

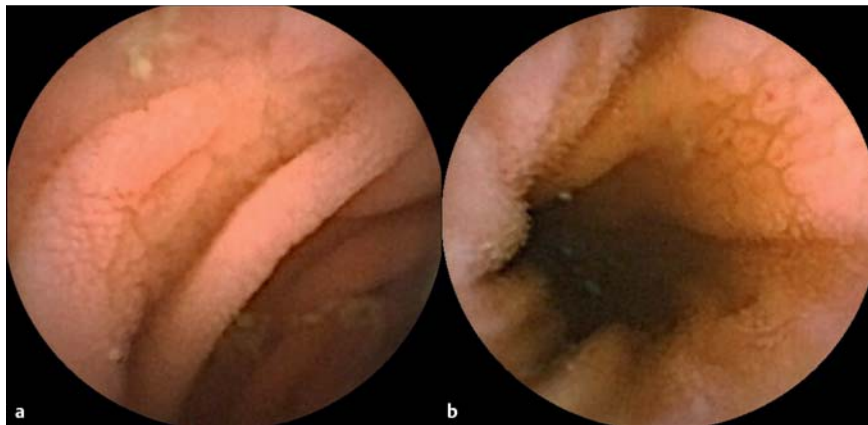
## Endoscopic findings of small-intestinal Epstein–Barr virus-associated T-cell lymphoproliferative disorder

A 71-year-old woman was admitted to our hospital in October 2009 with a 3-month history of severe diarrhea and weight loss of 5 kg with hypoalbuminemia. Computed

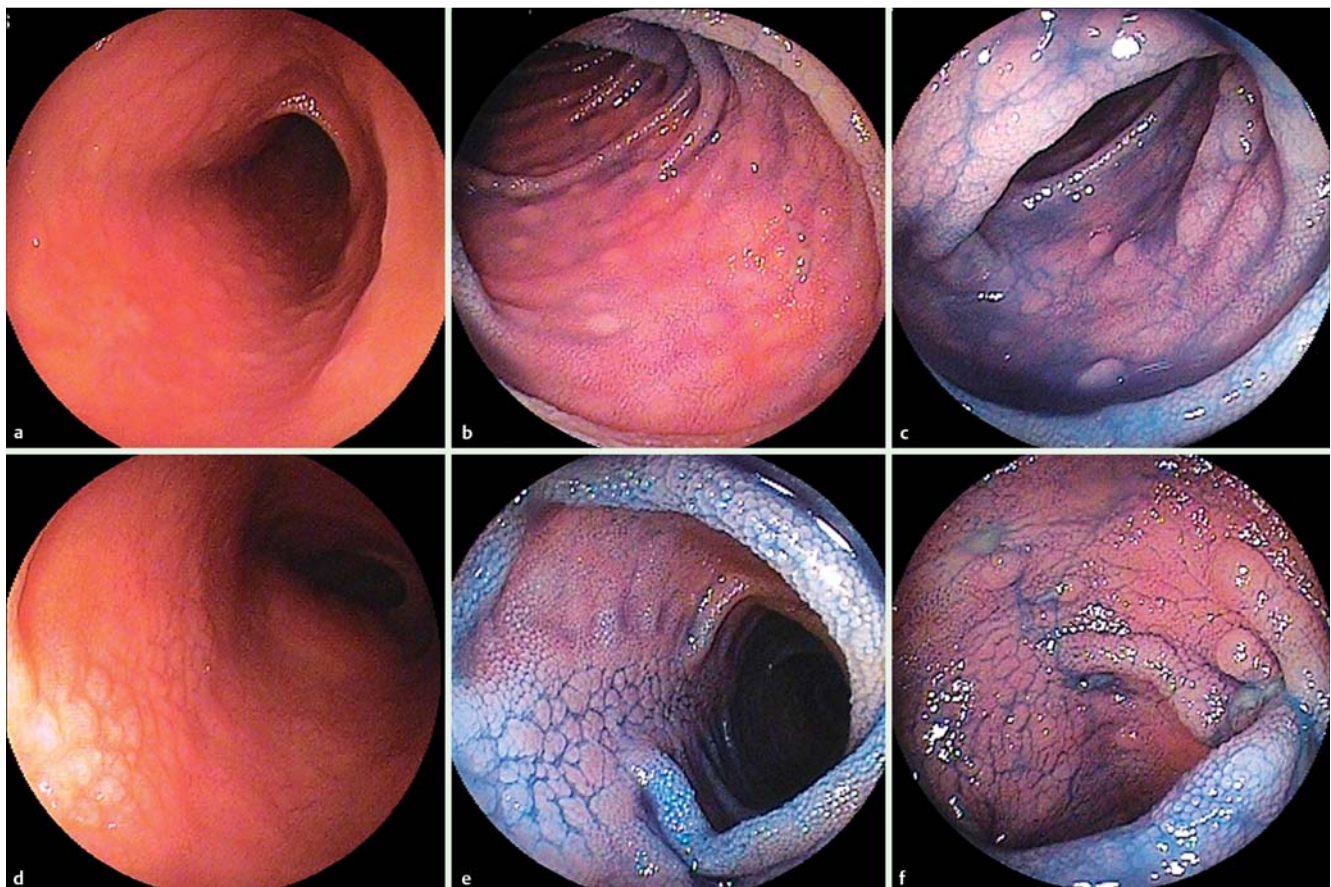
tomography showed diffusely thickened small-intestinal wall and intra-abdominal lymphadenopathy. Capsule endoscopy revealed flattened villi throughout the small

intestine (● Fig. 1). Double-balloon enteroscopy confirmed diffusely atrophic small-intestinal villi and clearly visible Peyer's patches (● Fig. 2). No neoplastic changes were observed on hematoxylin and eosin staining of the small-intestinal mucosa, but atrophic villous structures tentatively suggested celiac disease (● Fig. 3). Although blood tests indicated positivity for anti-gliadin antibodies, celiac disease was excluded as the patient's symptoms were not alleviated by being on a gluten-free diet for 1 month.

