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Management of an uncommon T-Cell lymphoma revealed by an anastomotic dehiscence in Crohn's disease: A case report

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ABSTRACT

INTRODUCTION AND IMPORTANCE: T-cell lymphoma degeneration in pancolic crohn's disease is scarce. It is mostly related to long-standing inflammatory bowel disease in patients under immunosuppressants. We reviewed the clinical, endoscopic, radiological and histologic data of the patient as well as the literature dealing with T-cell lymphoma arising from pancolic crohn's disease.
CASE PRESENTATION: We describe in this paper an unusual case of a female young patient who underwent emergency surgery for per endoscopic perforation of the right colon while being under azathioprine. She had a subtotal colectomy with ileostomy and sigmoidostomy. After six months, we restored the digestive continuity through an ileorectal anastomosis. She was kept in remission on azathioprine. After one year, she presented with a pelvic abscess revealing a dehiscence of the ileorectal anastomosis leading to a surgical drainage and resection of the anastomosis associated with terminal ileostomy and closure of the rectal stump. Pathology examination revealed T cell lymphoma arising from the ileorectal anastomosis.
DISCUSSION: Patients with long-standing IBD have an increased risk of developing colorectal cancer. The onset of a malignant lymphoma during the course of the CD is scarce. Some studies haves failed to identify crohn's disease as a risk factor of lymphoma whereas other ones have succeeded to. Immunosuppressants are reported to have carcinogenic effect. Rarely, lymphoma degeneration can be revealed by intestinal complications such as perforation like in our case.
CONCLUSION: Many studies reported lymphoma degeneration of crohn's disease after long-term immunosuppressant therapy. However, rapid T-cell lymphoma degeneration revealed by anastomotic dehiscence in crohn's disease made our case unique and interesting.

1. Introduction

Crohn's disease (CD) is a chronic inflammatory bowel disease that can affect any part of the digestive tract. It mainly occurs in young people. Furthermore, CD is associated with an increased risk of degeneration after a few years of evolution.

Literature has long studied the development of colorectal adenocarcinoma in inflammatory bowel diseases (IBD). However, there are wide variations between results reporting the incidence of this complication especially in long-standing CD [1]. Developing intestinal non-Hodgkin lymphoma in patients with IBD is scarce and fewly described in literature. We report herein a case of CD degenerated into an intestinal T lymphoma revealed by a dehiscence of an old ileo-rectal anastomosis in a 31-year-old female patient.

The case report has been reported in line with the SCARE criteria [2].

2. Case report

We report the case of a 31-year-old patient with a surgical history of appendectomy 15 years ago and an acoustic neuroma surgery 5 years ago, who is followed for a pancolic CD for 12 years. After 2 years of evolution of the disease, she presented with a severe acute colitis, which evolved favorably under medical treatment. She was then put on immunosuppressive drugs using initially 5ASA then Azathioprine for 6 years. She underwent in 2016 an emergency surgery for a per endoscopic perforation of the right colon. She had a subtotal colectomy with ileostomy and sigmoidostomy by median route with favorable outcomes. Six months later, we performed a complementary colectomy and we restored

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the digestive tract through a lateral ileorectal manual anastomosis. The postoperative course was uneventful. The patient was kept in remission on Azathioprine for one year with good drug tolerance.

In December 2019, she presented via ambulance with an acute diffuse abdominal pain evolving for two days with impaired general condition. The patient reported recent Six-times diarrhea per day during the previous week.

On physical examination, we found a 39 °C fever. The abdominal examination showed a diffuse abdominal tenderness with a guarding of the infra-umbilical area. Digital rectal exam revealed liquid blood-free stool but the ileorectal anastomosis was unreachable and therefore not evaluable. Tachycardia (120 bpm) and low blood pressure (08 / 05 mmHg) were found on cardiovascular exam. Increased respiratory rate (22 cycle / minute) was noticed. No other abnormalities on the remainder physical examination.

Laboratory tests showed a significant biological inflammatory syndrome with a high white blood cells count (18,000/ μl) and C-reactive protein level (150 mg/L). In addition, a 7.6 g / dl was shown up by biological results.

An abdominal-pelvic computed tomography was performed as a matter of urgency. It showed a mesenteric lymph node with necrotic center and a tissular mass of the left pericolic gutter measuring 4 * 3 cm. There was also an oblong uterine collection of 18 * 2 cm communicating with the anastomotic ileal loop through a fistula (Fig. 1).

