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Multiple primary tumors: Colorectal carcinoma and non-Hodgkin's lymphoma

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ABSTRACT

INTRODUCTION: Colorectal cancer (CRC) is the third most commonly diagnosed cancer, whereas lymphoma is the sixth leading cause of cancer death, 90% of which corresponds to non-Hodgkin's lymphoma (NHL). The association of these two primary tumors, a solid tumor with an hematological malignancy, is very uncommon.

PRESENTATION OF CASE: We report the case of a 47-year-old man who presented with abdominal pain, a right upper quadrant mass and 12 kg of weight loss in 9 months. The computed tomography (CT) showed a large intra-abdominal mass and a wall thickening at the rectosigmoid junction. A colonoscopic biopsy confirmed a colorectal adenocarcinoma and a laparoscopic biopsy of the intraabdominal mass confirmed a diffuse large B-cell NHL. After multidisciplinary discussion it was decided to treat first the NHL with 3 cycles of R-CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone). The patient experienced a good response with a 70% decrease in the intraabdominal mass and a negative PET/CT. Four months after diagnosis an anterior rectal resection was performed. The patient recovered uneventfully and was discharged 5 days after surgery. The patient finally died 20 months after surgery due to disease progression.

DISCUSSION: The association of CRC and NHL is an extremely rare scenario that represents a great multidisciplinary challenge with respect to treatment due to the scarce literature found on this topic.

CONCLUSION: When CRC and NHL are present, all the different disease patterns must be considered in a multidisciplinary and patient-oriented fashion, in order to decide the best therapeutic strategy for each individual.

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1. Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide and the fourth most common cause of death [1–3]. Only in the United States, around 140,250 individuals will be diagnosed with CRC during 2018, and 50,630 are expected to die from the disease [4]. On the other hand, Non-Hodgkin lymphoma (NHL) is the most common hematologic malignancy, ranking as the 7th most common cancer among males and the 6th most common cancer among females, with 70,800 new cases diagnosed in the United States in 2014 [5,6]. Diffuse large B cell lymphoma (DLBCL) is the most common histological subtype of NHL, accounting for 30% of NHL [7]. Extranodal or extramedullary disease occurs in up to 40% of patients with DLBCL, which is more likely to occur in the gastrointestinal tract and typically present with rapidly enlarging lymph nodal masses, most commonly in the neck or abdomen, and around 30% of patients present with B symptoms such as fever, night sweats and weight loss [7,8]. Despite that CCR and NHL are among the most frequent malignancies in adults, their synchronous occurrence is extremely rare.

We herein report a case of a patient with synchronous colorectal adenocarcinoma and diffuse large B-cell NHL. This manuscript is reported in line with the SCARE criteria [9].

2. Case report

We present a 47-year-old male with type 2 diabetes, arterial hypertension and occupational exposure to hydrocarbons, who presented with a 4-month history of progressively increasing abdominal pain in the hypogastrium associated with 12 kg of weight loss. At physical examination a mid-abdomen indurated mass was detected. Routine laboratory tests revealed a normo-

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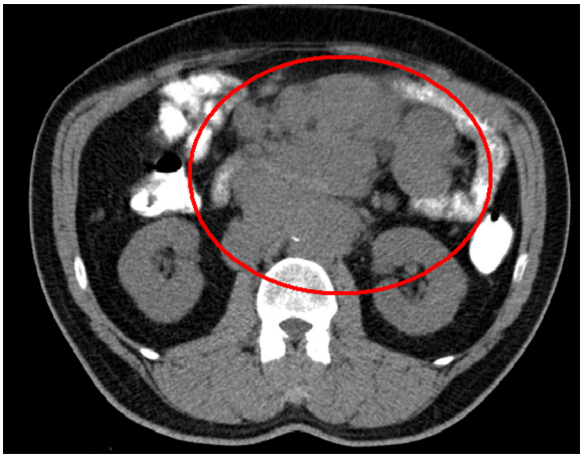

Fig. 1. Abdominal CT: Multiple retroperitoneal and mesenteric nodules forming a bulky conglomerate adenopathy.

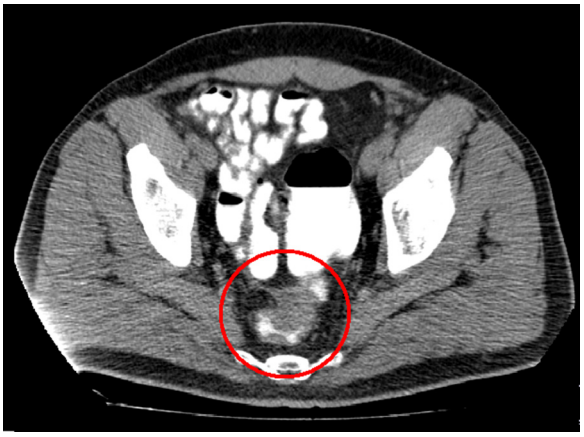

Fig. 2. Abdominal CT: focal wall thickening of the colon at the level the rectosigmoid junction.