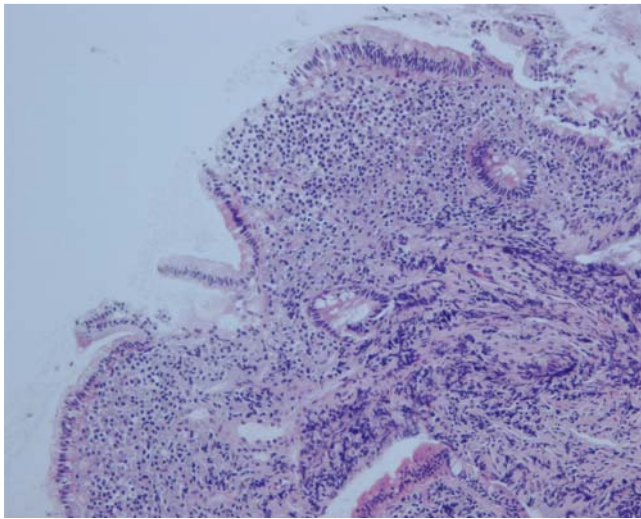
On the basis of suspected small-intestinal lymphoproliferative disorder we checked for Epstein–Barr virus (EBV) infection. High anti-EBV VCA-IgG and EA-IgG titers accompanied by a very high EBV-DNA load in the peripheral blood ( $6.3 \times 10^5$  copies/mL) suggested chronic active EBV infection. Southern blot analysis of EBV terminal repeats revealed monoclonal proliferation of the EBV-infected cells, which were shown by fluorescence-activated cell sorting (FACS) analysis to be CD4+T cells. EBV-encoded RNA in situ hybridization indicated a marked increase in the number of EBV-infected cells in the small-intestinal mucosa (● Fig. 4). Taken



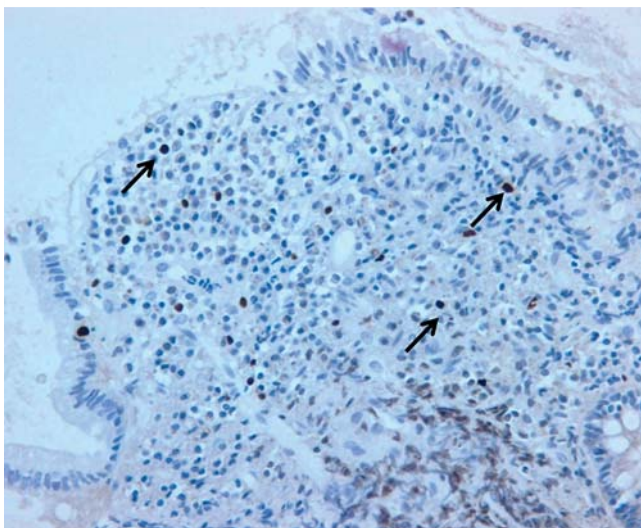
**Fig. 1** Capsule endoscopy findings in the small intestine. **a** Villous atrophy and flattening were found throughout the small intestine. **b** Red spots were observed in the lower small intestine.



**Fig. 2** **a–f** Double-balloon endoscopy findings in the small intestine. **a–c** Small-intestinal villi were diffusely flattened and atrophic. **d–f** Peyer's patches with swollen lymphoid follicles were clearly visible.



**Fig. 3** Small-intestinal mucosa; hematoxylin and eosin staining. Villous structures are tentatively suggestive of celiac disease. Many lymphocytes without neoplastic changes were seen beneath the epithelial layer.



**Fig. 4** In situ hybridization of the small-intestinal mucosa. Epstein–Barr virus (EBV)-encoded RNA in situ hybridization revealed a marked increase in the number of EBV-infected cells in the small-intestinal mucosa (arrows).

together, a final diagnosis of small-intestinal EBV-associated T-cell lymphoproliferative disorder was made. Despite sequential treatment with cyclosporine and CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone), the patient died in March 2010.

EBV-associated T-cell lymphoproliferative disorder is rare and has a poor prognosis, with a median survival of only a few months despite intensive chemotherapy [1,2]. In this case, proliferated B cells activated by EBV-infected CD4+T cells may have induced diffuse villous atrophy by damaging the small-intestinal mucosal structure, and yielded clearly visible small-intestinal Peyer's patches by increasing the volume of the lymphoid follicles. It is often difficult to differentiate small-intestinal lymphoproliferative dis-

orders from celiac disease, which also originates from activated T cells and often shows similar endoscopic findings [3–5]. This case suggested that to suspect EBV infection endoscopically followed by histological detection of EBV-encoded RNA is an efficient way to diagnose small-intestinal EBV-associated lymphoproliferative disorders.

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**Competing interests:** None

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#### Bibliography

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