

Profuse diarrhea after autologous stem cell transplantation for peripheral T-cell lymphoma, not otherwise specified: a case report

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Abstract

We report the case of a 59-year-old patient with a history of peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) presenting with profuse diarrhea 3 months after completing lymphoma treatment. After exhaustive workup a recurrence of the peripheral T-cell lymphoma in the gastrointestinal tract was diagnosed. Predominant gastrointestinal recurrence is a unique presentation of relapse of PTCL-NOS. To the best of our knowledge, no other case reports have covered predominant gastrointestinal recurrence of PTCL-NOS so far. (*Acta gastroenterol. belg.*, 2024, 87, 527-530).

Keywords: Peripheral T-cell lymphoma, not otherwise specified, lymphoma, autologous stem cell transplantation, gastrointestinal recurrence, endoscopy.

Introduction

Gastrointestinal lymphomas are a group of aggressive malignancies which are rare and challenging to diagnose. The incidence of T-cell lymphoma is 0.5-1 per million per year, the diagnosis is usually made in an advanced stage. The 1- and 5- year survival rates are 31-39% and 8-20%, respectively (1). Primary gastrointestinal lymphoma, presenting with predominant gastrointestinal involvement, accounts for only 1-4% of all gastrointestinal tract malignancies and 10-15% of non-Hodgkin lymphomas. However, the gastrointestinal tract is the most common site of extranodal involvement of lymphomas. Most non-Hodgkin lymphomas involving the gastrointestinal tract are however of B-cell lineage; T-cell lymphomas comprise only 4-6% (2-5). The predominant recurrence of PTCL-NOS in the gastrointestinal tract is extremely rare, to our knowledge no other cases have been reported.

Case

We report the case of a 59-year-old man with profuse diarrhea occurring 3 months after completing treatment for a peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS). The diagnosis of PTCL-NOS stage III (with mediastinal, paratracheal, iliac and inguinal adenopathies) was made in December 2022. Complete metabolic response was achieved after treatment with 6 cycles of polychemotherapy with cyclophosphamide,

doxorubicin, vincristin, etoposide and prednisolon (CHOEP), followed by consolidation with autologous stem cell transplant (ASCT) in July 2023. His past medical history further included a transcatheter aortic valve implantation because of a critical aortic valve stenosis and celiac disease for which he was following a strict gluten-free diet.

The patient was admitted in October 2023 due to profuse diarrhea and vague abdominal pain in the last four weeks. No rectal bleeding nor fever were reported. He did not travel abroad recently. His physical exam was unrevealing. The laboratory data showed a normal white blood cell count, mild increase of C-reactive protein (13.7 mg/L) and a minor decrease of renal function (creatinine 1.1 mg/dL, eGFR 73 mL/min). The patient was admitted for further diagnostic workup. Laboratory investigation revealed normal anti-tissue transglutaminase antibodies and an euthyroid status. Repetitive stool cultures were negative for common enteropathogens, *Clostridioides difficile* and parasites. Empiric treatment with azithromycin (500 mg once daily for three days) was started for a suspected infectious colitis. Due to ongoing diarrhea a gastroscopy was performed, which revealed mild inflammation of the duodenal bulb. Histological examination revealed an increase in intra-epithelial lymphocytes and minor flattening of the villi. During ileocolonoscopy, mild hyperemia of the ileal mucosa and profusely scattered small ulcers with otherwise normal appearing mucosa of the colon were seen. Guided biopsies revealed focal active ileitis and colitis, without signs of graft-versus-host disease. Immunohistochemistry for cytomegalovirus (CMV) showed some scarce positive nuclei. Treatment with ganciclovir (5 mg/kg twice daily during 11 days) was started, despite negative cytomegalovirus polymerase chain reaction (PCR) performed on colon biopsies. Unfortunately, high volume diarrhea with an output of more than five litres a day persisted. A further exhaustive workup was performed. PET-CT scan revealed reactive mesenteric lymphadenopathies and

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Submission date: 21/02/2024
Acceptance date: 06/05/2024

