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Case Report

J Clin Gynecol Obstet. 2018;7(3-4):81-83

Beyond HELLP: Peripartum Catastrophic Thromboembolism due to Hereditary Diffuse Gastric Cancer

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Abstract

Peripartum thrombocytopenia and thrombotic events are usually attributable to diseases like Hemolysis Elevated Liver Enzymes Low Platelets (HELLP) and thrombotic thrombocytopenic purpura (TTP). Malignancy is a rare cause and gastric cancer even more unusual. We report the case of a 28-year-old female with undiagnosed hereditary diffuse gastric cancer (HDGC) in the peripartum period initially presenting with nausea and blurry vision at 35 weeks' gestation. Following cesarean section 1 week later, she developed thrombocytopenia and elevated blood pressure; HELLP was diagnosed. Development of acute kidney injury, decreasing platelet count and anemia lead to consideration of TTP. Despite plasmapheresis she had no improvement, developed respiratory failure and had acute large vessel arterial and venous thrombosis with multiple cerebral, renal, splenic and lower extremity arterial infarctions. Deep venous thrombosis of lower limbs was also seen. She was placed on corticosteroids and anticoagulation. Following extensive workup, vegetations on mitral valve were seen on echocardiography and she was started on antibiotics for endocarditis. She deteriorated into refractory shock, multiple organ failure and died on postpartum day 8. Autopsy done revealed diffuse submucosal gastric adenocarcinoma (linitus plastica). Metastases were present on small bowel, fallopian tubes, ovary and the placenta. Mitral valve had marantic vegetations. Tumor cells showed CDH1 gene mutation. Such a diagnosis in pregnancy is very challenging due to overlapping symptoms leading to misdiagnosis. Here, thromboembolism was malignancy-related and rapid spread probably hormone-associated. The purpose of this report is to highlight the need to warrant investigation for cancer, among workup for other common conditions, for atypical thromboembolism in pregnancy.

Keywords: Peripartum; Thromboembolism; Gastric cancer

Manuscript submitted September 7, 2018, accepted September 17, 2018

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doi: https://doi.org/10.14740/jcgo512w

Introduction

Pregnancy-associated gastric carcinoma is a rare occurrence, accounting for 0.025-0.1% of all pregnancies [1]. The diagnosis is often delayed due to several contributing factors particularly the non-specific symptoms which may be misinterpreted as pregnancy-related, a lack of suspicion and the hesitancy associated with performing invasive procedures in pregnant patients [2]. Therefore, most, if any, are identified at a very advanced stage with poor prognosis and of those, only 45-56% undergo surgical resection [1]. Hereditary diffuse gastric cancer (HDGC), a subtype of gastric carcinomas, follows a germline mutation in the type 1 E-cadherin (epithelial) gene (CDH1) with 70% of individuals with said mutation at a life-time risk for developing diffuse gastric cancer [3]. It is suggested that in addition to environmental and genetic factors, pregnancy itself may prove to be a risk factor [4]. There exists minimal subject matter on HDGC and pregnancy. Consequently, we report the case of a 28-year-old woman with undiagnosed HDGC presenting in her third trimester with symptoms eliciting emergent C-section following which her condition rapidly deteriorated resulting in death. Diagnosis was made on autopsy.

Case Report

A 28-year-old Hispanic lady, gravida-2 para-1, presented to the obstetrics department with symptoms of nausea, vomiting and fatigue. She was in her third trimester at 35 weeks' gestation. Her previous pregnancy was uneventful with no significant past medical and family history. She had no prior history of smoking, alcohol or recreational drug use and was HIV-negative. Her current pregnancy was going well until the 35th week. She did not report any fever or weight loss. Further investigation showed low platelets on CBC following which she was diagnosed with a query of either Idiopathic Thrombocytopenic Purpura (ITP), Thrombotic Thrombocytopenic Purpura (TTP) or Hemolysis Elevated Liver Enzymes Low Platelets (HELLP), all of which require steroid therapy. She was therefore started on methylprednisolone, transfused with packed red blood cells and discharged home.

