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Case report

Synchronous adenocarcinoma and marginal zone B-cell lymphoma of the colon. A case report

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ABSTRACT

Introduction and importance: The association of colonic adenocarcinoma with lymphoma is a rare entity. The purpose of our presentation is to draw the attention of the endoscopist, and the surgeon, to the need to remove any suspicious lesions in the exploration for colorectal cancer. The pathologist should be warned about this association in the face of any unusual change in the lymphatic environment around an adenocarcinoma. In the slightest doubt, an immunohistochemistry (IHC) should be performed in order not to ignore this association.
Case presentation: A 77-year-old patient, who had adenocarcinoma of the right colic flexure, in whom a chance discovery of lymphoma was made intraoperatively. This combination was treated with chemotherapy targeting adenocarcinoma classified as pT4N1M0, ahead of the low-grade lymphoma malignancy. After two years, the patient presented with a recurrence as left lateral cervical lymphadenopathy and died in a picture of generalized paralysis.
Clinical discussion: Digestive lymphoma associated with adneocarcinoma is defined according to strict criteria according to DAWSON. It always precedes adenocarcinoma because it disrupts the subject's immunocompetence. His diagnosis is suspected when the lymphatic environment around the adenocarcinoma is disturbed. The confirmation is assured with the IHC. Treatment should target the most aggressive cancer.
Conclusion: The synchronous colonic occurrence of a MALT-type lymphoma and an adenocarcinoma is rare but possible. The pathologist must be alert to its existence. Treatment depends on the tumor stage of the adenocarcinoma but also on the lymphoma and its grade and any therapeutic decision should only be made in a multidisciplinary meeting.

1. Introduction and importance

Colorectal adenocarcinoma represents more than 95% of colorectal neoplasms, while the primary lymphomatous forms are rare and represent 0.2 to 0.4% of these neoplasms. [1]. Their association is exceptional, only about twenty cases are found in the literature [2–6].

We report here the 6th observation, of a synchronous localization of primary colonic lymphoma associated with mucous membranes (MALT) and of a liberkhünien adenocarcinoma of fortuitous discovery, in a 77-year-old patient. This work has been reported in line with the SCARE criteria [7].

2. Case presentation

A 77-year-old patient with a history of right renal lithiasis and benign prostatic hypertrophy treated medically with alpha-blocker, present colic-like abdominal pain associated with melena for one year. The patient haven't any familiar pathology and his social-economic condition is modest.

The clinical examination found, apart from a slight skin and mucous membrane pallor, a patient in general preserved condition, without a mass or palpable peripheral lymphadenopathy. The digital rectal examination was normal.

The biological assessment was unremarkable, especially haematological, finding a hemoglobin level of 12.3 g/dl, a number of leukocytes at 5450/mm^3 without an increase in lymphocytes (1640/mm^3). The

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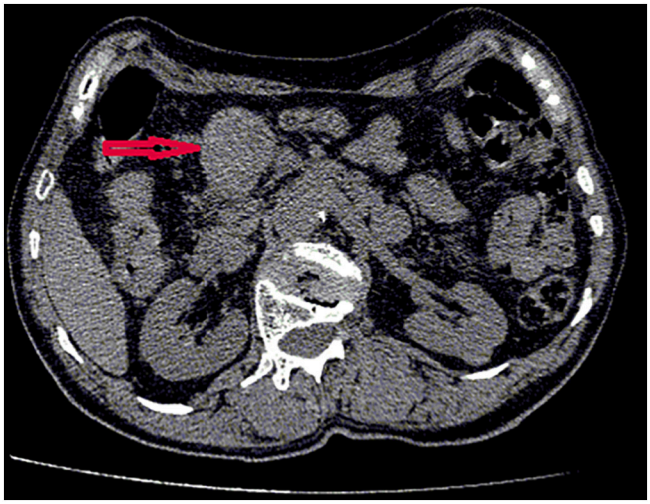

Fig. 1. Computed tomography showing a tissular mass of 42 mm (36 UH) corresponding to huge lymph node in the territory of the right colonic superior artery mimicking a duodenal duplicity (right arrow).

