

## SQUAMOUS CARCINOMA OF THE SMALL BOWEL IN A PATIENT WITH A TUMORAL BACKGROUND: METASTASIS?

### CARCINOMA EPIDERMÓIDE DO INTESTINO DELGADO NUM DOENTE COM HISTÓRIA DE DOENÇA ONCOLÓGICA MALIGNA: METÁSTASE?

 Andrea ILLAN<sup>1</sup>, Guadalupe PADILLA<sup>1</sup>, David LÓPEZ<sup>1</sup>, Rubén LENO<sup>1</sup>, Montserrat DÍAZ<sup>1</sup>

<sup>1</sup> Medical Oncology Department. Hospital Virgen del Puerto. Plasencia, Cáceres. Spain.

Correspondence: Andrea Illan (andrea88med@yahoo.es)

Received: 24/04/2021

Accepted: 01/03/2023

Published online: 1/05/2023

#### ABSTRACT

**Introduction:** Malignant tumor of the small intestine are extremely rare, with an incidence of less than one in 100,000 patients. The most frequency histology underlying is adenocarcinoma, followed by squamous carcinoma. **Methods:** We have carried out a review of the scientific literature about the main epidemiological, histological and diagnostic aspects of squamous cell carcinoma of the small intestine. **Results:** We present the clinical case of a 69-year-old man diagnosed with localized small cell carcinoma of the lung, with good response after concomitant chemoradiotherapy (QTRT). During the follow-up period, the patient presented with an acute abdomen due to intestinal perforation. Anatomopathological analysis (A-P) of the small intestine resection piece revealed squamous cell carcinoma with sarcomatoid features and stage pT4pNx. **Conclusions:** The interest of this case lies in the metachronous diagnosis of two primary tumors of different origin (small cell carcinoma of the lung and squamous cell carcinoma of the small intestine), being an unprecedented finding in the current scientific literature.

**Keywords:** *small bowel carcinoma, squamous cell carcinoma, small cell lung carcinoma.*

#### RESUMO

**Introdução:** Os tumores malignos do intestino delgado são extremamente raros, com uma incidência inferior a um em 100.000 doentes. O tipo histológico mais frequente é o adenocarcinoma, seguido do carcinoma escamoso. **Métodos:** A propósito de um caso clínico, realizamos uma revisão da literatura científica sobre os principais aspetos epidemiológicos, histológicos e diagnósticos do carcinoma espinocelular do intestino delgado. **Resultados:** Apresentamos um caso clínico sobre um doente do sexo masculino de 69 anos de idade com antecedentes de um carcinoma de pequenas células localizado do pulmão e com boa resposta após tratamento com quimiorradioterapia (QTRT) concomitante. Durante o seguimento, a doente apresentou quadro de abdómen agudo por perfuração intestinal. A análise anatomopatológica (AP) da peça de ressecção do intestino delgado revelou um carcinoma de células escamosas com características sarcomatoides e foi estadiado como pT4pNx. **Conclusões:** O interesse deste caso reside na ocorrência metacrónica de dois tumores primários de origem distinta (carcinoma de pequenas células do pulmão e carcinoma espinocelular do intestino delgado), Este facto revelou-se muito raro na literatura científica atual.

**Palavras-chave:** *carcinoma do intestino delgado, carcinoma espinocelular, carcinoma pulmonar de pequenas células.*



## INTRODUCTION

Neoplasms of the small intestine have a remarkably low incidence, actually occurring in less than one in 100,000 patients. The finding of tumors in this location is more likely to be distant metastatic lesions; in this case, the tumors that usually metastasize are, among others, carcinomas of the lung, mother, kidney and colon, as well as malignant melanoma.

The forms of clinical presentation are different and have also been reported (abdominal pain, perforation), although radiological examinations are performed on suspicion, computerized axial tomography (CT) and positron emission tomography (PET).