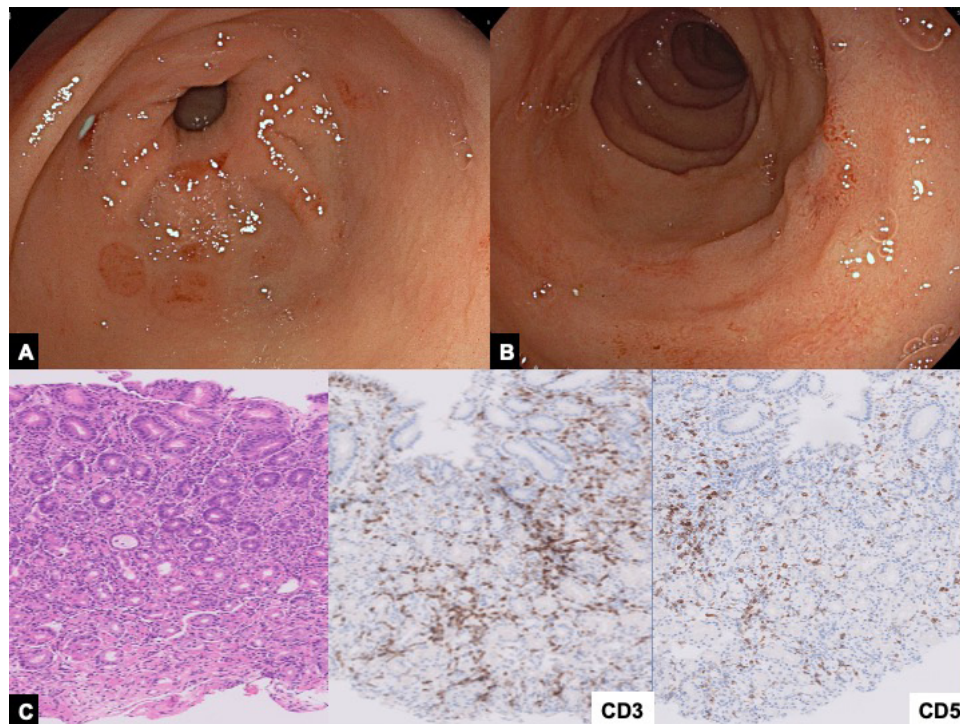


Figure 1. — Final gastroscopy. 1A: Round, focally raised erythematous lesions in the antrum with central erosions/ulcerations and surrounding erythema in the antrum. 1B: Superficial ulcerations in the duodenum with surrounding erythema, normal intervening mucosa. 1C: Biopsies of the stomach revealing a lymphoid infiltrate in the lamina propria with numerous atypical T-cells expressing CD3. The cells show also a loss of CD5, a T-cell marker.

a diffusely increased metabolism in the terminal ileum and right hemicolon. Because of his immunosuppressive status, a workup for rare opportunistic infections was done, including microscopic evaluation of a fresh stool sample (*Cyclospora cayentanensis*, *Cystoisospora belli*, *microsporidiosis*, *Entamoeba histolytica* and *Strongyloides stercoralis*), PCR (*Norovirus* and *Entamoeba histolytica*) and serologic testing (*Histoplasmosis* and *Strongyloides stercoralis*). All were negative. Repeat sigmoidoscopy showed persistent scattered superficial ulcerations of 5 to 10 mm with normal intervening mucosa, with histological signs of acute and moderate severe chronic inflammation with some apoptotic bodies but without crypt loss, granulomas or amyloid depositions. In situ hybridization was also negative for Epstein-Barr Virus (EBV). There were no arguments for a lymphoma. Colonic tissue PCR for EBV, CMV and *Mycobacterium tuberculosis* were all negative. Revision of the index duodenal biopsies, including periodic acid-Schiff (PAS) staining for *Tropheryma whipplei*, was also negative. An underlying neuro-endocrine tumor was excluded with negative serum vasoactive intestinal peptide (VIP), chromogranin-A and neuron-specific enolase (NSE), urine 5-hydroxyindoleacetic acid levels and a ⁶⁸Ga-DOTANOC PET-CT scan. Due to the development of thrombocytopenia and medical history of PTCL-NOS, a bone marrow puncture was performed. Neither cytology, flowcytometry nor histopathology revealed any arguments for recurrence of PTCL-NOS.