cytic and normochromic anemia, a globular sedimentation rate (GSR) of 46 mm and an elevated lactate dehydrogenase (LDH: 749 U/l). Tumor markers tests demonstrated an elevated serum carcinoembryonic antigen (CEA: 6 ng/mL). A CT-scan showed multiple retroperitoneal and mesenteric nodules forming a bulky conglomerate adenopathy measuring $24 \times 11 \times 10$ cm, and a focal wall thickening of the colon at the level the rectosigmoid junction (Figs. 1 and 2). A colonoscopy showed an ulcerated tumor, approximately 18 cm from the anal verge, and the biopsy of the lesion revealed a poorly differentiated adenocarcinoma. With regards to the intra-abdominal mass, a laparoscopic biopsy was performed and showed a germinal Center B-Cell like DLBCL (CD 20+, Ki-67 > 30%). The patient was discussed at multidisciplinary tumor board and given that the colon primary was asymptomatic it was decided to treat first the NHL with 3 cycles of R-CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone). After 3 months of treatment with good tolerance and absence of tumor lysis syndrome, a control PET-CT scan showed a reduction of more than 70% of the intra-abdominal mass and absence of metabolic activity within the lesion. Four months after diagnosis the patient underwent a low anterior resection with total mesorectal excision. Pathological examination confirmed a poorly differentiated adenocarcinoma, with tumor-free circumferential and distal margins, and 2 out of 18 lymph nodes with metastases (pT3-pN1-M0). The patient had an uneventful recovery and was discharged home in the 5th postoperative day. Eighteen months after surgery he experienced disease progression of his colorectal cancer in the peritoneum and liver and finally died at 20 months of follow-up after undergoing multiple lines of chemotherapy without response.

3. Discussion

Multiple primary malignant neoplasms (MPMN) are defined as two or more unrelated primary malignant tumors that originate from different organs and occur in the body at the same time or one after another [10]. A literature review on 1,104,269 cancer patients concluded that the prevalence of MPMN is between 0.73% and 11.7%, with an incidence that increases with age [11,12]. Each of the tumors must be distinct, and the probability of one being a metastasis of the other must be excluded [13]. Warren and Gates [13] proposed to classify MPMN as synchronous if the interval between tumors diagnosis is under 6 months, and metachronous if the interval is over 6 months. Metachronous presentation is more frequent than synchronous, with a ratio of 2.7 [14,15]. The synchronous occurrence of a solid tumor with an hematological malignancy is extremely rare, but even more so is the synchronous presentation of colorectal carcinoma and lymphoma, which has been estimated at 0.0002% [16]. We have herein reported a case of synchronous CRC and NHL, an extremely rare scenario.

The pathophysiology of MPMN remains poorly understood, but risk factors may include tobacco and alcohol intake, infections, immunosuppression, genetic predisposition, and toxic effects related to chemotherapy or radiotherapy treatments [16]. With regards to CRC and NHL, it has been suggested that lymphoma may be the initial event that suppresses the patient's defenses against the development of colorectal carcinoma [16–18]. On the other hand, Hirano et al. [19] reported a patient with hereditary nonpolyposis colorectal cancer who developed NHL after curative resection of CRC. In this case, both colon cancer and lymphoma showed microsatellite DNA instability, sharing alteration in a locus of chromosome 7 (D7S501) [19]. Nonetheless, the rarity of such cases prevents any firm conclusion regarding the pathophysiology of the relationship between lymphomas and colorectal adenocarcinomas.

Synchronous MPMN imply important therapeutic challenges, given that there is no standard treatment for the wide variety of presentations possible [12,20]. Depending on the tumor location and type of diseases involved, the treatment involves curative surgical resection of each cancer, radiotherapy and/or chemotherapy [12,13,16,20]. When CRC and lymphoma occur simultaneously, attention is usually drawn first to the symptoms of the colorectal carcinoma [17]. This was not the case of our patient, in whom the symptoms were derived exclusively from the mid-abdomen indurated mass, which was the NHL. Therefore, the management of our patient was individually tailored for simultaneous optimal treatment of both conditions discussing his medical records at a multidisciplinary tumor board. After considering the tumor stage of both diseases and the performance status of the patient, it was decided to initially treat the lymphoma given that the colon cancer was asymptomatic and colorectal resection was technically difficult at that moment. Even though the patient finally died of disease progression due to very aggressive tumor biology, he successfully completed three courses of R-CHOP chemotherapy with good response and reached uneventfully the surgical resection of its synchronous colorectal primary.

4. Conclusion

The synchronous association of colon cancer and diffuse large B-cell non-Hodgkin's lymphoma is an extremely rare scenario, which poses a great challenge with regards to the appropriate treatment

sequence. All the different disease patterns must be considered in a multidisciplinary and patient-oriented fashion, in order to decide the best therapeutic strategy for each individual.

Conflicts of interest statement

None.

Funding

None.

Ethical approval

Single case retrospective studies where all data is anonymized are exempt from ethnical approval at our institution. However, patient written informed consent was obtained for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor in-Chief of this journal on request.

Consent

Written informed consent was obtained for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor in-Chief of this journal on request.

Author contribution

Study conception and design: Diana A. Pantoja Pachajoa, Marco Antonio Bruno.

Acquisition of data: Diana A. Pantoja Pachajoa, Marco Antonio Bruno.

Analysis and interpretation of data: Diana A. Pantoja Pachajoa, Fernando A. Alvarez, Facundo Mandojana.

Drafting of manuscript: Diana A. Pantoja Pachajoa, Fernando A. Alvarez, Germán Viscido.

Critical revisión: Fernando A. Alvarez, Germán Viscido, Facundo Mandojana, Alejandro Doniquian.

Authors give final approval of the version to be submitted: Fernando A. Alvarez, Alejandro Doniquian.

Registration of research studies

Case Report.

Guarantor

Diana A. Pantoja Pachajoa.
Facundo Mandojana.
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