We decided then to perform a CT-scan-guided biopsy of the tissular mass. Pathology examination findings were suggestive of peritoneal tuberculosis. However, no formal diagnosis could be set on these pathological results. Moreover, CT-Scan guided drainage of the uterine collection was performed and has brought pus. Radiological treatment was associated with broad-spectrum antibiotics combined with resuscitation. Bacteriological examination of the purulent fluid collected isolated a multi-sensitive *Escherichia Coli* allowing adaptation of antibiotic therapy.

The patient was therefore put on anti-tuberculosis treatment, complicated on Day eight by a drug-induced hepatitis. Several attempts to reintroduce anti-tuberculosis therapy have failed.

A proctoscopy was compulsory to explore the remnant part of the rectum and the ileorectal anastomosis. It showed multiple ulcerations at the level of the anastomosis with no other abnormalities noticed during the exam.

Faced with the absence of clinical, biological and radiological improvement during three weeks of management, a university hospital assistant decided to operate the patient with the aim of performing surgical drainage of the collection with eventual resection of the fistulized ileorectal anastomosis.

Through a median incision, we found a pelvic shield made of small agglutinated handles clogging an anastomotic hemicircumferential dehiscence that feeds a collection of 3 cm (Fig. 2). There was also a whitish 2 cm nodule at the level of the right pericolic gutter and a mesenteric lymph node of 6 cm that were resected for pathological study.

We therefore decided to perform a resection of the ileorectal anastomosis, with closure of the rectal stump and preparation of a right iliac terminal ileostomy. We left in place a wide drainage in the pelvis.

Histological examination of the specimen concluded that there was a morphological and immunohistochemical aspect consistent with small intestinal T lymphoma of the NOS type (CD3 +, CD30 +, ALK-) without any argument in favor of associated tuberculosis disease (Fig. 3).

The parietal nodule and the mesenteric mass removed are free from any tumor proliferation or tuberculosis involvement.

The evolution was favorable and post-operative course was uneventful.

The patient was discharged on Day 10 postoperatively, and was referred to oncology department in order to benefit from adjuvant treatment. Six months follow up showed no recurrence under anthracycline-containing chemotherapy (CHOP: cyclophosphamide, doxorubicin, vincristine and prednisone).

3. Discussion

The association of cancer and CD is well documented. Many studies confirmed that patients with long-standing IBD have an increased risk of developing colorectal cancer [3]. The results vary widely between different studies. Jess et al. [4] reported a meta-analysis of intestinal cancer risk in crohn's disease based on population-based studies revealing an overall increased risk of both colorectal cancers and small bowel cancers among patients with CD with standardized incidence ratios (SIR) ranging from 0.9 to 2.2. These findings stress the importance of endoscopic follow-up and treatment of patients with operated or not IBD.

Although the type of lymphoma most frequently described with immunosuppressants is large cell B lymphoma, non-Hodgkin's T lymphoma has been described in individuals with IBD with a demonstrated combination of therapy or treatment with Azathioprine alone.

Digestive T cell lymphomas represent 13%–17% of all gastrointestinal lymphomas [5]. They almost all occur in the small intestine especially the jejunum but remain less frequent than B lymphomas in this location [5,6].

The onset of a malignant lymphoma during the course of the CD is a very rare finding. Almost all papers reported are case reports [7]. Crohn's disease has long been suspected in the genesis of non-Hodgkin's lymphoma of the digestive tract. However, most studies have failed to demonstrate this claim.

Two large-scale Swedish studies have failed to identify CD as a risk factor for lymphoma [8,9]. On the other hand, a recent American study [10] identified crohn's disease as a risk factor for non-Hodgkin's lymphoma but this study gathered a population of elderly patients with severe forms of the disease.

Immunosuppressive therapies used to control CD such as thiopurines have now been shown to be a risk factor for non-Hodgkin's lymphoma. This risk is increased in male patients and the elderly [11].

The risk of non-Hodgkin's lymphoma can be overlooked by the clinician in the face of the significant improvement in quality and life expectancy in young subjects whose Crohn's disease is kept in remission thanks to maintenance therapy based on Azathopirine [12].

Maintaining such a level of immunosuppression is associated with a carcinological risk. Thus, the use of thiopurines is clearly associated with a risk of developing lymphoma [13]. In 2011, 43 cases of lymphoma were described among the 16,023 patients treated with immunosuppressants for IBD [13]. The type of lymphoma most often diagnosed was large cell B lymphoma (44%), then follicular lymphoma (14%) then Hodgkin's lymphoma (12%).

