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CASE REPORT

Transformation of jejunoileal follicular lymphoma into diffuse large B-cell lymphoma detected using double-balloon enteroscopy

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Accepted 21 June 2018

SUMMARY

Jejunoileal follicular lymphomas (FLs) are rare and have been reported to undergo histological transformation (HT). We report a case of jejunoileal FL transformation into diffuse large B-cell lymphoma (DLBCL). An 82-year-old woman presented with a 5.5 cm ulcerated jejunal mass, identified through double-balloon enteroscopy. The histopathology report revealed diffuse atypical lymphoid cells, which confirmed the presence of DLBCL. Neoplastic follicles confirmed the presence of FL. Genetic analysis revealed a match between the FL and DLBCL. Following a segmentectomy and chemotherapy, the patient is in remission. Based on this case, we should consider the possibility of jejunoileal FLs transforming into DLBCL.

BACKGROUND

In extranodal B-cell lymphoma, the gastrointestinal (GI) tract is the most frequently involved site.[1] In most cases of intestinal follicular lymphoma (FL), the lesions are located in the duodenum. However, jejunoileal FL is a rare entity, with an estimated frequency of 1%–3% among non-Hodgkin lymphomas (NHLs) of the GI tract.[2] It can be differentiated from other GI lymphomas such as mucosa-associated lymphoid tissue (MALT) lymphomas and high-grade lymphomas by its characteristic immunohistochemical pattern and genetic analysis. Compared with nodal FL, GI-FL were shown to be unique in that they had ongoing hypermutations as in nodal cases, but the mechanisms involved in the hypermutation were quite different.[3] GI-FL is usually localised and can be followed up without any therapy in most cases. There have been few reports of histological transformation (HT) of jejunoileal FL. We report the case of transformation of jejunoileal FL into diffuse large B-cell lymphoma (DLBCL) detected using double-balloon enteroscopy (DBE). The procedures followed were in accordance with the Declaration of Helsinki and the study was reviewed and approved by The National Hospital Organization Kure Medical Center and Chugoku Cancer Center and informed consent was obtained from the patient.

CASE PRESENTATION

An 82-year-old Japanese woman was experiencing nausea with vomiting after eating meals since a month. She had also experienced 4 kg weight loss in a month; she then visited our hospital. She had no significant medical history. She was conscious and had no fever. On physical examination, she exhibited tenderness in the abdomen without obvious rebound tenderness or guarding. Her bowel sounds were slightly decreased. CT revealed a 5.5 cm mass in the small intestine and swelling of the paraaortic and inguinal lymph nodes (LNs). Retrograde DBE showed multiple whitish nodules in the ileum. Furthermore, a follicular dendritic cell pattern was identified in the biopsy specimen obtained from the ileum. Inguinal LN and bone marrow biopsies also showed FLs. She exhibited no B symptoms. Peroral DBE revealed a large ulcerated mass in the jejunum (figure 1), and a follicular dendritic cell pattern was identified in the biopsy specimen. The patient was subsequently diagnosed with jejunum obstruction due to FL, and a jejunum segmentectomy was performed (figure 2). Histopathology showed that

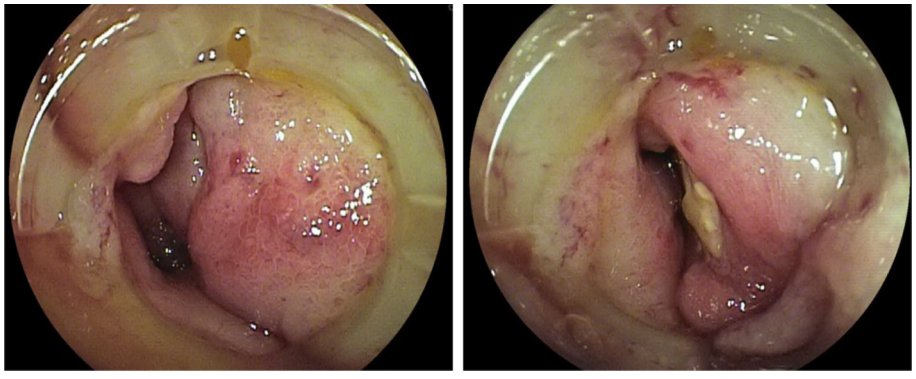

Figure 1 Peroral double-balloon enteroscopy shows stenosis due to a large ulcerated mass in the jejunum.

