Endoscopic diagnosis of a colonic localisation of a mantle cell lymphoma

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Abstract

Extra-nodal localisations of mantle cell lymphomas are most frequently found in the gastrointestinal tract. It is therefore important for an endoscopist to be familiar with the endoscopic image of a mantle cell lymphoma. In this case series of three patients with colonic involvement of mantle cell lymphoma, we discuss the endoscopic diagnosis. (Acta gastroenterol. belg., **2022,** 85, **632-634**).

Keywords: colonoscopy, gastrointestinal lymphoma, polypoid lesions.

Introduction

Hematological malignancies such as lymphomas can present throughout the entire gastrointestinal tract (1, 2). As a matter of fact, one of the most frequent extra-nodal presentations of mantle cell lymphomas particularly, is in this gastro-intestinal tract (3,4). The typical image on colonoscopy is that of a lymphoid polyposis. These polyps are most frequently visible in the ascending colon, followed by the ileum, stomach and duodenum. In the stomach not only polyposis-like images are encountered, but also gastritis and ulcerative lesions are seen with mantle cell lymphoma. The image of polyposis in the colon, should be differentiated from adenomatous polyposis and benign lymphoid hyperplasia (4-6).

Less than 10% of all non-Hodgkin lymphomas are mantle cell lymphomas. They are B-cell lymphomas which vary significantly from asymptomatic to very aggressive tumours (7). The median age at presentation is approximately 60 years and there is a 2:1 ratio for men (3,7,8). Despite the heterogeneity regarding the aggressiveness, few patients survive without an allogenic stem cell transplant (7,8) although the life expectancy can still be many years.

Almost all cases of mantle cell lymphoma are caused by a genetic mutation, i.e. a translocation t (11;14) (q13; q32), resulting in an overexpression of cyclin D1. However, the literature also describes other molecular abnormalities causing a cyclin D1 negative form of mantle cell lymphoma (3,4,7,8).

Mantle cell lymphomas are considered incurable unless patients receive an allogenic stem cell transplant. Nevertheless, maintenance therapy with rituximab can increase survival rate. In older patients this survival benefit is only observed after use of rituximab-cyclophosphamide, doxorubicine and vincristine (R-CHOP) induction therapy. Rituximab is given during 3 years after stem cell transplantation or chemo-immunotherapy in the elderly (3,7).

Case history

Case 1

73-year-old male, with weight loss. Medical history was unremarkable. Routine blood tests showed an important leucocytosis and slight anaemia. Flowcytometric examination showed a monoclonal B-cell population with an abnormal kappa-lambda ratio pointing towards an indolent non-Hodgkin lymphoma without further immunophenotyping. Given the minor complaints and lymph nodes < 5 mm on imaging, a watchful waiting policy was suggested. Two years later he complained of diarrhoea. Computed tomography (CT) scan of the abdomen showed an increase in size and number of lymph nodes and a thickening of the terminal ileum (Fig. 1 panel A). Colonoscopy was performed. Terminal ileum oedema and an aberrant mucosa were seen. Scattered across the transverse colon and throughout the rectum, multiple sessile polyps were encountered (Fig. 1 panel B). Microscopic analysis showed a colonic localisation of a mantle cell lymphoma. This patient showed a translocation t (11,14) as frequently encountered with this type of lymphoma. Considering the colonic presentation, we started treatment with rituximab- bendamustine (RBENDA) and rituximab maintenance. He received 6 dosages of R-BENDA with rituximab as maintenance therapy for 3 years. Follow-up of the colonic lesions was performed with colonoscopy two yearly. In the follow-up time, the lesions in the colon gradually decreased, with only an occasional polypoid lesion still present. Four years after diagnosis the patient remains in remission.