In addition, the use of azathioprine or 6-mercaptopurine increased the risk of developing lymphoma by 4–5. On the other hand, the correlation between the occurrence of lymphoma and the use of an anti TNF is more disputed due to the use, often in parallel, of anti TNF and thiopurines in most patients [14]. A meta-analysis of 26 studies had described 13 cases of non-Hodgkin's lymphoma in adults treated with anti TNF for CD. Compared to the risk in the general population of developing lymphoma (1.9 per 10,000 person-years), the risk under anti TNF therapy was 3 times higher (3.2 per 10,000 person-years). Nevertheless, among the cases, 66% were also on thiopurines at the time of the diagnosis of lymphoma.

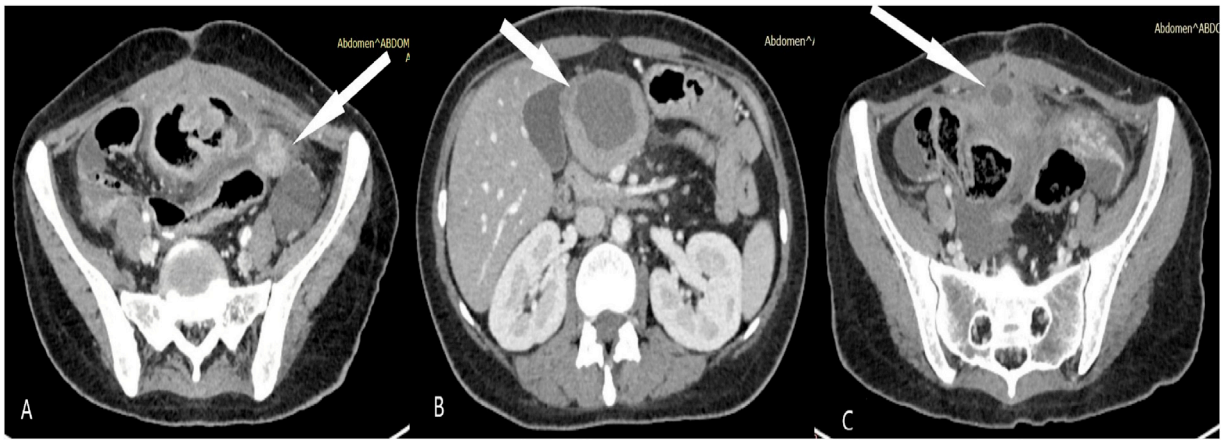

Fig. 1. Abdominal-pelvic CT-scan. **a**: Tissular mass of the left pericolic gutter. **b**: Mesenteric lymph node with necrotic center.**c**: Uterine collection communicating with the anastomotic ileal loop.

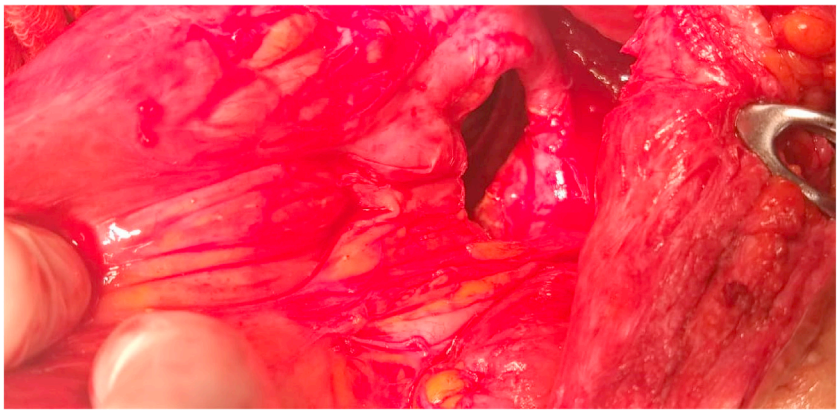

Fig. 2. Anastomotic dehiscence.

