LATE CUTANEOUS METASTASES FROM GASTRIC CARCINOMA

METÁSTASE CUTÂNEA TARDIA DE ADENOCARCINOMA GÁSTRICO

JOSÉ PINTO[1], LILIANA DUARTE[2], MARTA FERREIRA[2], ROSA SIMÃO[3], CONCEIÇÃO MARQUES[3], LUÍS FILIPE PINHEIRO[4], CARLOS CASIMIRO[5],

[1] Interno de Formação Específica, Centro Hospitalar Tondela-Viseu
[2] Assistente Hospitalar, Centro Hospitalar Tondela-Viseu
[3] Assistente Graduada, Centro Hospitalar Tondela-Viseu
[4] Assistente Graduado Sénior, Centro Hospitalar Tondela-Viseu
[5] Director de Serviço, Centro Hospitalar Tondela-Viseu

ABSTRACT

Cutaneous metastases from primary gastric carcinoma are uncommon, generally occur late in the course of the disease and have a poor prognosis. We report a long-term survival of a patient with cutaneous metastases from a gastric carcinoma. A 56-year-old patient, previously diagnosed with a poorly differentiated signet-ring cell gastric carcinoma staged as ypT3N3aM0, who underwent total gastrectomy with Roux-en-y reconstruction and extended lymphadenectomy (D2) 7 years prior, with no evidence of disease recurrence. At presentation, physical examination revealed firm erythematous nodular lesions in the face and neck, and palpable adenopathy in the left axilla. Laboratory workup showed mild anemia, and the tumour markers were negative. The staging PET-CT scan revealed left axillary and right inguinal lymph nodes metastases. The patient underwent a complete resection of the facial lesion, and the histopathology of the specimen was compatible with cutaneous metastases of signet-ring cell gastric adenocarcinoma. The patient received postoperative chemotherapy with clinical remission at 24 months follow-up. This case report of long-term survival in a metastatic gastric carcinoma emphasizes that although cutaneous metastases are rare, they should be considered when assessing suspicious lesions in patients with a history of gastric carcinoma.

Keywords: *Gastric; Carcinoma; Cutaneous; Metastases;*

RESUMO

As metástases cutâneas de adenocarcinoma gástrico são raras e apresentam-se mais frequentemente num estadio tardio da doença. Apresentamos o caso clínico de um doente do sexo masculino, de 56 anos, com antecedentes de adenocarcinoma pouco diferenciado da pequena curvatura gástrica estadiado como ypT3N3aM0, em 2011, submetido a gastrectomia total com montagem em Y-de-Roux e linfadectomia D2. Realizou quimioterapia peri-operatória (epirrubicina, oxaliplatina e capecitabina). Follow-up clínico, analítico e imagiológico sem evidência de recidiva, aos 7 anos pós-diagnóstico. Ao exame objectivo, com adenopatia palpável na região axilar esquerda. Analiticamente com discreta anemia, sem elevação dos marcadores tumorais. Proposta excisão das lesões, em Consulta de Decisão Terapêutica, revelando metastização cutânea de primário gástrico. A TAC toraco-abdomino-pélvica e a PET revelaram metastização ganglionar axilar esquerda e inguinal direita. Realizou quimioterapia adjuvante, com boa resposta. Este caso mostra que as metástases cutâneas, embora raras, devem ser consideradas na avaliação de lesões suspeitas em doentes com história de carcinoma gástrico.

Palavras-chave: *Carcinoma; Gástrico; Metástases; Cutâneas*

INTRODUCTION

According to 2018 data from World Health Organization, gastric cancer is the sixth most frequently diagnosed cancer worldwide and the third cause of death from all malignancies. Advanced gastric cancer frequently metastasizes to the regional lymphatic nodes, the liver, the peritoneal cavity and the lungs[1], with cutaneous metastases being rare, with a reported incidence of 0.8-1% [2,3].

We report a case of late cutaneous metastases presenting 7 years after the diagnosis of a primary gastric cancer, in a patient who underwent surgical resection and perioperative chemotherapy, with clinical remission at 24 months follow-up after systemic therapy.

CASE REPORT

A 56-year-old male patient, without any family history of gastric cancer, was diagnosed with poorly differentiated signet-ring cell gastric carcinoma of the cardia with locoregional metastatic lymph nodes staged as ypT3N3aM0. The patient underwent total gastrectomy with Roux-en-y oesophagojejunostomy reconstruction and extended lymphadenectomy (D2). The patient received 3 cycles of chemotherapy with epirubicin, cisplatin, and oxaliplatin before and after the surgery. The annual follow-up with computed tomography (CT) and laboratory tests showed no sign of recurrence or metastases.

Seven years after the initial diagnosis, the patient presents with 2 firm nodular lesions in the face and neck, of 2 months duration. The lesions were nonpruritic and painless. The physical examination revealed 2 erythematous nodular lesions, measuring 2x2cm, in the face and the lateral cervical region (Figure 1 and 2). There was also a palpable left axillary lymph node, with no evidence of other pathological findings. Laboratory tests showed mild anemia and negative tumour markers. A staging PET-CT revealed left axillary and right inguinal lymph nodes metastases, and no sign of local recurrence.