Regarding primary tumors of the small intestine, the histologies most frequently found in the A-P exam are adenocarcinoma and squamous cell carcinoma. In relation to the epidermoid subtype, multiple and different pathogenic mechanisms for the development of squamous cell carcinoma of the small intestine have been described in the literature.

We present the clinical case of a 69-year-old man diagnosed metachronous of two primary tumors of different primary origin (small cell carcinoma of the lung and squamous cell carcinoma of the small intestine), being a finding found in the current scientific literature.

## MATERIAL AND METHODS

We have carried out a review of the scientific literature about the main epidemiological, histological and diagnostic aspects of squamous cell carcinoma of the small intestine. For this, we have used the main search engines (PubMed, Cochrane), finding practically all reports of clinical cases and scientific reviews on them.

## CASE REPORT

We present the clinical case of a 69-year-old man with a personal history of hypertension, diabetes mellitus II, dyslipidemia and acute fibrinolyses anterolateral myocardial infarction in 2009. Among his toxic habits, a smoking habit of 50 years/package stands out, as well as ex-moderate drinker (10 beers daily). Among his personal history, it should be noted that his father died of lung cancer at the age of 70.

The patient began a study based on a 6-month evolution constitutional syndrome (with 30 kg weight loss) accompanied by a productive cough. His primary care physician (MAP) performed an analysis, with anemia with transfusion needs (Hb of 8.9 g/dl) and was referred to the Emergency Department of our hospital. Chest radiography (Rx) revealed a right hilar mass. It was decided to enter Internal Medicine for study.

CT confirmed the findings of right parahilar mass with invasion of the right upper lobar bronchus, with compromise and stenosis of the upper lobar pulmonary artery and right main bronchus. It was also observed: a distended abdominal aorta with a small saccular aneurysm, 38 x 43 x 38mm: T x AP x L, immediately after the left renal artery was removed and another fusiform aneurysm, immediately posterior with extension to the iliac bifurcation, 65 x 65 x 92mm: T x AP x L, with 43mm eccentric light and a peripheral wall thrombus. In addition, a dubious 3cm focal thickening of the duodenal antrum was visualized (upper digestive endoscopy without findings, although random biopsies were taken, which were negative for malignancy).

Given the radiological findings, a diagnostic bronchoscopy was performed, resulting in the anatomical-pathological diagnosis (A-P) of the bronchial biopsy of small cell lung carcinoma; the immunohistochemical profile was as follows: CAM5.2 +, TTF-1-, chromogranin-, synaptophysin +, CD56 +, Ki67 > 75%.

CT and nuclear magnetic resonance imaging (MRI) ruled out brain metastases, although they did



confirm the presence of chronic vascular lesions at the supra and infratentorial levels. The whole body bone scan (GOCE) denied osteoblastic metastases.

Therefore, with clinical judgment of limited small cell carcinoma of the lung, he was referred to outpatient medical oncology consultations. The patient referred as the only usual frontal headache clinic. Concomitant chemoradiotherapeutic treatment (QTRT) based on cisplatin D1 and etoposide D1-3 was considered weekly. The patient received 4 cycles of QT and 70 Gy total dose of RT on the chest injury. The tolerance to the treatment was regular. In fact, the patient required admission for febrile neutropenia of respiratory origin up to two occasions; transfusion of blood products was also required in three cycles for grade II anemia.

After the end of the concurrent treatment, the control CT experienced a greater partial response. Given this, prophylactic holocranial irradiation was proposed, as stated in the international clinical guidelines for the treatment of small cell lung cancer, with a total of 25 Gy and spread over 10 sessions.

Subsequently, he began a program of follow-up. With a 4 months-progression-free interval, the patient went to the emergency department for abdominal pain and nausea of hours of evolution. On physical examination, the abdomen was shown in a table. Blood tests showed leukocytosis with left deviation and C-reactive protein (PCR) of 320 mg/l. An urgent abdominal CT was requested, which was compatible with pneumoperitoneum of probable right colonic origin (although a jejunal or ileal loop located in the right hemiabdomen could not be ruled out as a location); the abdominal aortic aneurysm revealed no changes or complications.

