

Case Report

Muscle Metastases Revealing Gastric Signet Ring Cell Carcinoma: Case Report and Review of the Literature

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Abstract

Advanced stomach cancer remains a serious disease with a poor prognosis. Skeletal muscle metastases of gastric carcinoma are extremely rare and may be revealing the disease. The signet ring cell carcinoma is defined by the presence of proportion of independent cells greater than 50%. In an advanced stage it has a more aggressive character with a greater risk of lymph node invasion or distant metastasis. The needle biopsy is required for diagnosis. The chemoresistance of SRCC appear as elements of poor prognosis. The armamentarium includes further the antitumor chemotherapy, radiotherapy and palliative care adapted to the patient's clinical context.

Keywords: Muscle Metastasis; Signet Cell Carcinoma; Gastric Cancer; Chemoresistance

Abbreviations

SRCC: Signet Ring Cell Carcinom; CT: Computer Tomography; MRI: Magnetic Resonance Imaging; FDG -PET: Fluorodeoxyglucose (FDG)-Positron Emission Tomography; FOLFOX: 5-Fluoro-Uracile, Leucovorin and Oxaliplatin; FOLFIRI: 5-Fluoro-Uracile, Leucovorin and Irinotecan

Introduction

Gastric cancer is the second most common digestive cancer after colorectal cancer and the fourth leading cause of cancer death worldwide [1].

The most common metastatic sites are regional lymph nodes, liver, peritoneum, lung and bone. Gastric cancer can cause unusual metastases, such as gums, irises, testicles, muscles or even the meninges [2,3]. Muscular metastases are rare, only sporadic cases have been reported in the literature [4,5].

We report, in one patient, the case of a gastric adenocarcinoma with signet ring cells, which was revealed by the presence of muscular metastases.

Case Presentation

This is a 54-year-old Caucasian woman with a history of arterial hypertension who was admitted in July 2018 to manage a painful abdominal swelling affecting the right flank evolving for 2 months in a context of paroxysmal epigastralgia. On admission, she was 160cm tall and weighed 65kg. She had a temperature of 36.4°C, heart rate 82beats/min, blood pressure 140/70 mmHg. The abdominal examination found a hard and sensitive mass of the right flank, which was fixed in relation to the deep plane, the ganglionic areas were free, and the rest of the examination was without particularity.

Therefore, she received abdominal pelvic CT demonstrating irregular nodular thickening of the right transverse and the right rectus muscles of the abdomen with edematous diffuse infiltration of the next subcutaneous fatty tissue and a diffuse thickening of

the cardiotubercotic and fundic region of 2cm thick (Figure 1). Subsequently, an ultrasound-guided biopsy of muscle swelling was conducted. The histological result with immunohistochemical complement (anti-CK7 +, anti-CK20 +, WT1-, ACE +, CDX2 + antibody) was in favor of muscle metastasis of gastric signet ring cell carcinoma (Figure 2 and 3). Endo-gastroduodenal fibroscopy showed a non-stenosing ulcerobourgnnant antral process. The histological diagnosis of the gastric biopsy showed a signet ring cell carcinoma with a background of chronic gastritis HP- and the HER2 status was negative.

At this stage, a full-body CT with contrast and PET-scan (Figure 4) had excluded other distant metastases from gastric carcinoma, and the ACE/CA19-9 tumor markers were negative.

After a multidisciplinary evaluation, considering the advanced stage of the disease (stage IV) and the absence of gastrointestinal complications, including gastrointestinal bleeding or gastric stenosis, a modified FOLFOX-4 regimen (J1-J15) was administered as first-line chemotherapy. After 3 cycles, the clinical and radiological evaluation by thoraco-abdominopelvic CT showed a reduction

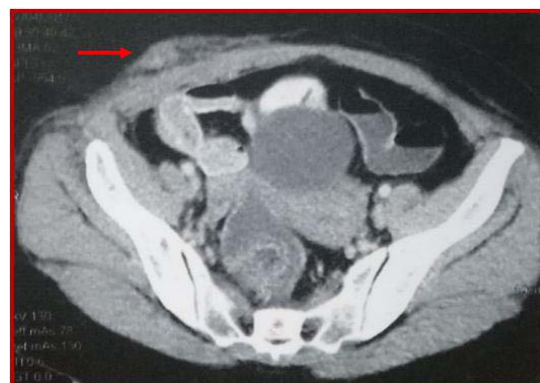


Figure 1: Abdominal pelvic CT shows irregular nodular thickening of the right transverse and the right rectus muscles of the abdomen.