Figure 1 – **Cutaneous metastatic lesion in the forehead presenting as a reddish-colored elevated nodule**

Figure 2 – **Cutaneous metastatic lesion in the neck with 2cmx2cm dimension**

Based on these findings, the case was presented in the Cancer Multidisciplinary Team Meeting and surgical resection of the facial lesion, with diagnostic intent, was proposed to the patient. Surgical resection of the lesion and a flap repair was performed without complications and the patient was discharged 2 days after the surgery (Figure 3). The histopathologic and immunohistochemistry analysis of the specimen confirmed the diagnosis of cutaneous metastases from a signet-cell ring gastric adenocarcinoma. The HER2 status was negative.

Figure 3 – **Surgical resection of the frontal lesion and flap reconstruction**

Figure 4 – **Complete regression of cutaneous cervical lesion after adjuvant chemotherapy**

Considering the presence of lymph nodes metastases and a remaining cervical cutaneous lesion the patient received 12 cycles of postoperative chemotherapy with cisplatin and a De Gramont combination of fluorouracil and leucovorin. At more than 24 months of clinical, analytical, and radiological follow-up the patient remains free of disease (Figure 4).

DISCUSSION

Despite the improvement in its diagnosis and treatment, gastric cancer remains a serious condition associated with high mortality. Metastases from primary gastric cancer are associated with advanced disease with a median-survival without treatment of 3 – 5 months, an average of 11.4 weeks in the case of cutaneous metastases[4], depending on the primary cancer, the presence of other regional or distant metastases, the number and dimensions of the lesions, and the performance status of the patient[5] as well.

We report a rare case of 7 years disease-free survival of a stage IIIb undifferentiated-type gastric carcinoma presenting with late cutaneous metastases, with a remarkable response to systemic therapy.

As previously discussed, cutaneous metastases from gastric cancer are quite uncommon, with the most frequent metastatic sites being the liver, peritoneal cavity, lymph nodes, and lungs. They usually manifest as non-specific erythematous nodular lesions in the head, neck, chest, abdominal wall and rarely in the extremities and inguinal groove[4–8]. They are also described as erysipelas-like and cellulitis-like lesions[9], zosteriform lesions[7] and as lesions resembling a contact dermatitis pattern[10].

Several mechanisms can explain the occurrence of cutaneous metastases from internal organs carcinomas: hematogenous or lymphatic spreading, direct tissue invasion of primary cancer and intra-operative iatrogenic implantation[1,5].

In this case, the dermatotropism of the metastatic cells can be explained by the interaction of the chemokines and their receptors between the tumour cells and the skin cells in a process not fully understood but certainly with a crucial role in the development of "selective" metastases[11–13].

Given the plurality of lesions associated with cutaneous metastases from gastric carcinoma, the diagnosis is based on clinical suspicion confirmed by histopathological and immunohistochemical

analysis. Gastric cancers express some adenoepithelial and/or gastrointestinal markers including EMA, AE1/AE3 and CK7[8], which were all positive in our case.

After the diagnosis is established it is important to rule out other metastases and exclude local recurrence. A staging PET-CT scan is the most accurate staging modality for detection of solid organ and lymph node metastases[5]. A full laboratory workup including tumour markers is also important for staging.

There are several treatment options for metastases from primary gastric carcinoma depending on the number and dimensions of the lesions, the presence of other regional or distant metastases and the performance status of the patient.

For isolated lesions, resection followed by a careful follow-up can be performed with a curative intent[1]. For painful or haemorrhagic lesions, surgical resection can also be performed as a palliative treatment. For multiple, extensive or recurrent lesions, or if associated with another solid organ or lymph node metastases, systemic chemotherapy is the most commonly used treatment.[5,6,14]

Depending on the immunohistochemistry and molecular profile of the lesions, immunotherapy and molecular-targeted therapies can be attempt, usually not as first-line therapy.[15,16]

In our case, we decided to perform surgical resection of one of the lesions with diagnostic intent. The patient also underwent postoperative chemotherapy due to the presence of other cutaneous lesions and metastatic lymph node involvement, with clinical remission at 24 months follow-up.

The evidence about what chemotherapy regimens should be used in this particular case is sparse, but combination therapy (eg, oxaliplatin plus leucovorin and short-term fluorouracil [FOLFOX regimen], fluorouracil plus cisplatin or S-1 plus cisplatin) has shown better results than monotherapy. The role of radiotherapy as an adjuvant in the treatment of cutaneous metastases from gastric cancer is not yet understood. Although the prognosis after occurrence of cutaneous metastases is poor, we report a long-term survival after systemic therapy.

CONCLUSION

Cutaneous metastases should be considered when assessing suspicious lesions in patients with a history of gastric carcinoma. Once the histopathological diagnosis is confirmed, PET-CT scan is mandatory to exclude the presence of other metastases or local recurrence. Therapeutic options include local resection, chemotherapy, radiotherapy and/or immunotherapy/molecular targeted therapy depending on the number and dimension of the lesions, the presence of other regional or distant metastases and the patient's performance status.

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Correspondência:
JOSÉ PINTO
e-mail: josecarlospereirapinto@gmail.com

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