A trial with systemic corticosteroids (methylprednisolone 40 mg once daily for three days) in view of a possible chronic inflammatory bowel-like disease was ineffective. Concerning his history of autologous stem cell transplantation for a peripheral T-cell lymphoma and the negative workup so far, the possibility of a local recurrence of the T-cell lymphoma was kept in mind. On repeat upper endoscopy, round, focally raised lesions with central ulcerations and surrounding erythema in the stomach and the duodenum were found (Figure 1). Histologic examination revealed an increased infiltrate in the lamina propria with atypical lymphocytes. Ileocolonoscopy showed a severe pancolitis and terminal ileitis with diffuse deep ulcerations with spontaneous bleeding (Figure 2). Colonic biopsies now revealed an atypical T-cell lymphoid infiltrate with loss of CD5 expression and 15% CD30 positivity. These combined findings were highly suggestive of a local recurrence of the peripheral T-cell lymphoma. The T-cell receptor gene rearrangement also revealed presence of the same clonal population as at initial diagnosis.

Although previous bone marrow examination could not confirm invasion of T-cell lymphoma, a new bone marrow core biopsy eventually found the presence of scarce CD30+ lymphocytes, suspicious for discrete invasion of the T-cell lymphoma.

Based on the biopsies of the stomach, duodenum and colon, a recurrence of the peripheral T-cell lymphoma in the gastrointestinal tract was diagnosed. The patient was

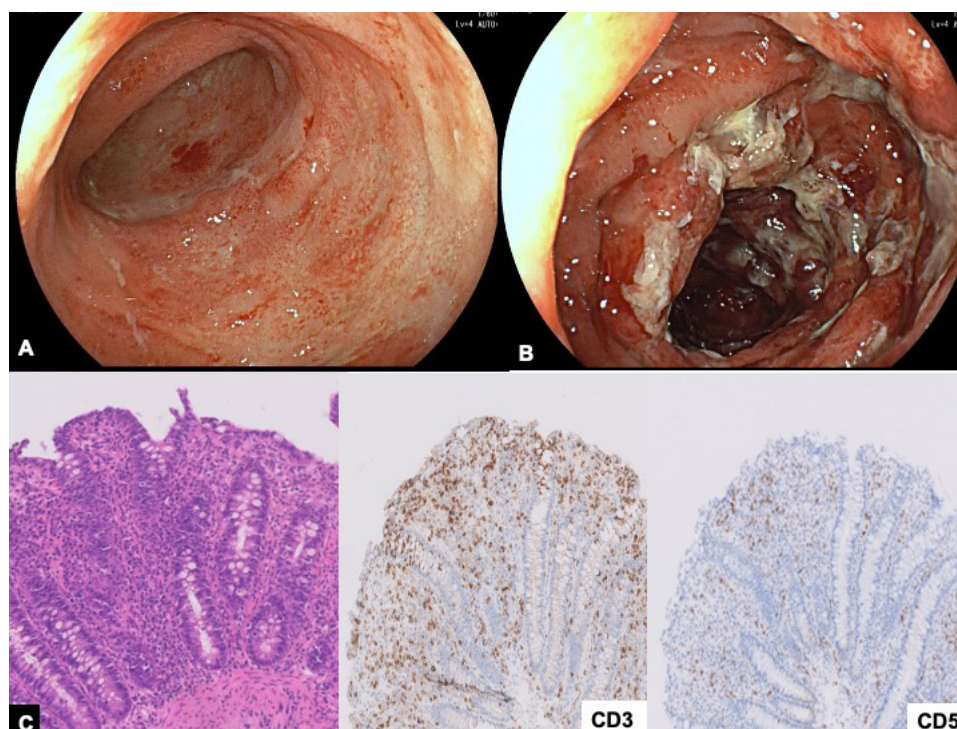


Figure 2. — Second ileocolonoscopy. 2A: Erythematous mucosa in the terminal ileum with deep circular ulcerations with spontaneous bleeding. 2B: Erythematous mucosa in the colon with circular deep ulcerations with spontaneous bleeding. 2C: Biopsies of the colon. In the lamina propria of the colon numerous atypical T-cells (CD3) are found, which show a nearly complete loss of CD5, a T-cell marker.

referred to the hematology department and chemotherapy (gemcitabin/cisplatinum) was commenced shortly after the final diagnosis was obtained.