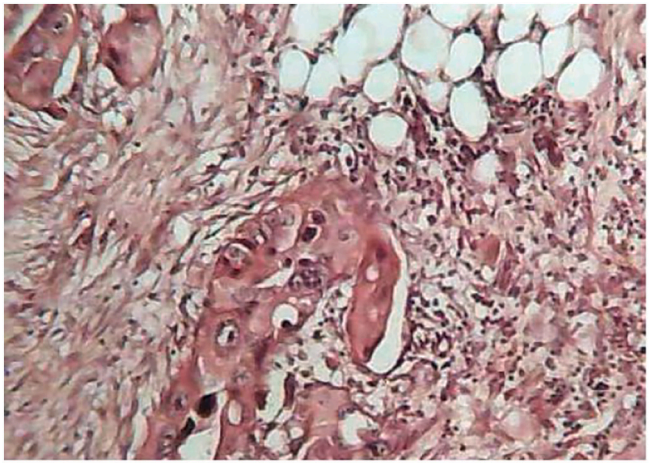

Fig. 2. H&E (×200) Infiltrating, well-differentiated adenocarcinomatous proliferation surrounded by a fibrous reactive stroma, containing some polymorphic reactive inflammatory elements.

dosage of tumor markers was normal, in particular that of the Carcino-Embryonic Antigen estimated at 2.3 IU/L. Colonoscopy showed the presence in the right colon flexure of an ulcerative and stenosing tumor process which is associated with sessile polyps of 10 mm long axis a few centimeters downstream. Histological study of the biopsy samples taken revealed the presence of a well-differentiated colonic adenocarcinoma.

As part of the extension assessment, a thoraco-abdomino-pelvic computed tomography (TAP CT) did not find any secondary locations, but only a mass of 42 mm long axis, sub-duodenal, tissue density (36 HU) not enhancing after injection of contrast product which may correspond to digestive duplicity (Fig. 1).

Intraoperative exploration revealed a stenosing process of the right colic angle. Ten cm downstream of this first process, there is a second mass of three cm long axis located at the level of the transverse colon. The remainder of the intraoperative exploration revealed the presence of a large lymphadenopathy, 05 cm in diameter, well encapsulated, located on the territory of the right superior colonic artery (RSCA), in intimate contact with the inferius duodenal genu. It was the latter training that was mistaken for duodenal duplicity on CT. Furthermore, no ascites or secondary localizations were found.

A right hemicolectomy widened to the left was performed by a senior

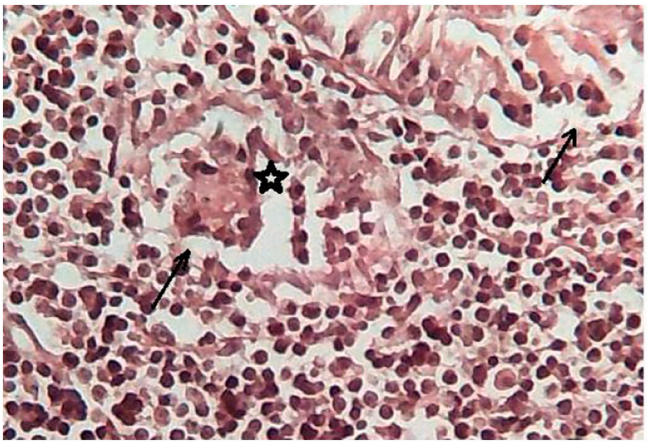

Fig. 3. H&E (×200) Lymphomatous proliferation made up of small monomorphic lymphocytes with images of lymphoepithelial destruction (star) and exocytosis (arrows).

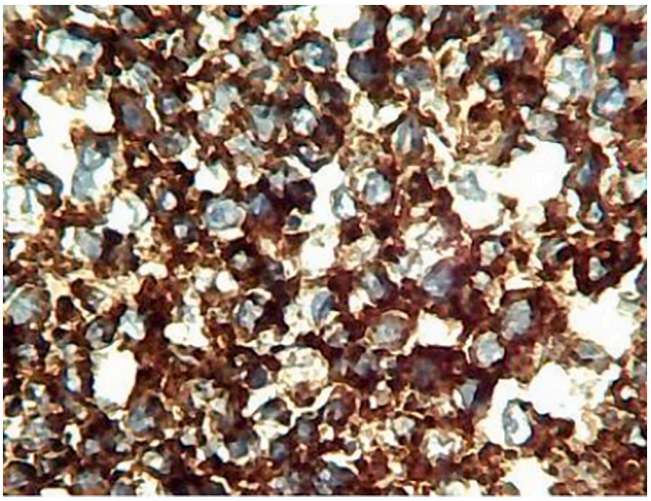

Fig. 4. Intense and diffuse expression of lymphoma cells with anti-CD20 (×400).

surgeon in a teaching hospital with lateral ileo-transverse anastomosis and subhepatic drainage by a DELBEY blade. The post-operative period was uneventful.