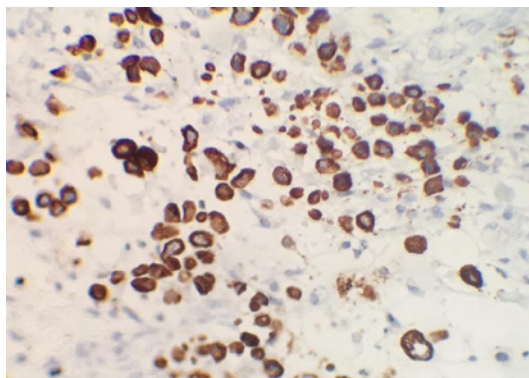


Figure 2: Higher magnification (x200) reveals poorly differentiated signet ring cell carcinoma composed of single, non-cohesive, round and vacuolated cells.

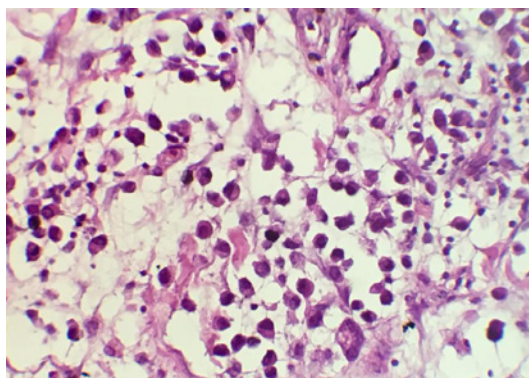


Figure 3: Immunohistochemical complement; Microphotograph showing intracellular mucin within tumor cells. Nuclear atypia and mitosis are also visible. [PAS, x400].

in gastric thickening and metastatic muscle thickening. The consultation with the surgeons did not retain the indication of carcinologic excision. After receiving an additional cycle, the patient objectified the appearance of a rapidly progressive swelling affecting the left flank and the left iliac fossa (Figure 5) and the appearance of a left vulvar swelling. A lesion progression was also retained on the Thoraco-Abdomino-Pelvic CT data showing the appearance of a new lesion in the left rectus muscle (Figure 6) and on the vulvar biopsy data confirming a secondary localization of a signet ring cell carcinomatous process compatible with known gastric origin (AC antiparacytokeratin +).

Considering the conservation of the patient performance status, a second-line chemotherapy was selected based on FOLFIRI regimen (J1-J15). The patient is currently under treatment.

Discussion

Despite recent advances in cancer therapy, advanced stomach cancer remains a serious disease with a poor prognosis. It is an adenocarcinoma in 95% of cases and, in 20% of cases, it is accompanied by overexpression of the HER2 receptor. The signet ring cell carcinoma (SRCC) is defined by the presence of proportion of independent cells (weakly cohesive cells or also called ring-shaped cells) greater than 50%.

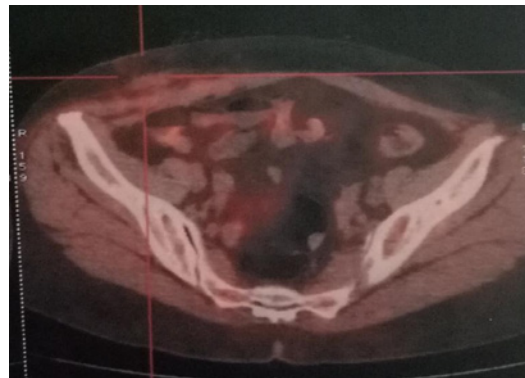


Figure 4: FDG-PET SCAN image exclude other distant metastases from gastric carcinoma.