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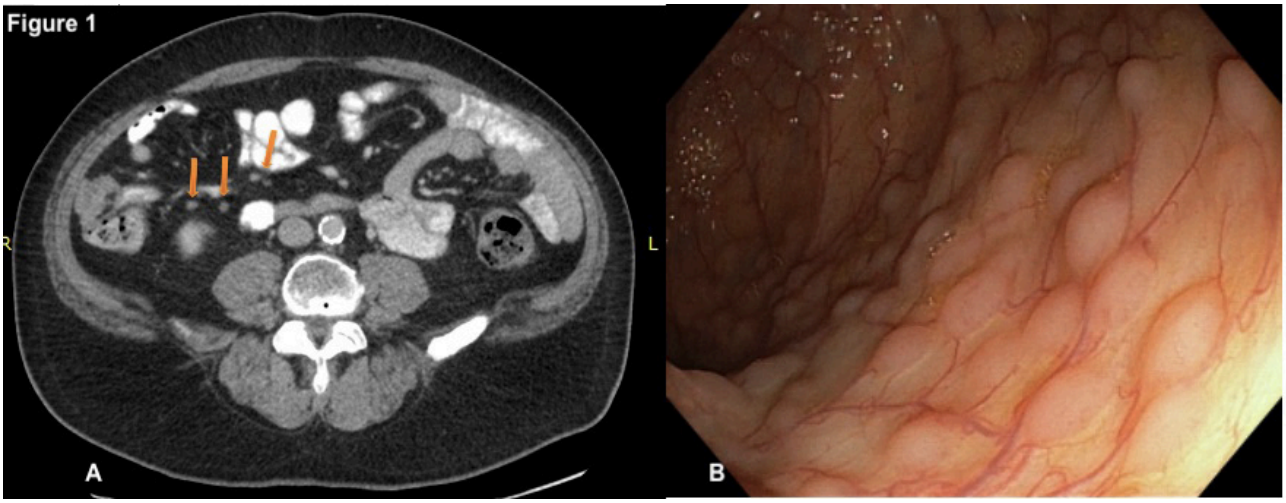

Figure 1. — Panel A (left): CT abdomen shows multiple lymph nodes increasing in size and number over time. Panel B (right): Colonoscopy shows diffuse polypoid lesions. Microscopic evaluation showed mantle cell lymphoma.

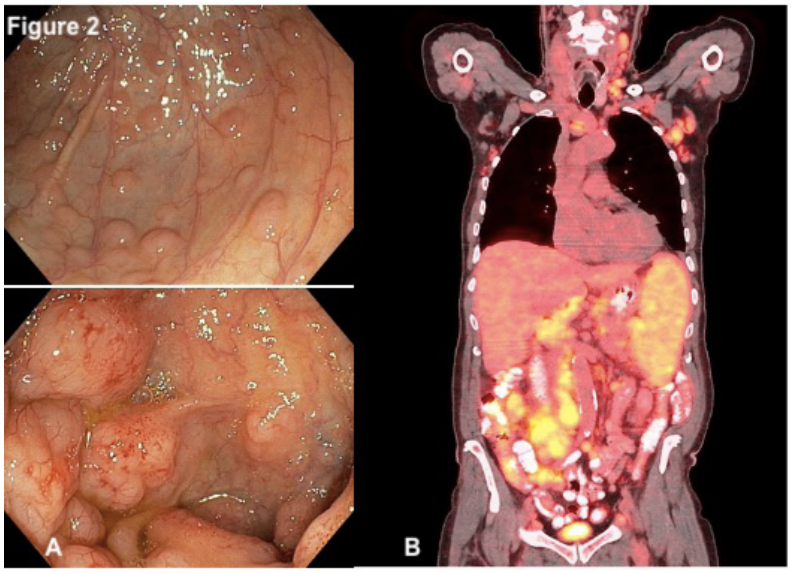

Figure 2. — Panel A (left): Multiple sessile polyps on colonoscopy turning out to be mantle cell lymphoma. Panel B (right): PET CT shows multiple adenopathies above and below the diaphragm with involvement of the colon and the spleen.