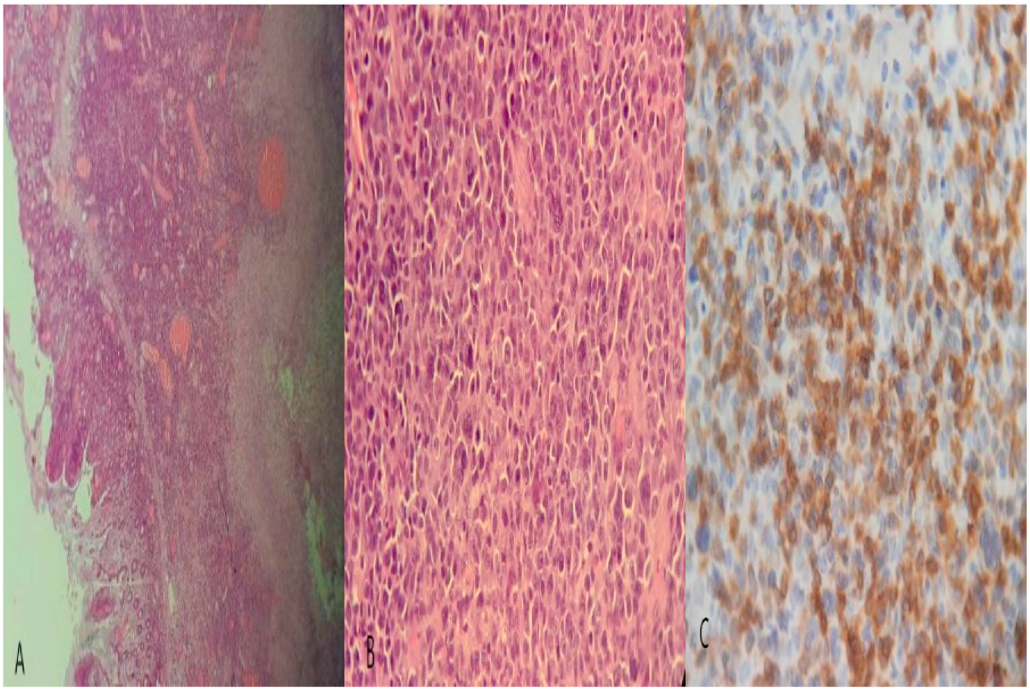

Fig. 3. Pathological findings of resected specimen. **a**: Hematoxylin Eosin x 10: intestinal mucosa site of a diffuse lymphoid proliferation. **b**: Hematoxylin Eosin x 40: pleomorphic lymphoid cells, sometimes large, with atypical nuclei. **c**: Immunohistochemistry x 40: tumor cells express CD3 intensely.

Finally, the TREAT study [15] is the only prospective study that continues to compare the side effects of infliximab with those of other therapies in more than 6000 patients treated for CD since 1999. The last update of this study in 2014 did not report any correlation between the use of infliximab and the risk of neoplasia but confirmed that immunosuppressive treatments, alone or in combination with biotherapies, increased the carcinogenic risk with odds with respective ratios of 4.19 and 3.33.

Similarly, Herrinton et al. reported that combotherapy increased the risk of developing lymphoma by a factor of 6 compared to the risk of the general population [13].

Non-Hodgkin's lymphomas can be complicated by intestinal perforation, especially after the initiation of anti-tumor chemotherapy, but the perforations can complicate the natural history of a lymphoma. These perforations most often occur in the small intestine and generally require emergency surgery [16]. Perforation is also known as a rare acute surgical emergency complicating the natural history of the CD, occurring in 1–3% of cases [17]. However, in other cases, perforation of a cancer, endoscopic perforation or anastomotic failure may occur.

In our patient, the perforation happened at the level of the ileo-rectal anastomosis which was the seat of lymphoma complicating the CD.

Surgical resection is currently the standard treatment with a mortality of less than 4% compared to 41% of mortality observed in the past after simple sutures of the perforation [18]. We opted for a resection of the ileo-rectal anastomosis with closure of the rectal stump and preparation of an ileostomy associated with wide drainage of the pelvis given the peritoneal contamination and the immunocompromised site. The restoration of delayed digestive continuity was necessary in our view.

4. Conclusion

The appearance of lymphoma occurred in this case, in a young patient put on Thiopurines for 6 years with an evolution towards degeneration is relatively rapid compared to what is generally reported in the literature. The non-Hodgkin's lymphoma discovered fortuitously in pathology study was responsible for an anastomotic dehiscence which was blocked by the small handles carrying out a real plastron. To our knowledge, no publication has dealt with a case of dehiscence of an anastomosis at 3 years of follow-up due to degeneration in T lymphoma which makes this case all the more interesting.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

Not applicable.

Consent

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.

Author contribution

Anis Haddad: Performed Surgery.
Ahmed Ben Mahmoud: Writing - Original draft.
Houcine Maghrebi: Supervision.
Baya Chelly: Data interpretation of the pathological findings.
Mohamed Jouini: Supervision.
Montasser Jameleddine Kacem: Supervision - Reviewing.

Registration of research studies

Not applicable.

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Provenance and peer review

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