Candida Esophagitis in an Immunocompetent Pregnant Woman

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ABSTRACT

Background: Nausea and vomiting are common during the first half of pregnancy and usually require only supportive measures. When symptoms are progressive and weight loss occurs, treatable causes should be sought by means of upper gastrointestinal endoscopy. We report a case of an immunocompetent gravida with invasive Candida albicans esophagitis.

Case: The immunocompetent primigravida developed progressive nausea, vomiting, epigastric pain, and a 4.1 kg weight loss during the second trimester of pregnancy. Treatment with metoclopramide and cimetidine for presumed gastroesophageal reflux was not effective. The patient had normal T-cell CD4 and CD8 subsets and was human immunodeficiency virus (HIV) antibody negative. Upper gastrointestinal endoscopy revealed C. albicans esophagitis which was treated with oral nystatin. The esophagitis had resolved completely when reassessed postpartum. The use of histamine2 blockers is associated with an increased risk for fungal esophagitis and may have been a contributing cause in this case.

Conclusion: Pregnant patients with persistent nausea, vomiting, and weight loss should be evaluated by endoscopy for fungal esophagitis.

KEY WORDS
Candida albicans esophagitis, hyperemesis gravidarum, pregnancy complications, gastrointestinal

We report a case of Candida albicans esophagitis in an immunocompetent gravida. We are unaware of other reports of this infection complicating pregnancy. We suggest that Candida esophagitis be included in the differential diagnosis of refractory nausea, vomiting, and weight loss during pregnancy.

CASE REPORT

A 37-year-old primigravida woman with a history of leiomyomata presented for prenatal care at 8 weeks gestation with a uterus that was 20 weeks size. At the age of 31 years, she had a positive tuberculin skin test and a normal chest radiograph. She refused isoniazid prophylaxis. Physical examination at that time showed a healthy, thin, black woman with a weight of 58.6 kg and a height of 167.5 cm. Pelvic ultrasonography showed a single, viable, 9.5-week fetus in a gestational sac near the cervix and a large fundal leiomyoma with dimensions of 17 × 10 × 13.5 cm. All routine prenatal laboratory values were normal. The patient declined human immunodeficiency virus (HIV) antibody screening. An amniocentesis done at 15 weeks showed a normal karyotype, 46 XX, and a normal alpha feto-protein.

In the second trimester, she developed increasing uterine pain, tenderness, and loss of appetite. By 17 weeks gestation, her weight had decreased 1.8 kg to 56.8 kg.
Fig. 1. Histologic section of esophagus demonstrating invasive Candida infection. Acute inflammation and necrotic material are present in the lamina propria. Hematoxylin and eosin stain. ×40.

Despite enteral supplementation, her weight decreased to 54.5 kg by 22 weeks gestation. She had nausea, vomiting, and a sensation of obstruction in her throat, but denied odynophagia. The uterus was markedly tender and was 30 cm at 22 weeks gestation. Degeneration of the leiomyomata was diagnosed.

Hemoglobin was 10.7 g/dl, white blood cell (WBC) count 8,800/mm$^3$ with a normal differential, platelets 613,000/mm$^3$, total protein 5.6 g/dl, and albumin 2.6 g/dl. All blood chemistries and liver function tests were normal. Ultrasound showed no hepatobiliary abnormalities and confirmed appropriate fetal growth.

Peripheral hyperalimentation was administered. Gastroesophageal reflux was diagnosed and cimetidine, 400 mg b.i.d., and metoclopramide, 10 mg 30–45 min before meals and at bedtime, were prescribed. Her symptoms resolved temporarily; she gained 2 kg. She refused further parenteral nutrition.

At 27 weeks gestation, nausea, vomiting, and weight loss recurred. She had no oral thrush or vaginal candidiasis. She denied having odynophagia, retrosternal pain, hematemesis, or fever. The uterine fundal height had increased to 38 cm. The 1-hr post-50 g glucola blood glucose was 151 mg/dl. A 3-hr glucose tolerance test met criteria for the diagnosis of gestational diabetes (fasting 77 mg/dl, 1-hr 194, 2-hr 167, and 3-hr 90). In order to provide adequate calories, we placed no restrictions and continued the Ensure (Ross Laboratories, Columbus, OH). Subsequent fasting and postprandial serum glucose concentrations remained normal. A 10 French-feeding tube was inserted for enteral hyperalimentation. The tube became kinked and stopped functioning after 1 week. The patient refused reinserterion of the tube until 32 weeks gestation. Upper gastrointestinal endoscopy (for placement of a second feeding tube) revealed the classic patchy white exudates of Candida esophagitis. No feeding tube was placed. Fungal culture and histologic section confirmed invasive C. albicans infection (Figs. 1, 2). Treatment was initiated with nystatin suspension, 500,000 units swish and swallow q.i.d. Metoclopramide and cimetidine were discontinued.
The patient's and her spouse's serum HIV antibody enzyme-linked immunosorbent assay (ELISA) tests were negative. The complete blood count (CBC), T-cell panel, and serum protein electrophoresis were normal. The WBC count was 10,600/mm³; lymphocytes were 18% of total (normal 15–40%); T-helper cells (CD4) were 48% (normal 32–56%); and T-suppressor cells (CD8) were 24% (normal 17–40%). Skin testing for mumps showed 30 mm of erythema at 48 hr after injection; coccidioidin caused no reaction. Chest radiograph was normal. During the course of antifungal therapy, the patient's dysphagia decreased, but her oral intake remained poor and abdominal pain increased. She remained euglycemic. After fetal maturity was confirmed, a cesarean delivery was performed at 36.5 weeks for breech presentation and increasing abdominal pain.