Case 2

The second patient had no complaints. In 2014 screening colonoscopy revealed 1 polyp which was resected. Surprisingly, microscopic examination showed an indolent non-Hodgkin lymphoma without clear subtype. Considering the absence of other abnormalities and the lack of symptoms, a watchful waiting policy was advised. Two years later he underwent a follow-up colonoscopy which showed a diffuse polyposis. No other abnormalities were revealed on clinical examination, most notably no adenopathies. Microscopic analysis showed a B cell non-Hodgkin lymphoma, suggestive for a mantle cell lymphoma. The lymphoma was staged as stage II. Treatment was started with RCVP, i.e., rituximab combined with cyclophosphamide, vincristine, and prednisolone. At the current time he has received eight cycles of this therapy and remains in remission.

Case 3

The third patient, an 85-year-old man with weight loss, constipation and fatigue since a couple of months. Colonoscopy was performed which showed diffuse polypoid lesions throughout the colon (see Fig. 2 panel A), macroscopically mimicking nodular lymphoid hyperplasia. Biopsies were taken, and a few polyps were resected for microscopic analysis.

Microscopic evaluation showed a lymphoid hyperplasia without evident germinative centres. Further characterization confirmed the diagnosis of a mantle cell lymphoma.

Positron emission tomography (PET)-CT was done for staging. This showed an advanced mantle cell lymphoma with adenopathies above and below the diaphragm with involvement of the colon and the spleen, leading to a stage IV disease (see Fig. 2 panel B). There

was a diffusely enhanced tracer uptake of the skeleton without focal bone lesions, possibly signifying bone marrow invasion. A discrete pleural effusion on the left was seen related to pleural involvement.

The patient has started a treatment with ibrutinib, a protein kinase inhibitor.

Discussion

The diagnosis of hematologic diseases based on colonoscopic findings is rather infrequent (9-11). Mantle cell lymphoma can affect the gastrointestinal tract as primary or secondary lymphoma, the latter primarily affecting the lymph nodes. Gastrointestinal involvement with secondary mantle cell lymphoma is seen in up to 90% of patients and they are often asymptomatic. Primary gastrointestinal MCL is even more rare with very aspecific symptoms. Most frequently described are abdominal pain, diarrhoea, abdominal masses, gastrointestinal blood loss, weight loss and fatigue (12).

As the colonic presentation of a mantle cell lymphoma can be the first and only presentation of this potentially lethal disease, endoscopists must be aware of this endoscopic image on colonoscopy. Classic alarm symptoms of weight loss, anorexia, night sweats etc. can be absent at first, making the endoscopic image the only clue which should not be ignored. It can present as a variety of lesions such as ulcerations, polyps, gastritis and submucosal lesions (6). The most frequently encountered form is that of multiple polyposis as described in our series. The most frequently involved sides are colon, small bowel, stomach and rectum. However, often the mucosa appears macroscopically normal.

Misinterpretation of this image as benign lymphoid hyperplasia is possible when the endoscopist is not familiar with the image of a colonic lymphoma. This could potentially lead to lack of biopsies and delay of the necessary therapy.

Endoscopists may also have a role to play in the staging. PET-CT scan is generally used. Current guidelines do not recommend standard endoscopy in the work-up of mantle cell lymphomas. In previous studies it was demonstrated however that PET-CT has a low sensitivity for gastro-intestinal involvement (13,14). Patients can however be asymptomatic and yet they seem to have a worse prognosis. Knowledge of involvement of the gastrointestinal tract is therefore clinically important. Up to 50% of patients have normal appearing mucosa (15). Therefore standard biopsies in the staging of a mantle cell lymphoma can be of added value.

Endoscopy can also contribute to early detection of recurrence (14). Small or microscopic lesions can develop in the gastro-intestinal tract as a first sign of progression. As stated above, the standard radiological techniques can often not detect these. Endoscopic follow-up therefore offers an opportunity to direct patients to early salvage treatment without delay.

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