Figure 5: Rapidly progressive swelling affecting the left flank and the left iliac fossa.

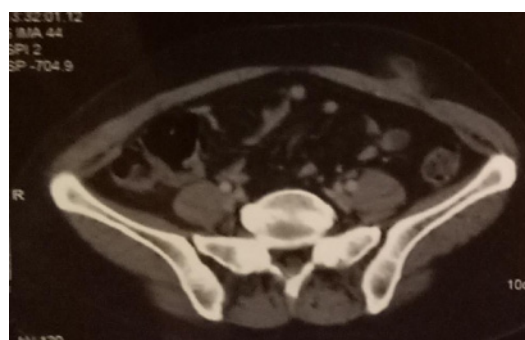


Figure 6: Thoraco-Abdomino-Pelvic CT data shows the appearance of a new lesion in the left rectus muscle.

SRCC appears as a separate entity affecting more often women and at a younger age (median age at diagnosis: 61.9 years) [5] and preferentially sits in the antrum and body of the stomach. In addition, it may be related to a genetic predisposition in carriers of the CDH1 gene mutation encoding E-cadherin. At an early stage, SRCC is a type of gastric cancer with a similar prognosis as the rest of gastric carcinoma subtypes, but in an advanced stage it has a more aggressive character with a greater risk of lymph node invasion or distant

metastasis. The presence of muscle metastases is rarely described in the literature [5]. The primary cancers commonly associated with muscle metastases are lung, kidney, bladder cancers, and carcinomas of the gastrointestinal tract. The anatomical predilection sites for occurrence of muscle metastases are the lower limbs [6,7]. In the literature, cases that associate gastric cancer with muscle metastases are rare, and most of the cases described have a histological profile of SRCC and are associated with advanced disease and poor prognosis. Several other unusual sites of metastasis of gastric cancer have been reported in the literature such as pancreatic, cutaneous, parotid, gingival, mammary, testicular, uterine and fallopian tube metastasis [8,9].

To date, although skeletal muscle is a hypervascularized tissue and constitutes more than half of the body mass, there are no clear explanations justifying the scarcity of muscle metastases. Several factors could make skeletal muscle hostile to metastatic spread, such as unconstant muscle blood flow, pressure changes due to muscle contractions, inhibition of tumor proliferation by lactic acid, muscle pH, and portal filter that can prevent the peripheral spread of the disease apart from the presence of hepatic metastasis [10-12].

Muscular metastases can be discovered incidentally during a radiological assessment in asymptomatic patients or more generally by the presence of a hard and painful mass [13,14]. They may also be indicative of an undiagnosed primary tumor, as in our case, with or without other detectable metastases [4,5,7,15].

Although most skeletal muscle metastases are detected by CT, MRI is considered superior to CT in terms of characterization of muscle abnormalities [7,8,14].

When the skeletal muscle metastasis is the initial presentation, as in our patient, the biopsy is considered obligatory for diagnosis as long as the mass is accessible [6,13].

The medical treatment of advanced gastric cancers is essentially based on chemotherapy, to which can be added other therapeutic options including radiotherapy, to relieve pain or to reduce the size of muscular metastases, and surgical excision which can be proposed in selected patients with a symptomatic isolated mass in the absence of other metastatic locations [6,7]. However, several SRCC data from gastric adenocarcinoma studies suggest chemoresistance in this histological subtype [16,17].

Metastatic SRCC have a poor prognosis and depend mainly on metastatic spread. In our case, rapid progression with the appearance of other sites of muscle metastasis after only four cycles of chemotherapy, even in the absence of visceral metastases, made surgical excision or other local treatment impossible.

Conclusion

Skeletal muscle metastases of gastric carcinoma are extremely rare and may be revealing the disease. As in our case, the needle biopsy is required for diagnosis. In addition, any painful tumefaction must

make suspect the presence of muscular metastases. These as well as the chemoresistance of SRCC appear as elements of poor prognosis. The armamentarium includes further the antitumor chemotherapy, radiotherapy and palliative care adapted to the patient's clinical context.

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