To cite: Nishimura T, Kuwai T, Imagawa H, *et al*. *BMJ Case Rep* Published Online First: [*please include* Day Month Year]. doi:10.1136/bcr-2018-224467

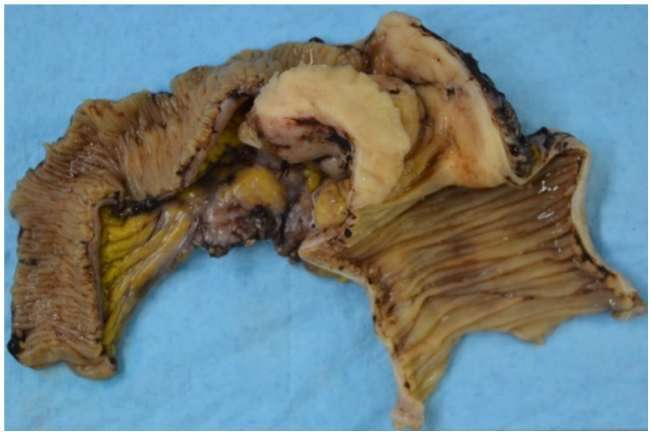

Figure 2 The resected jejunum tumour measured 60×50 mm.

60% of the tumour cells were composed of diffuse infiltrates consisting of large-sized atypical lymphoid cells, and neoplastic follicles were present elsewhere (figure 3). Immunohistochemical findings revealed the former was DLBCL, and the latter was FL. Tumour cells presented CD20+ (figure 4A), CD3- (figure 4B.), CD5- (figure 4C.), CD10+ (figure 4D), BCL2+ (figure 4E) and cyclin D1- (figure 4F) by immunohistochemistry and the Ki-67 labelling index was high (80.89%) (figure 4G.). At this point, the patient was diagnosed with DLBCL. PCR analysis showed that the clone of the inguinal LN FL was identical to the DLBCL tumour cell. Immunoglobulin heavy chain rearrangement peaks of both samples were detected at the same size (300 nt). The patient was diagnosed with DLBCL transformed from FL. The patient received postoperative rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone treatment.

DIFFERENTIAL DIAGNOSIS

Using DBE.

TREATMENT

A jejunum segmentectomy and postoperative chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone).

OUTCOME AND FOLLOW-UP

The LNs reduced remarkably, and no new lesions have emerged so far.

DISCUSSION

In this report, we have presented the case of jejunoileal FL that had transformed into DLBCL. Miyata-Takata *et al* recently reported on the case of DLBCL transformed from primary duodenal FL.[3] After that report, Kitabatake *et al* also reported the development of DLBCL from FL of the duodenum in endoscopic findings.[4] Although there are a few reports of cases transformed from duodenal FL, a case of transformed jejunoileal FL is rare. The reason why the jejunoileum is not usually evaluated in detail for a check-up if abdominal symptoms are absent is because of anatomical difficulties with diagnostic approaches to the jejunoileum. On the contrary, the GI tract is the most commonly involved extranodal site of NHLs. Compared with the prognosis of nodal FL, the prognosis of intestinal FL (including duodenal FL) is excellent. Intestinal FL shares characteristics with MALT lymphomas,[5] and patients with intestinal FL are usually managed using the watch-and-wait strategy, in resemblance to those with MALT lymphoma of the intestine. However, intestinal DLBCLs usually cause perforation and stenosis, which is suggestive of poor prognosis. Therefore, if it is possible for intestinal FL to transform to DLBCL, it needs to be detected as soon as possible and requires regular careful monitoring. In the present case, intestinal FL underwent severe stricture in the small intestine because it transformed from FL to DLBCL.

