CASE REPORT

Advanced Esophageal Carcinoma Expressing Human Chorionic Gonadotropin (HCG-b)

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ABSTRACT

Human Chorionic Gonadotropin (HCG; HCGb) is expressed by various solid malignancies, including lung, pancreas, gastric and cervical cancers. Some previous studies suggest that this indicates an adverse prognosis. However, most of these studies evaluated HCGb expression by immunohistochemical methods, and the clinical significance of elevated levels of serum HCGb is not known. It may indicate a particularly aggressive disease. This phenomenon has not yet been studied in esophageal cancers. Here we present a case of a middle-aged woman with a poorly differentiated esophageal carcinoma that expressed HCGb, and elevated levels of the hormone appeared in her serum. These elevated serum levels were associated with a very aggressive clinical course.

KEY WORDS

Esophageal cancer, Human chorionic gonadotropin, HCG

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A 46-year-old lady with a history of cholelithiasis presented with worsening, colicky epigastric and right upper quadrant abdominal pain that had persisted for four to five months with no aggravating or relieving factors. She had associated nausea, loss of appetite and a 40-pound weight loss. She denied fevers, chills, vomiting, diarrhea, urinary complaints or jaundice. She had regular but heavy menstrual cycles and had four healthy children. Significant family history included ovarian cancer in her mother and lymphoma in her sister. Our patient had never smoked, or abused alcohol/drugs.

On physical examination, she was afebrile, pale but in no distress, with a regular heart rate of 82/min and a respiratory rate of 18/min. Her blood pressure was 161/92 mmHg. Systemic examination indicated normal lung, heart and neurological functions. An abdominal exam revealed tenderness in the epigastrium and right upper quadrant with no guarding or rigidity, no shifting dullness, no masses or organomegaly and normal bowel sounds. Pelvic examination was normal.

Laboratory analysis showed normal serum electrolytes and lipase, as well as normal renal and liver function. Hemoglobin was 8.6 g/dL (normal = 11.7-14.9 g/dL) with

an MCV of 68/fL (normal = 81.8-96.9/fL). Serum ferritin was 88.7 ng/ml (normal = 11-307 ng/ml) with a serum iron of 9 mg/dL (45-182 mg/dL), low percent saturation and a total iron binding capacity of 225 mg/dL (normal 250-425 mg/dL) consistent with anemia of inflammation. A urine pregnancy test was positive with an HCGb level of 190 milli-International Units (mIU). A transvaginal ultrasound showed multiple fibroids but no evidence of uterine or tubal pregnancy. A spontaneous abortion was suspected. However serial HCGb levels showed a plateau with levels of 156 and 166 mIU, a finding that is inconsistent with spontaneous abortion. A CT scan of chest/abdomen/pelvis showed irregular thickening of the distal esophagus and gastric cavity with multiple liver metastases, predominantly in the left hepatic lobe with periportal and retroperitoneal adenopathy. All tumor markers CEA, CA 19-9, CA-125 and alpha-fetoprotein were normal. An esophago-gastro-duodenoscopy showed a large ulcerated mass in the distal esophagus, extending to the lesser curvature of the stomach. Biopsy indicated a poorly differentiated carcinoma with some squamous differentiation on immunohistochemistry. The tumor was also stained for HCGb and was strongly positive, confirming the ectopic secretion of HCGb by the tumor.

The patient had an esophageal stent placed, which was then replaced with a jejunal feeding tube. She developed post-operative wound infection, which was treated with debridement and antibiotics. She was started on chemotherapy with cisplatin and 5-fluorouracil for one cycle, but as her tumor progressed, she experienced worsening dysphagia and pain, and her functional status rapidly declined. She enrolled in hospice services two months after the initial diagnosis.

Discussion

Ectopic HCG (HCGb) secretion has been reported in several types of tumors, including cervical, gastric, pancreatic, ovarian and lung cancers, and several studies indicate that its expression is associated with a graver clinical outcome as well. However, the prognostic significance of ectopically secreted serum levels of HCG in patients with esophageal cancers remains unknown. We present a case of HCG-secreting esophageal carcinoma with a very aggressive clinical course.