Anatomopathological study of the surgical specimen found, on the one hand, an ulcerative budding tumor process of 6 cm long axis, located at the level of the right colonic angle and corresponding to a well differentiated lieberkuhnian adenocarcinoma and on the other hand, an infiltrating parietal tumor process, located 10 cm downstream from the first, corresponding to a small cell B lymphoma of the MALT type. The latter is represented by a significant lymphomatous proliferation, transparietal, of diffuse and vaguely nodular architecture, made of small monomorphic lymphocytic cells, centrocytic in appearance, little mitotic, intensely and diffusely expressing CD 20 but not CD 5, CD23, cyclin D1 and CD10. Images of lymphoepithelial destruction are also associated (Figs. 2, 3 and 4). Due to the lack of reagents, no molecular study looking for a translocation was carried out.

The lymph node dissection brought back 17 lymph nodes, 16 of which were reactive and one lymphomatous. As for the large sub-duodenal mass, located on the ACSD territory, it corresponded to a lymph node metastasis of the adenocarcinoma described above. Thus, the adenocarcinomatous process was classified as pT4aN1M0 according to the TNM (Tumor Node Metastasis) classification of the International Union Against Cancer (UICC) version 2011.

Table 1
Diagnostic criteria for primary colonic lymphoma defined by Dawson et al. [8].

1. A normal chest x-ray
2. Absence of hepatomegaly or splenomegaly
3. Absence of superficial lymph nodes
4. Normal white blood cell count
5. Colonic tumor mass with regional lymph nodes

In view of this fortuitous discovery of the lymphomatous process and as part of its extension assessment, the ear, nose and throat (ENT) examination and the bone marrow biopsy (BMB) performed, did not find any sign of dissemination. The eso-gastro-duodenal fibroscopy showed, after studies of biopsy fragments, a Helicobacter pylori gastritis, of moderate intensity and atrophy associated with foci of intestinal metaplasia. This clinical case was discussed at the multidisciplinary meeting in oncology (MMO) and adjuvant chemotherapy based on 08 courses of Capecitabine was started after informed consent of the patient. The drug tolerance was well. Follow-up was carried out every 3 months with clinical, radiological and biological examination.

The patient presented two years later a recurrence which has been manifested by a malignant left latero-cervical node and bilateral lung metastases.

3. Clinical discussion

Primary colon lymphoma is rare and accounts for 0.2–0.4% of all colonic tumors [1–8]. It is defined by DAWSON [8] according to strict criteria (Table 1). Its synchronous association with an adenocarcinoma is exceptional and represents a diagnostic surprise [4–20].

Physiopathologically, and according to several authors, there is no known common etiological factor between adenocarcinoma and lymphoma and their association is pure coincidence [6–20]. But for SHIGENO, the presence of lymphoma would disrupt the local environment and favor the development of a second adjacent cancer [9]. According to CORNES, adenocarcinoma generally coexists or follows lymphoma but never precedes it [10], suggesting that lymphoma by impairing the subject's immunocompetence could accelerate the malignant degeneration of an existing precancerous lesion. However, no correlation between immunodeficiency and the activation of an oncogene or the activation of a tumor suppressor gene has not been found [11]. In addition, rare cases of association with Helicobacter pylori infection, tuberculosis or ulcerative colitis have been described in the literature [6,15–16].

In fact, only 5 cases of primary synchronous colonic association of MALT-type lymphoma and adenocarcinoma have been reported [4–6], of which 4 were women and whose ages varied between 68 and 77 years (Table 2).

The symptomatology is not specific; a notion of fatigue, anemia and/or fecal blood loss, whether occult or not, are often reported.