The patient underwent emergency surgery using an exploratory laparotomy with findings of intestinal perforation in the middle third of the small intestine, with an inflammatory reaction on the right mesocolon and free purulent zero fluid. A partial resection of the small intestine was carried out, with a definitive AP result compatible with a squamous carcinoma with sarcomatous areas of

2.3 cm, with extensive areas of necrosis, affecting the entire thickness of the wall, reaching the serous surface and with the radial edge in contact with the tumor. The pathological staging was pT4pNx.

The patient presented a favorable postoperative period. He presented disorientation due to an acute confusional syndrome that was managed by psychiatry with haloperidol drops. Twelve days after discharge, the patient re-entered the hospital for symptoms of cognitive decline and disorientation according to the family. The vital signs showed minimal hypotension and a fever of 38.5 °.

On physical examination, the patient appeared disoriented and with a defense maneuver upon palpation of the left abdominal flank. The analysis revealed leukocytosis with neutrophilia and PCR of 21 mg/l. A new emergency abdominal CT scan was requested again, describing dilatation of the thin loops and thickening of the wall in the mesogastrium in possible relation with intestinal loop suffering.

The patient underwent exploratory laparotomy and partial resection of the greater omentum with findings of:

- Surgical wound with purulent collection in all its extension
- Necrotic greater omentum of 6 × 6 cm in the mesogastrium,
- Apparent microfuge at cecum level with small collection and fibrin at that level
- Cecum dilatation

The patient presented adequate postoperative evolution, but was readmitted four days after discharge due to candidiasis in the surgical wound. The patient experienced other episodes of an acute confusional syndrome, reduced reactivity to stimuli and interaction with the environment progressively after the last discharge. In addition, at home, he developed incoherent language, animal-like visual hallucinations, and falls to the ground. The patient was dependent for basic activities of daily life.



Body CT was requested, which ruled out recurrence of the central nervous system. The patient was brought to Medical Oncology Consultations on a stretcher, showing performance status (PS) of 3-4, with incongruous speech and tending to sleep. Patient admission and treatment with intravenous corticosteroid therapy without clinical improvement were proposed. He was assessed by Neurology during hospitalization. The diagnostic judgment was compatible with encephalopathy and behavioral alterations of a multifactorial cause (history of enolism, probable previous cognitive impairment, unfiltered, small cerebral vessel disease, pharmacological toxicity and sequelae due to prophylactic holocranial radiotherapy), in addition to confusional episodes in the context of hospitalization. The prognosis of this multifactorial entity was dire.

Given the general situation of the patient (small cell carcinoma with thoracic disease in response but persistent, epidermoid carcinoma of the intestine pT4, PS 3-4 and limiting cognitive impairment, dependent on basic activities of daily living), we contacted the Palliative Care Unit for control and monitoring in socio-sanitary residence.

## DISCUSSION

In relation to the large extension and surface area of the gastrointestinal tract, malignant tumors of the small intestine are remarkably rare<sup>1</sup>, with an overall incidence of less than one in 100,000 patients. It is more frequent in metastatic lesions<sup>2</sup>.

The tumors that most frequently metastasize to the small intestine<sup>2</sup> may include carcinomas of the lung, breast, kidney, and colon; Malignant melanoma can also metastasize to the small intestine.

Several pathogenic mechanisms are contemplated for the development of squamous cell carcinoma of the small intestine: 1) malignant transformation of the heterotopic squamous epithelium, 2) Stem pluripotential cells differing from malignant

squamous cells, 3) squamous metaplasia due to chronic mucosal damage that leads to malignant changes, 4) transformation from adenocarcinoma to adenosquamous carcinoma and eventually to squamous cell carcinoma.

