Gastric Cancer in a Pregnant Woman Presenting with Low Back Pain and Bilateral Erythematous Breast Hypertrophy Mimicking Primary Inflammatory Breast Carcinoma

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Abstract. This report describes the first case of a pregnant woman presenting low-back pain and breast pain associated with bilateral erythematous breast hypertrophy, proving to be the result of metastatic disease from a gastric carcinoma. A 30-year-old pregnant woman was admitted complaining of persistent severe low back pain, breast pain and concomitant bilateral erythematous breast hypertrophy, mimicking primary inflammatory breast carcinoma. During the caesarean section, widespread disease was found and finally metastatic gastric cancer was detected. Pregnant women with gastric cancer may present symptoms that are considered common during pregnancy. Common symptoms that present warning characteristics, such as the persistent severe pain observed in the presented case, should be carefully investigated as they may be the only warning signs and symptoms of rare ominous conditions such as gastric cancer.

In a pregnant woman, breast metastasis from gastric carcinoma mimicking primary inflammatory breast carcinoma represents an exceptional clinical event. Gastric carcinoma during pregnancy is rare, with an incidence of 0.1% of all gastric cancer cases (1, 2). In addition, breast metastasis is rare and accounts for 1.3-2% of all breast cancer cases (3), and even more so when the metastasis is from extra-mammary tumours, especially those mimicking primary inflammatory breast carcinoma.

This report describes, to the Authors’ knowledge, the first case of a pregnant woman with metastatic breast disease from a gastric carcinoma, presenting breast metastasis mimicking primary inflammatory breast carcinoma as the first sign of pregnancy-associated gastric cancer.

Case Report

A 30-year-old, pregnant woman was admitted during week 37 of gestation to the Department of Obstetrics and Gynaecology (Arcispedale S. Maria Nuova di Reggio Emilia, Italy) for further evaluation. Her clinical history included three previous admissions to this Department. She had been admitted in week 32 of gestation presenting symptoms of preterm labour and low-back pain (LBP). At that stage, tocolytic therapy and prophylaxis from respiratory-distress syndrome were administered, while an examination by an orthopaedic consultant attributed her LBP symptoms to pregnancy-related mechanical changes in the lumbopelvic area and postponed further evaluation until after the delivery.

At week 35 of gestation, the patient was admitted with suspicion of premature membrane rupture and subsequently discharged when this was not confirmed by instrumental evaluation.

At week 36 of gestation, the patient was assessed with suspicion of premature membrane rupture and subsequently discharged when this was not confirmed by instrumental evaluation.

At week 37 of gestation, the patient reported the onset of breast pain and persistent LBP. Physical examination revealed bilateral erythematous breast hypertrophy (Figure 1A) and bilateral axillary lymphadenopathy. At the time, the attending clinician attributed these symptoms to pregnancy-related hormonal hyperstimulation. Blood test and ultrasound examinations were prescribed. The ultrasound examination revealed non-specific bilateral small axillary lymphadenopathy of probable inflammatory nature.

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Key Words: Gastric cancer, low back pain, pregnancy, bilateral erythematous breast hypertrophy.
In order to relieve the patient of the severe LBP, labour was induced. The induction was performed with a vaginal device for the controlled release of dinoprostone (Propess 10 mg; Ferring Pharmaceuticals, Malmo, Sweden). After 21 h of labour, foetal distress was suspected and the patient underwent caesarean section (CS) giving birth to a healthy 2.850-kg male (Apgar score, 9/10).

The CS was followed by an exploration of the abdominal and pelvic cavities. This revealed ascites and multiple nodules on the greater omentum, abdominal-pelvic peritoneum and appendix. On that occasion, peritoneal fluid was collected, multiple biopsies were performed and placenta and foetal adnexa were sent for histological examination. Breast needle biopsies were also performed.

Assay of tumour markers detected increased CA 19-9 (4194 UI/ml). Lumbar sacral MRI of the pelvis showed small hypo-intense lesions in T1-weighted images. Breast needle biopsies revealed a focal infiltration of small/medium-sized pleomorphic cells with linear (Figure 1B) or microacinar (Figure 1C) arrangement. Higher magnification showed scattered signet-ring tumour cells (Figure 1D). Immunohistochemical investigation revealed positivity for E-cadherin and negativity for cytokeratin (CK) 34βE12, oestrogen receptor (ER) and progesterone receptor (PR). The proliferative fraction detected by Ki-67 was notably high (90%). Fluorescence in situ hybridisation (FISH) analysis revealed no amplification of HER-2/neu gene. Omental and peritoneum biopsies revealed massive infiltration by an adenocarcinoma with signet-ring pattern and endolymphatic invasion (Figure 2A). Immunohistochemistry revealed a positive reaction for CK AE1/AE3, CK 19, CK 7, CK CAM 5.2, focal positivity for CDX2 (Figure 2B). Moreover, immunohistochemical staining was negative for thyroid transcription factor-1 (TTF-1), CK 20, ER and PR. Placenta and foetal adnexa were free of metastatic disease.

With the clinical picture pointing towards a primary gastric tumour, the patient underwent a gastroscopy which revealed a deep ulcer at the greater curve of the corpus (Figure 3A). The histopathological examination of the gastric biopsies revealed a poorly differentiated adenocarcinoma with a signet-ring component (Figure 3B-D).