The diagnosis of lymphoma was made for the various observations only on an operative specimen, as in our patient, whereas the various biopsies carried out only found adenocarcinomatous proliferation. This testifies to the interest of the sampling, the quality of the endoscopic progression, given that 73% of lymphomas are located in the cecum [1–3] as well as the rigorous assessment of the tumor environment, difficult on biopsy.

For this, two remarks should be made to the pathologist: The first is that not all periadenocarcinomatous lymphoid infiltrate is synonymous with a stroma reaction; and that the destructive, diffuse and monotonous nature of the infiltrate, as described in our observation, should alert the pathologist and should be the subject of immuno-phenotyping, in order to make the diagnosis of malignancy.

The second is that all the lymph nodes in the dissection which are not metastatic should not be considered systematically as reactive; and that any erasure of the architecture giving rise to suspicion of lymphomatous infiltration should be subject to immunohistochemical testing.

Table 2
Table summarizing the various cases reported in the literature of a synchronous localization of a colonic adenocarcinoma and a MALT type lymphoma.

Cas	Age/Sex	Symptoms	Localisation and TNM stade of ADNK	Localisation Lymphoma/adénocarcinoma	Lymph nodes	Bone narrow biopsy	Traitement	Remission (Months)
1[4]	77/Female	Asthenia	Right colic angle T2N0M0	Right colic angle (0 cm)	(+) NP/14	–	Surgery	Good
2[5]	75/Female	Anemia, Asthenia, Rectorragie	Low rectum TisN0M0	Low rectum (0 cm)	2/22	–	Surgery	Not precised 20
3[5]	71/Female	Anemia Loss of weight	Right colon T3N0M0	Right colon (0 cm)	22/34	–	Surgery	48
4[5]	72/Male	Anemia	Right colon T1N0M0	Right colon (? cm)	12/12	+	Surgery + Chemotherapy	18
5[6]	68/Femme	Rectorragie	Right colic angle T?N0M0	Right colic angle (0 cm)	0/3	–	Surgery	2
6[*]	77/Male	Colic Melena	Right colic angle T4aN1M0	Transverse colon (10 cm)	1/17	–	Surgery + Capecitabine	6

The discovery of a double tumor location thus requires an assessment of the extension of both lymphoma (BOM, ENT examination, upper and lower digestive endoscopies and TAP CT) and adenocarcinoma [4–6].

The surgical treatment of colonic adenocarcinoma is well codified, that of lymphoma is less so as evidenced by the various articles found [2–19]. What cleaning? And what are the resection margins? Thus, in the event of two contiguous synchronous localizations, colonic excision with a sufficient margin of safety (as in our case, right hemicolectomy widened to the left) made it possible to have healthy surgical limits. On the other hand, and in the event of spaced tumor locations (right and left colon for example), a total colectomy with ileorectal anastomosis seems more appropriate. In the event of associated inflammatory colonic disease, total coloproctectomy with ileoanal anastomosis should be the rule according to NISHIGAMI [16].

As for adjuvant therapy, the most progressive and/or the most aggressive tumor should be targeted [4–6]. In our case and given the advanced stage of the adenocarcinoma (T4aN1M0), the low-grade malignancy and localization of the lymphoma, we opted only for chemotherapy targeting the adenocarcinoma. It should also be noted that in certain situations, the first treatment of a digestive lymphomatous pathology associated with an adenocarcinoma resulted in a tumor dissemination of the latter and the appearance of liver metastases, which further complicated the management [12].

Rigorous long-term monitoring of the two entities must be ensured periodically. Any recurrence (metastatic, lymph node or peritoneal) detected should be histologically labeled and actively treated surgically and/or medically.

4. Conclusion

The synchronous colonic occurrence of a MALT-type lymphoma and an adenocarcinoma is rare but possible. The pathologist must be alert to its existence. Treatment depends on the tumor stage of the adenocarcinoma but also on the lymphoma and its grade and any therapeutic decision should only be made in a multidisciplinary meeting.

This work has been reported in line with the PROCESS criteria [21].

Written informed consent was obtained from the patient 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.

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Ethical approval

The ethics committee of our institution has approved this publication.

Author contribution

All authors approved the case report.

Guarantor

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Declaration of competing interest

No one.

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