Examination of the small intestine is critical when NHL lesions are found in the GI tract because better therapies could be selected based on the findings. Capsule endoscopy (CE) and DBE can detect jejunoileal lesions of lymphoma, but biopsy samples can only be obtained using DBE. Due to advances in DBE, various types of malignant lymphomas of the small intestine have been observed at very early stages.[6] CT is also useful; however, it is difficult to monitor FL in its early stage using CT. Kodama *et al* recommended monitoring FLs as long as possible because of the risk of relapse.[7] Akiyama *et al* have reported a similar case involving the duodenum. They suggest that the life-time follow-up that is usually performed for patients with nodal FL should also be provided to patients with duodenal FL.[8] Even though jejunoileal lesions were

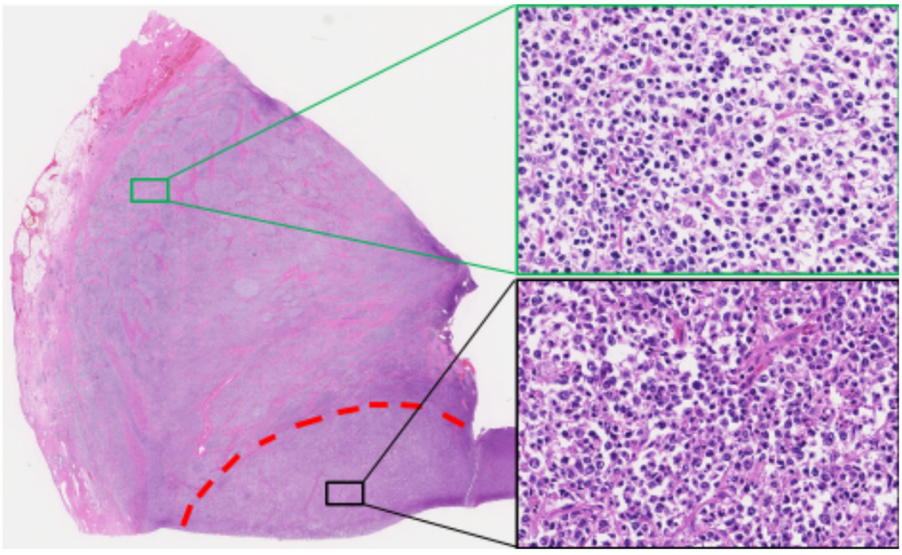

Figure 3 There were two tumour components: DLBCL (black square) and FL (green square). DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma.

