direct 1.42 mg/dL), with abnormal liver function tests (ALKP 111, GGT 83, AST 127, ALT 316 U/L). Both amylase and lipase were elevated (362 and 579 U/L, respectively). Blood gases showed a combination of metabolic and respiratory alkalosis with high anion gap metabolic acidosis (pH 7.51, pCO₂ 38.3, bicarbonate 30.4). CRP was 1.31 mg/dL.

Point of care ultrasound performed in the ER showed a hyperdynamic heart with “kissing ventricles” pattern and a small IVC diameter suggestive of hypovolemic state.

The patient was treated in the trauma room by fluid resuscitation, with rapid improvement of clinical state and vital signs, and after stabilization was admitted to the gynecology ward.

During her hospitalization, the patient presented with the

following problems:

Hypovolemic Shock, Acute Kidney Injury (AKI) and Electrolyte Imbalance

As described, the patient presented with hypovolemic shock, with elevated urea and creatinine (previous creatinine was normal) and extensive electrolyte imbalance. She was treated in the ER with boluses of normal saline (3 liters total) and four additional liters in the next 24 hours.

Due to AKI a relevant workup was performed: Urinalysis revealed elevated protein/creatinine ratio of 867, urine osmolality was 378 mEq/L, sodium was 30 mEq/L, potassium 8 mEq/L and chloride 21 mEq/L (note that urine was obtained >24 hours after admission, post fluid resuscitation). Urine microscopy 5 days after admission (sampled from a catheter inserted in the ER) showed no casts or red blood cells, with multiple white blood cells and rod-shaped bacteria. Abdominal ultrasound (US) showed no pathological findings of the urinary system, and renal vein duplex was normal.

During hospitalization, blood tests showed improvement and then resolution of renal functions, and electrolyte imbalance resolved with fluid correction, except for hypokalemia and hypomagnesemia that required IV supplementation. The patient was treated with cefuroxime for suspected urinary tract infection (urine culture was later positive for *Escherichia coli* susceptible to this treatment).

Pancreatitis

A previous event of pancreatitis in 2010 was presented with central abdominal pain and vomiting. CT scan showed moderate pancreatic inflammation with no visible stones in the biliary system, triglycerides were normal. The patient was treated symptomatically and was discharged two days later in good condition.

As described above, labs on arrival showed mixed liver function abnormalities and elevated amylase and lipase. The following days these increased up to amylase of 1057 U/L and lipase of 378 U/L.

The patient completed the following workup: Blood triglycerides were 381 mg/dL and alcohol levels (obtained 4 days after admission) were <10 mg/dL. Abdominal US showed normal liver size and texture, gallbladder with no stones or inflammation and normal intra and extra-hepatic bile ducts; Pancreas was only partially demonstrated, and the head of pancreas showed no gross findings.

The patient was initially treated with IV fluids and no oral intake, with rapid improvement: the vomiting resolved, and enteral nutrition was renewed, bilirubin normalized and other liver and pancreatic functions improved significantly.

Thyrotoxicosis

On 3rd day of hospitalization, due to persistent tachycardia despite fluid correction, thyroid functions were obtained and revealed TSH<0.008 uIU/mL with elevated free T3, free T4 and thyroglobulin (up to 7.8 pg/mL, 4.5 ng/dL and 245 ng/mL, respectively).

Past medical records showed normal thyroid functions, including two months earlier. On targeted questioning the patient reported palpitations and constipation, and denied neck pain, fever or exposure to contrast material. Targeted physical exami-

nation revealed tachycardia, tremor, possible mild lid lag and non-pitting pedal edema (only described after receiving large volume of IV fluids for several days); neck palpation revealed no apparent goiter or nodules. Blood tests for antithyroglobulin and anti-thyroid peroxidase antibodies were negative. A neck US showed thyroid gland with normal size and texture and with no apparent nodules, doppler demonstrated slightly increased blood flow to both lobes of the gland.

The patient was treated symptomatically with increasing doses of beta-blocker until reaching normal heart rate. Repeated blood tests showed spontaneous thyroid function improvement and therefore anti-thyroid treatment was not initiated, and on discharge T3 and T4 level normalized.

Pregnancy with Poor Prenatal Care

As noted, the patient was in the 17th week of her 7th pregnancy with poor prenatal care until the current event. While hospitalized, a fetal ultrasound was performed, showing a single fetus with biometry correlating with 17 weeks gestation, normal fetal heart rate, movements and amniotic fluid volume, and an anterior placenta.