For the diagnosis of primary squamous cell carcinoma, metastases should be excluded. Personal history is a key factor. However, a history of previous malignancy does not necessarily imply that the lesion of the small intestine is metastatic<sup>1</sup> especially when the tumor or the primary neoplasm outside the intestine has been diagnosed at an early stage and the time or interval is long until the discovery of the lesion in the small intestine. At the A-P level, most metastatic tumors are located in the submucosa, while the mucosa is largely affected by primary squamous cell carcinomas of the small intestine. Immunohistochemistry does not differ<sup>1</sup> from metastatic and primary entities.

Garwood et al. reviewed cases with small bowel perforation due to forgiveness derived from this metastatic lung carcinoma and found that perforations occurred more frequently in the jejunum<sup>2,3</sup> in 53% of cases; the underlying histologies represented adenocarcinoma in 23.7%, squamous cell carcinoma<sup>3</sup> in 22.7%, large cell carcinoma in 20.6%, and small cell carcinoma of the lung in 19.6% of cases.

They may appear in intestinal duplication type congenital anomalies or Merkel<sup>4</sup> diverticulum. Furthermore, Nandedkar et al. present the rare<sup>5</sup> form of presentation of a primary tumor in the small intestine in the form of an ulcer and not as a protrusion towards the lumen.

As in the clinical case that we present with metastatic or primary small intestine tumors with patients who have these are tumors and who initiate acute abdominal symptoms, they should be evaluated to rule out intestinal perforation<sup>6</sup>.

PET<sup>1,7</sup> and the combination with CT is the staging test to rule out other entities that result in the lesion in the small intestine being metastatic.



## CONCLUSIONS

The finding of primary squamous cell carcinoma of the small intestine is rare in the scientific literature and in routine clinical practice. The clinical case that we contribute also presents the peculiarity of appearing metachronous during the follow-up of a

localized small cell lung carcinoma. The presentation was based on clinical and radiology compatible with intestinal perforation, requiring urgent surgical intervention and exeresis, at least, macroscopic, of the lesion. However, given his comorbidities and functional deterioration, the patient was not a candidate for another complementary treatment.

## REFERENCES

1. Wang FD, Wang ZW, Xue HD, Wu HW, Zhang Y, Yu JC, Jin ZY. Primary Squamous Cell Carcinoma of the Small Intestine: Pathogenesis and Clinical Features. *Chin Med J (Engl)*. 2016 Sep 5;129(17):2131-3. doi: 10.4103/0366-6999.189067. PMID: 27569244; PMCID: PMC5009601.
2. Sun DS, Shin OR, Ku YM, Kim YS, Seo KJ. Squamous cell carcinoma of the small bowel manifesting as a jejunal perforation: a case report. *Int J Clin Exp Pathol*. 2014 Aug 15;7(9):6345-9. PMID: 25337289; PMCID: PMC4203260.
3. Garwood RA, Sawyer MD, Ledesma EJ, Foley E, Claridge JA. A case and review of bowel perforation secondary to metastatic lung cancer. *Am Surg*. 2005 Feb;71(2):110-6. PMID: 16022008.
4. Mumtaz S, Ahmad Z, Fatima S, Qureshi A. Squamous cell carcinoma in the small intestine. *BMJ Case Rep*. 2011 May 12;2011:bcr0120113762. doi:10.1136/bcr.01.2011.3762. PMID: 22696720; PMCID: PMC3094779.
5. Nandedkar SS, Trivedi KK, Malukani K. Primary squamous cell carcinoma of the small intestine. *J Cancer Res Ther*. 2013 Oct-Dec;9(4):739-40. doi: 10.4103/0973-1482.126477. PMID: 24518732.
6. Chao TC, Chao HH, Jan YY, Chen MF. Perforation through small bowel malignant tumors. *J Gastrointest Surg*. 2005 Mar;9(3):430-5. doi: 10.1016/j.gassur.2004.09.022. PMID: 15749607.
7. Friedman E, Kwan MR, Cummins L. Squamous cell carcinoma of the transverse duodenum. *Gastrointest Endosc*. 1986 Apr;32(2):99-101. doi: 10.1016/s0016-5107(86)71766-5. PMID: 3710107.