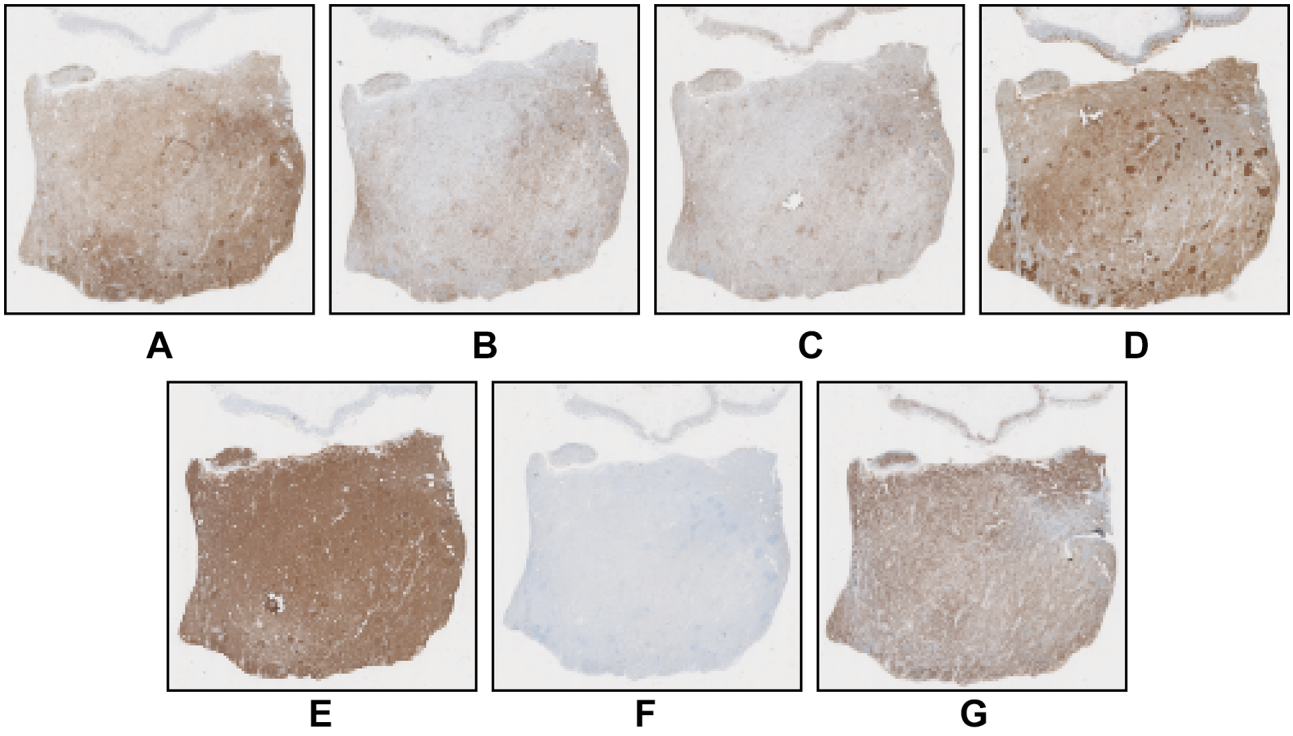

Figure 4 Immunohistochemistry revealed cells that were: (A) CD 20+, (B) CD3-, (C) CD5-, (D) CD10+, (E) BCL2+, (F) cyclin D1 and (G) Ki-67.

found in this case, we can assume that life-time follow-up would also be beneficial for our patient. Currently, there are insufficient data regarding optimal intervals for these examinations. However, El-Galaly *et al* have reported that the 10-year cumulative risk of FL HT was 22%.[9] Therefore, we recommend monitoring every 6 months at least. As DBE is widely used, the detection rate of jejunoileal FL has increased. The characteristic endoscopic appearance is a polypoid nodule.[10] On the contrary, DLBCL can cause ulcers, stenosis and perforation.[11] They require a completely different treatment strategy, so it is very important to confirm using DBE.

In summary, the final diagnosis of the present case was DLBCL that had transformed from jejunoileal FL. We have reported a case of HT from jejunoileal FL detected using DBE. There is no doubt that the clinical watch-and-wait strategy for intestinal FL without obstruction should be implemented. Furthermore, no matter how anatomically difficult diagnostic approaches may be, such as in the jejunoileum, they need to be followed up via DBE or CE regularly.

Learning points

- Jejunoileal follicular lymphoma (FL) transformation into diffuse large B-cell lymphoma may occur and therefore should be considered in patients with intestinal FL. The life-time follow-up that is usually performed for patients with nodal FL should also be provided to patients with intestinal FL.
- No matter how anatomically difficult diagnostic approaches may be, such as in the jejunoileum, intestinal FL need to be followed up via double-balloon enteroscopy or capsule endoscopy regularly.

Acknowledgements The authors thank Naoko Matsumoto for assistance in administrative support.

Contributors TK assessed the patient. TN and HI wrote the manuscript. HK critically reviewed the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Reminder of important clinical lesson