The patient was initially admitted to the gynecology ward and treated by a multidisciplinary team, including internal medicine specialist and endocrinologist-gynecologist, and was later transferred to the internal medicine ward for additional workup and observation. Following clinical and laboratory improvement, the patient was discharged with a course of oral beta-blocker and magnesium treatment, until heart rate and electrolytes normalized. The patient was recommended to continue laboratory follow-up and full prenatal care with additional endocrinologist-gynecologist surveillance.

Following discharge, the patient did not make regular visits to her gynecologist for routine prenatal follow-up. However, she did attend the high-risk pregnancy (HRP) clinic every few weeks. During these visits, the patient showed normalization of liver, pancreas, and thyroid functions; due to high blood pressure without proteinuria, labetalol treatment was started.

Around 32 weeks gestation, due to measurement of severe high blood pressure, the patient was admitted to the HRP ward for monitoring and evaluation. During hospitalization lab results were normal except for a urine protein/creatinine ratio of 371 mg/gr. Obstetric ultrasonography showed a bilateral notch on uterine artery doppler with no additional maternal or fetal abnormal findings. Twice-daily fetal heart rate monitoring was normal. The patient's medical treatment was adjusted by increasing doses of labetalol and a course of betamethasone was given. Due to *Escherichia coli*-positive urine culture the patient was treated with nitrofurantoin.

On the fourth day of hospitalization, a spontaneous rupture of membranes and vaginal bleeding occurred, and the patient was transferred to the delivery room. On fetal monitor and US the fetus was found to have no pulse, and antepartum death was diagnosed. Later pathological examination of the placenta revealed mild acute chorioamnionitis and signs of maternal-side under-perfusion with subchorionic fibrin thrombi and retroplacental hematoma.

Discussion

This is a rare case of severe acute pancreatitis episode during pregnancy, presenting with hypovolemic shock and consequent AKI, rapidly corrected with IV fluids.

The etiology of pancreatitis was not identified upon basic workup in current and previous episodes, although common etiologies were ruled out, including biliary origin, alcohol consumption, hypertriglyceridemia and gross anatomical pancreatic abnormalities. Although the patient presented with hypercalcemia on admission, this is not likely to be the cause, as it was most probably secondary to severe dehydration and indeed was rapidly corrected with IV fluids.

Although rare, acute pancreatitis can present as a complication of pregnancy. Biliary disease is still the main etiology accounting for two-thirds of cases of pancreatitis during pregnancy and is associated with better outcomes [5]. Other less common etiologies associated with pregnancy include acute fatty liver of pregnancy, hypertriglyceridemia of pregnancy (primarily in combination with familial hypertriglyceridemia), preeclampsia and hyperemesis gravidarum [6]. Biliary disease was ruled out in our patient as previously described, as well as the first three pregnancy-related etiologies: Liver size and texture were normal on imaging and transaminases were normalized rapidly during hospitalization, only slight elevation of triglyceride was noted, and patient did not fill diagnostic criteria for preeclampsia.

Hyperemesis Gravidarum (HG) is associated with amylase and lipase elevation in 10-15% of patients, and can increase up to five-fold of normal levels [7]. HG on its own does not usually cause hypovolemic shock and AKI [8], although in combination with pancreatitis it can lead to adverse outcomes. The diagnosis of HG as the cause of current event is supported by the fact that the patient's main complaint at presentation was vomiting that appeared on previous pregnancies and persisted throughout current pregnancy, as well as the combination of liver and thyroid function abnormalities also known to be associated with HG[9]. Against this diagnosis is the fact that HG only occurred during 2nd trimester of the patient's pregnancy, when it usually resolves by the end of 1st trimester [10], together with previous history of pancreatitis when she was not pregnant.

Immunoglobulin G4-related disease, an immune-mediated fibro inflammatory condition, may affect multiple organs, including the pancreas, thyroid and kidneys [11,12]. Type 1 (IgG4-related) autoimmune pancreatitis may present as acute, recurrent, or chronic pancreatitis. The fact that this was her second event of pancreatitis in combination with multiple-organ involvement raise the option of this diagnosis. However, Riedel's thyroiditis associated with this syndrome does not match the patient presentation, as it is usually chronic, with hypo- rather than hyperthyroidism in most cases, and with a firm neck mass not observed in current case [13]. That, and the absence of other characteristic organ involvement, make this diagnosis less probable although possible.