One week after discharge, she again presented to the hospital with confusion, nausea and anemia. On subsequent evaluation, she was found to have acute kidney injury (AKI), thrombocytopenia and hypofibrogenemia for which she was taken in for emergent caesarian section for possible HELLP syndrome

(hemolysis, elevated liver enzymes and low platelets). However, following the procedure, her symptoms persisted with an additional blurring of vision. She had no abdominal pain, headache or fever. A repeat CBC was consistent with thrombocytopenia (23,000), anemia (hemoglobin of 7.9), AKI with creatinine of 1.9, fibrinogen of 150 and liver function tests (LFTs) mildly elevated (100s). An MRI was done demonstrating an occipital cerebrovascular event in the posterior cerebral artery distribution accounting for the blurry vision. Neurology was brought on board and the decision to start plasmapheresis for presumed TTP was made due to the AKI and worsening hematological tests. She was transferred to our department for further investigation and management.

Despite plasmapheresis she did not show improvement. Over the course of 24 h, she developed respiratory failure with new lung infiltrates and hypoxemia requiring intubation. Subsequently, she became hypotensive, was unresponsive to fluid challenge and was started on vasopressors for refractory shock. Hematology/oncology was consulted due to the presence of schistocytes on blood smear and an abdominal CT was done which was suggestive of lymphadenopathy. Clinically, she developed cyanosis of her lower extremity as well as further decline in mental status. Further investigation identified tibial artery occlusion and multiple new cerebral infarcts on head CT. She was tested for antiphospholipid antibody syndrome, placed on corticosteroids and anticoagulation. Blood cultures were positive for pneumococcus and echocardiography revealed mitral valve vegetations. She was, therefore, started on antibiotics for endocarditis. Her condition continued to decline rapidly. She started bleeding vaginally requiring IR embolization. She ultimately developed multiple organ failure with bradycardia despite efforts which progressed to asystolic arrest on post-partem day 8. Following her death, an autopsy was performed which revealed diffuse submucosal gastric adenocarcinoma (linitis platica) with extensive transperitoneal metastases on the diaphragm, small bowel, fallopian tubes, ovaries and the placenta. Multiple cerebral, renal, splenic and lower extremity infarcts were seen. Mitral valve had marantic vegetations and there was necrosis of the liver. Tumor cells shower CDH1 mutation indicative of HDGC.

Discussion

Although there has been a reported declining trend in the occurrence of gastric cancers [5], it continues to remain a leading cause of cancer-related mortality, more so in Asian countries [6]. It is a disease primarily in patients aged over 50 years [2]; however, approximately 10% occurs in those less than 45 years of age [7] with a female predominance [8]. Pregnancy-associated gastric carcinoma is an uncommon occurrence, accounting for up to 0.1% [2, 9] with HDGC being even rarer with a mutation in CDH1 gene affecting E-cadherin expression [3].

There exist common presenting signs and symptoms in patients which elicit a suspicion of gastric carcinoma inclusive of nausea, vomiting, dysphagia, dyspepsia, early satiety, epigastric pain, weight loss and melena [2]. However, most of these are commonly seen at some point in pregnancy and are therefore misinterpreted and attribute to the delay in diagnostic workup. Alternatively, in the early stages, it has been shown that up to 80% of patients are asymptomatic, further delaying diagnosis [10]. A study was done by Maconi et al which resulted in a mean delay of 29.3 ± 39.9 weeks in the diagnosis of gastric cancer in young patients with no alarm symptoms [11]. Pregnancy-related hormones have also been suggested as contributing factors towards the growth and pathogenesis of gastric cancers [12, 13].

Our patient developed thromboembolism which was secondary to malignancy and showed a rapid spread which may have been due to the hypercoagulable state induced by pregnancy hormones. A study done showed thromboembolism in malignancy, commonly known as Trousseau's syndrome, having the second highest incidence in relation to metastatic gastric cancer (10.7 events per 100 patient-years) following pancreatic cancer (20) [14]. The exact etiology is unknown, but the expression of tissue factor on tumor cells has shown to be an important factor as seen in gastric, colon, pancreatic, lung and breast carcinomas [15]. Another study done on Asian gastric cancer patients resulted in a 2-year cumulative incidence of venous thromboembolism (VTE) of 0.5% in stage I disease, 3.5% in stage II-IV(M0) and 24.4% in stage IV(M1) with most common being 62% intra-abdominal VTEs [16].

Previous studies done have shown that among pregnant women, the highest risk for thromboembolism lies in the postpartum period [17] with the most recognized risk factors being age, race, thrombophilia, lupus, heart disease, sickle cell disease, obesity, electrolyte imbalance, infection and transfusion [18]. However, very limited subject matter is available for the incidence of pregnancy-related gastric cancer and thromboembolism. Consequently, atypical thromboembolism in pregnancy should warrant investigation for cancer among workup for other common conditions.

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