HCGb expression correlates with reduced tumor cell apoptosis, and increased expression may be involved as well in tumor vascularization and dissemination in patients with invasive cervical squamous carcinoma.¹ Moutzouris et al showed that HCGb expression increased with tumor invasiveness and that such tumors were relatively resistant to treatment.² Others found that the a false positive urine pregnancy test was neither sensitive nor specific enough to be used as a tumor marker for lung and esophageal cancer.³ However, another report indicated that elevated HCGb levels in serum and urine correlated with established tumor markers like CA 19-9 and carcinoembryonic antigen in patients with pancreatic and biliary cancers.⁴

Most studies of HCG expression in invasive cancers have been based on immunohistochemical analysis, yet the practical role of this hormone in any tumor may differ depending on the histological type. One study showed that 53% of patients with malignant gastric tumors had cells that were immunohistochemically positive for HCG; the positivity was more apparent in poorly differentiated tumors than in well differentiated tumors and more common in antral tumors than in other locations. This study did not find any prognostic significance of HCG secretion by the tumors.⁵ Another immunohistochemical study of colon cancers showed that patients with positive HCG had significantly worse survival compared to those with negative HCG production. The authors also found higher HCG positivity in patients with poorer tumor differentiation as well as more advanced disease in those individuals who had lymph node metastasis, peritoneal metastases and liver metastasis than patients without metastases. HCG positivity also correlated significantly with Dukes staging; Dukes stage D tumors had significantly higher rates of HCG expression compared to lower stages.⁶ Others reported that metastatic pancreatic adenocarcinomas had a >50% inci-

dence of HCG positivity and that HCG positive tumors had statistically significantly worse survival rates compared to those that were negative for HCG.⁷

HCGb secretion by esophageal carcinoma is rare, although some investigators identified positive cells by immunohistochemistry. Three cases of HCGb-secreting esophageal squamous cell carcinoma were described by Birkenfeld et al.⁸ Immunohistochemical positivity was noted in 71% of the 42 esophageal squamous cell cancers, along with significantly greater positivity in tumors with lymph node metastasis, but serum or urine levels were not reported.⁹ The immunohistochemical expression of HCG in esophageal cancers has been confirmed and the greater positivity correlated with poorly differentiated squamous histology in lymph node metastases, but no correlation with serum levels of HCG has been reported.¹⁰ HCG production is rarely reported in esophageal adenocarcinomas, although one immunohistochemical study reported HCGb positivity in adenosquamous esophageal cancers in both well differentiated and poorly differentiated squamous cell carcinomas.¹¹

Conclusion

Our patient had a rapidly deteriorating clinical course with an aggressive HCGb-expressing, poorly differentiated metastatic esophageal carcinoma. Our findings confirm previous studies of colon and pancreatic carcinomas that suggest a poor outcome for patients with HCGb-secreting tumors. Because there are, as yet, no studies that link elevated serum levels of HCG with prognosis in esophageal cancers, further evaluation is needed to determine if HCG secretion detected by serum analysis is a potential prognostic marker for invasive esophageal cancers.

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Pojava hemofilije A u vreme koronarno-arterijskog premoštavanja

APSTRAKT

Ekspresija humanog horionskog gonadotropina (HCG; HCGb) je ustanovljena u različitim solidnim malignim tumorima, uključujući pluća, gušteraču, želudac i karcinom cerviksa. Neke predhodne studije sugerišu da ovo ukazuje na nepovoljnu prognozu. Međutim, većina ovih studija je procenjivala ekspresiju HCGb imunohistohemijskim metodama, dok je klinički značaj povišenog nivoa HCGb u serumu još uvijek nepoznat, a može ukazivati na posebno agresivnu bolest. Ovaj fenomen još uvijek nije proučavan kod raka jednjaka. Prikazali smo slučaj srednjovječne žene sa slabo diferenciranim karcinomom jednjaka, ekspresijom HCGb i povišenim nivoom hormona u serumu. Povišen nivo ovog hormona bio je udružen sa veoma agresivnim kliničkim tokom.

KLJUČNE REČI

Karcinom jednjaka, humani horionski gonadotropin, HCG.