An abdominal computerised tomography (CT) scan revealed severe ascites with multiple nodules on the mesenteric adipose tissue, dilatation of the renal pelvis and the proximal right ureter, and bilateral lymphadenopathy of the iliac and inguinal lymph nodes. A chest CT scan showed bilateral pleural effusion, pericardial effusion, multiple small lymphadenopathy of the axillary and supraclavicular lymph nodes and evidence of metastatic bone disease. Finally, there were no signs of cancerous tissue in the lungs.
Figure 2. Massive omental infiltration by signet-ring adenocarcinoma. A: Signet-ring tumour cells showing intracytoplasmic mucin demonstrated by PAS immunohistochemical stain (after diastase) (×400). B: Immunohistochemical positivity for CDX-2 (×200).

Figure 3. Endoscopic (A) and histological (B) (haematoxylin-eosin staining, ×200) and high power (C) (×400) aspects of the gastric lesion. The positive immunoreaction for CK AE1/AE3 (D) is helpful for discovering carcinomatous cells (×200).
Postoperatively, the patient received a blood transfusion and was given antihypertensive medications.

Ten days after the CS, a head CT scan was performed because of the onset of tonic clonic seizures. The findings were inconclusive. The patient was discharged 26 days after CS with a diagnosis of inoperable gastric cancer. She received only palliative therapy. She died 71 days after being discharged.

**Discussion**

Only 27 cases of breast metastasis of gastric cancer have been reported since 1908 (4).

This report described the first case of breast metastasis mimicking primary inflammatory breast carcinoma of gastric signet-ring adenocarcinoma in a pregnant woman.

Under the age of 40, gastric cancer is more common in women than in men, with an incidence ratio of 2.5 to 1. Gastric cancer in women presents proximal localisation, poor differentiation and prognosis (5, 6).

Common gastric cancer risk factors such as *Helicobacter pylori* infection and smoking, which play an important role in the development of this pathology in men, cannot be held entirely responsible for the presentation of gastric cancer in younger women (7). Accordingly, in the literature, there is no general consensus for other gastric risk factors, such as those that are pregnancy-specific. In fact, the role of pregnancy-related hormonal changes in the pathogenesis of pregnancy-related gastric cancer, such as the steady increase of oestrogen, remains unclear and controversial (8, 9). Although hormonal changes during pregnancy are thought to result in an overall protective action, with the reduction of gastric-acid production (10), pregnancy-related immunosuppression may be thought to play a role in the development of the carcinoma (11).

The diagnosis of gastric cancer requires normally more than six months from the onset of the first symptoms; in pregnancy, it is further delayed due to the misinterpretation of nonspecific symptoms. Symptoms such as nausea and gastric pain are easily associated with the natural course of the pregnancy and are not a cause of concern for the patient or the clinician. The patient in this report complained of LBP because of the onset of tonic clonic seizures. The findings were inconclusive. The patient was discharged 26 days after CS (Figure 2). At the same time, the breast biopsies that were performed confirmed the presence of signet-ring cell adenocarcinoma (Figure 1).

Differentiating between a primary and a metastatic signet-ring adenocarcinoma of the breast represents a clinical challenge. In fact this type of cancer can be either of breast or gastric origin. Of relevance, the breast cancer would represent a lobular subtype of cancer and may result in gastric metastasis. Therefore, immunostaining analysis is essential to distinguish between primary and metastatic lesions. Commonly, breast signet-ring cell adenocarcinomas are positive for CK7, ER, PR and gross cystic disease fluid protein (GCDFP15) (13). In the present case, breast and abdominal localisation were morphologically identical. ER and PR negativity and CDX-2 positivity suggested an intestinal tract origin.

The final diagnosis of the primary gastric cancer was confirmed by the endoscopic biopsies (Figure 3). An endoscopic examination is safe in pregnancy and recommended for complicated cases such as atypical and severe refractory dyspepsia continuing beyond week 16 of gestation, nausea and vomiting that do not respond to traditional therapies, or suspicious symptoms of malignancy.

Gastric cancer treatment in pregnancy should be planned according to the guidelines of Ueo et al. (14) based on the stage of the carcinoma and the progression of the pregnancy (7). Immediate surgical intervention for gastric cancer should be the treatment of choice before week 24 of gestation. Accordingly, from week 25 to 29 of gestation, immediate resection is recommended in cases when the cancer is advanced, despite the risks to the foetus. After week 30 of gestation, the foetus should be delivered before radical surgery is performed on the gastric cancer (7).

Survival rates in cases of gastric cancer are strictly bound to the diagnostic times. Early detection is critical. The literature shows that 80% of the patients diagnosed die in the first year and the 3-year survival rate is only 8% (15).

The described case confirms the complexity of the presentation of the gastric cancer in a pregnant woman, the diagnostic challenge and poor survival rate. Late diagnosis of gastric cancer in pregnancy inevitably results in a poor prognosis. In addition, the breast involvement described in this case renders the prognosis poorer still as it is considered
a sign of widespread disease. All symptoms usually referred by the patients (nausea, vomiting, or, as in the present case, persistent LBP and breast pain) are non-specific and common in pregnancy. The persistency or severity of common symptoms should prompt clinicians to perform further tests and instrumental examinations, such as gastroscopy, MRI scans and tissue biopsy. Even though in the described case an earlier diagnosis would not have improved survival, it may have led to a more effective pain therapy with an improvement of the quality of life.

Although this is a unique and anecdotal case, the present case report is useful for clinicians because the clinical course of the patient is representative of this disease, especially in Western countries, where gastric cancer is a rare and may be misdiagnosed.

To conclude, the described case suggests that closer attention should be paid to all symptoms presented by the patient, particularly to persistent and worsening symptoms. During pregnancy, common presenting complaints may be the only signs of an underlying ominous pathology. No symptoms should be easily dismissed by the clinician because of their common association with uncomplicated pregnancy. Any of these complaints may be the only signs available to the clinician to early detect the underlying pathology early.

References


Received November 18, 2010
Revised December 23, 2010
Accepted December 24, 2010