Additional evaluation is needed to determine the cause of recurrent pancreatitis, including high quality imaging, genetic testing for hereditary pancreatitis and immunological workup including IgG4; meanwhile, however not typical, HG as a contributor for current event cannot be ruled out.

Another unresolved issue presented in this case was the transient thyrotoxicosis. Features suggestive of Grave's disease including goiter, specific ocular findings and typical antibodies were not found, and further investigations ruled out multinodular goiter or toxic adenoma. Radionuclide uptake studies could not be performed due to pregnancy, and alternative test with color-flow doppler ultrasonography showed increased blood

flow suggestive of hyperthyroidism rather than destructive thyroiditis.

Homology between the hCG beta-subunits and TSH may result in hyperthyroidism in pregnant women during the period of highest serum hCG concentrations, around 10-12 weeks of gestation. One entity included under the "hCG-mediated hyperthyroidism" group is HG-related hyperthyroidism, due to relatively high hCG levels in these patient [14,15]. Vomiting as presenting feature, the increased blood flow on doppler US and the absence of other findings suggestive of Grave's disease support this diagnosis, as well as the fact that thyroid functions resolved spontaneously over time. However, the relatively severe thyroid function disturbance, and specifically T3 elevation, that persisted beyond first trimester, the presence of overt thyrotoxicosis symptoms and the fact that thyroid functions were normal earlier in current pregnancy does not usually correlate with this entity [16].

"Shock thyroid" is a radiological entity described as a rare manifestation of the 'hypovolemic shock complex' on computed tomography (CT) [17,18]: On two case series a total of seven patients were described with hypovolemic shock and with a secondary CT showing heterogeneous enhancement of the thyroid with a collection of homogenous fluid surrounding the gland. Thyroid function tests were not obtained except for one patient with normal levels. One hypothesis regarding these CT findings is that the hypotension stimulated a profound thyroid response in attempt to maintain cardiac output by increasing heart rate. Another hypothesis is that the patients' poor hemodynamic status may have led to inadequate thyroid gland perfusion with subsequent cellular damage. Both theories may result in a transient thyrotoxicosis state that, as noted, has not been investigated in most patients. In current case the emphasis was on clinical and laboratory findings and CT scan was not performed due to her pregnancy. Although US did not reveal fluid collection or edema of the gland, the clinical course preceding the diagnosis and the rapid resolution following treatment may be consistent with the diagnosis of "shock thyroid".

Finally, the possible connection between the described event and later adverse pregnancy results should be discussed. The patient had six previous successful pregnancies and births with no adverse events, except for DVT following her sixth birth. Unfortunately, the current pregnancy ended with antepartum fetal death around 15 weeks following the described event, with clinical and pathological findings suggestive of placental abruption and hypoperfusion. The patient had multiple risk factors known to be associated with stillbirth, including older age [19,20], multiparity [21], obesity and hypertension (specifically connected to placental abruption) [20]. Poorly-controlled hyperthyroidism is also associated with increased pregnancy complications including stillbirth [22], although transient thyrotoxicosis as seen here was not found to be associated with placental abruption or stillbirth [23]. Furthermore, the association between acute pancreatitis episode during pregnancy and adverse fetal outcomes has been previously described, with a marked correlation between pancreatitis severity and fetal risk [24-26]. Finally, the role of the patient's inherited thrombophilia as a risk factor for stillbirth is controversial, with inconsistent results in both prospective and retrospective studies [27-33], although it cannot be ruled out as a contributor.

Conclusions

This case reviews a unique course of a 39-year-old pregnant

woman presenting on second trimester with an uncommon combination of vomiting, hypovolemic shock, pancreatitis and thyrotoxicosis. Although a clear common cause to all presenting components was not found, a few optional explanations were reviewed including pregnancy-related and unrelated causes, with a possibility that a combination of some of these causes could have led the complete picture. Later poor pregnancy outcome may be attributed to the combination of multiple risk factors that were found in this patient, as well as a possible and previously described connection to the presented acute event at an earlier stage of pregnancy. We hope this study will contribute to the understanding of the causes and possible outcomes of acute and severe illness presenting during pregnancy.

Declarations

Declarations of interest: none.

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