The female infant weighed 2,848 g and had Apgar scores of 9 and 9 at 1 and 5 min, respectively. There was a single fundal leiomyoma which extended to the left hemidiaphragm. There was no evidence of Candida esophagitis when upper gastrointestinal endoscopy was performed 3 days postpartum.

Five months postpartum, a myomectomy was performed. The leiomyoma weighed 852 g and measured 15 × 15 × 7 cm. Pathologic examination revealed a hyalinized and infarcted leiomyoma. A preoperative HIV antibody test remained negative.

**DISCUSSION**

We were unable to find other reports of Candida esophagitis during pregnancy in immunocompetent or immunocompromised patients. This diagnosis should be considered in patients with refractory nausea, vomiting, and weight loss during pregnancy. This patient did not have the common symptom of odynophagia or the presence of oral thrush. The nystatin therapy improved the dysphagia, and a repeat endoscopic examination confirmed resolution of the esophagitis. The patient's dysphagia and the histologically proven Candida

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Fig. 2. High-power view of Figure 1. Histologic section of esophagus demonstrating invasive Candida infection. Pseudohyphae are present within necrotic debris. Silver methenamine stain. ×450.
esophagitis cannot be attributed to the mass effect of
the gravid uterus and leiomyoma, although these
may have caused some of her epigastric discomfort.

Histamine$_2$ blockers are widely used and are
usually well tolerated. A significant association
exists between treatment with histamine$_2$ blockers
and the presence of fungal esophagitis. The
prevalence of fungal esophageal infection was 12 of
72 (16.7%) among patients exposed to histamine$_2$
blockers, whereas only 3.5% of patients unexposed
to the drug had fungal esophageal infection. The
association is somewhat unexpected because cimetidine
has been shown to enhance cell-mediated immu
nity in humans. Cimetidine augmented delayed
hypersensitivity responses to skin tests including the
Candida antigen in humans with duodenal-ulcer
disease. In 4 adult patients with chronic mucocu
taneous candidiasis, cimetidine stimulated the im-
une response to Candida antigen and the pro-
duction of leukocyte migration inhibitory factor,
although lymphocyte transformation was not af-
fected. Cimetidine and ranitidine are FDA cate-

光阴category B drugs; their use during pregnancy should
be limited to instances in which the benefit justifies
the risk.

Type I diabetes mellitus has been associated with
Candida esophagitis. Although this patient met cri-
teria for gestational diabetes mellitus, because she
remained euglycemic, we do not think that her
glucose intolerance was severe enough to be a cause
for the fungal esophagitis. Perhaps the combina-
tion of pregnancy, diabetes mellitus, and treatment
with a histamine$_2$ blocker may increase the risk for
Candida esophagitis.

Immunocompetent pregnant patients who have not
responded to routine therapy for gastroesoph-
ageal reflux should undergo upper gastrointestinal
endoscopy to diagnose Candida esophagitis. If they
have been treated with histamine$_2$ blockers, they are
at increased risk for esophageal fungal infection.

In immunocompromised pregnant patients, upper
gastrointestinal endoscopy is particularly im-
portant to identify opportunistic esophageal infec-
tions. As HIV infection becomes more common in
obstetrical patients, Candida esophagitis and other
opportunistic infections will be encountered more
frequently. At this time, Candida esophagitis is the
acquired immunodeficiency syndrome (AIDS)-indica-
tor disease for 15% of HIV-infected adolescents
and adults.

Although this patient responded to oral nystatin
therapy, immunocompromised patients frequently
need prolonged systemic therapy with fluconazole,
ketoconazole, or amphotericin B. The safety of
these systemic drugs during pregnancy has not been
established.

ACKNOWLEDGMENTS

We thank Samuel H. Pepkowitz, M.D., for assis-
tance in preparing the photomicrographs.

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