Unfortunately, regarding the poor prognosis of the disease, 5 days after initiating chemotherapy, the patient opted for a palliative policy.

Discussion

According the World Health Organization (WHO) classification, PTCL-NOS represents a heterogeneous category of nodal and extranodal mature T-cell lymphomas that do not fit any of the specifically defined entities of mature T-cell lymphomas (6). Patients diagnosed with PTCL-NOS typically present with peripheral lymph node involvement, often accompanied by advanced disease with B-symptoms. While lymph nodes are the primary site of manifestation, the skin and gastrointestinal tract are also frequently involved. Unfortunately, PTCL is associated with an aggressive disease course and a poor prognosis when compared to B-cell lymphomas (2,7).

Primary gastrointestinal lymphoma typically refers to lymphoma primarily involving the gastrointestinal tract. It is a very rare presentation, accounting for only 1-4% of all gastrointestinal tract malignancies. However, gastrointestinal involvement as an extranodal manifestations of lymphoma is more common, accounting for 30-40% of cases and can occur in almost any type of lymphoma subtype. Most non-Hodgkin lymphomas involving the gastrointestinal tract are of B-cell lineage;

T-cell lymphomas comprise only 4-6%. A typical example of intestinal T-cell lymphoma is enteropathy-associated T-cell lymphoma, typically occurring in patients with pre-existing enteropathy. The most commonly involved sites of gastrointestinal lymphoma are the stomach (60-75%), followed by the small intestine (20-50%) and colorectum (4-6%) (2-5).

Patients with primary gastrointestinal lymphoma mainly present with non-specific symptoms, encompassing fever, diarrhea, hematochezia, unexplained weight loss or abdominal pain. Acute bowel perforation is a common complication. Cross-sectional imaging of T-cell lymphomas might reveal thickening of the luminal wall, mucosal ulcerations and nodularities closely resembling those observed in Crohn's disease and mucosa-associated lymphoid tissue lymphomas (MALTomas) (1). Morphological characteristics of gastric lymphoma lesions can be diverse, varying from a single or multiple ulcerative lesions, diffuse mucosal hyperemia and erosive lesions to a submucosal tumour or a mass (4). Typical endoscopic features of ulcerative colonic T-cell lymphoma are diffuse or segmental extensive mucosal ulcerations in the background of edematous mucosa, that can easily be confused with other disorders like Crohn's disease, intestinal tuberculosis or nonspecific colitis (8,9). Histology reveals a substantial infiltration of inflammatory cells, often posing additional difficulty in the identification of the subset of lymphoma cells. One of the characteristic features of ulcerative colon T-cell lymphoma is the increased count of

intraepithelial lymphocytes. However, this can also be found in collagenous colitis, microscopic colitis, Crohn's disease and celiac disease (8).

A primary T-cell lymphoma of the gastrointestinal tract has been reported in case reports (1-4,7,8). However, we report a case of a primarily gastrointestinal relapse of PTCL-NOS presenting with profuse diarrhea. To the best of our knowledge, this has not been reported previously.

In summary, our case illustrates the challenges in diagnosing a recurrence of a peripheral T-cell lymphoma in the gastrointestinal tract, due to the rarity of this entity and non-specific clinical presentation. Exhaustive workup with serologic testing, imaging, bone marrow biopsy and multiple endoscopies were initially unable to clearly identify the disease recurrence. Adequate biopsies and multidisciplinary discussions with the hematologists and pathologists were crucial in making the final diagnosis. Because of the challenging differential diagnosis based on clinical, endoscopic and histological presentation, close endoscopic surveillance and repetitive inspections may be of great importance. So, the possibility of a gastrointestinal lymphoma should always be kept in mind in patients with colonic ulcerative conditions.

Conflict of interest statement

The authors have no relevant conflicts of interest to declare.

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