Annals of Hematology (2019) 98:1501–1503
https://doi.org/10.1007/s00277-018-3543-y

LETTER TO THE EDITOR

Locally distributed multicentric plasmacytomas in the ileum secondary to lymphoma chemoimmunotherapy

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Received: 24 October 2018 / Accepted: 5 November 2018 / Published online: 8 November 2018

Dear Editor,

Extraosseous (extramedullary) plasmacytomas (EPs) are rare and typically solitary plasma cell neoplasms originating from extraosseous organs, commonly involving the mucous membranes of the upper air passages [1, 2]. We report a case of multicentric ileal EPs in a patient who had previously received chemoimmunotherapy for diffuse large B cell lymphoma (DLBCL).

A 69-year-old man with a history of DLBCL presented with intermittent diarrhea and appetite loss. He had received six cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone seven years ago, which resulted in complete remission. Laboratory tests showed an increased level of serum lactate dehydrogenase (986 U/L; reference range, 124–222 IU/L) and severely decreased levels of albumin (1.8 g/dL; 4.1–5.1 g/dL) and cholesterol (35 mg/dL; 142–248 mg/dL). Immunoelectrophoresis did not reveal monoclonal proteins in the serum and urine. Upper gastrointestinal endoscopy and colonoscopy showed normal findings. ^{18}F-fluorodeoxyglucose positron emission tomography with computed tomography did not detect abdominal lesions. Three weeks later, he presented with acute abdominal pain and underwent emergency surgery for small intestine perforations. Intraoperative findings showed a number of multicentric, whitish, flat tumors across the ileum, with two pinhole perforations at approximately 80 and 140 cm proximal to the ileocecal valve (Fig. 1a). Resection of the perforated segments with end-to-end anastomoses was performed. The resected specimen contained multiple tumorous lesions that were composed of monotonous sheets of medium-sized lymphoid cells (Fig. 1b, c). Some atypical cells resembled plasma cells. Immunohistochemical analysis revealed abnormal cells expressing CD56, MUM1/IRF4, and cytoplasmic kappa light chain (Fig. 1d–f). They were negative for CD19, CD10, and CD20. Flow cytometry analysis showed that the infiltrating cells were positive for CD38 and CD56, confirming the immunohistochemistry results. A diagnosis of EP was made. Southern blot analysis revealed rearrangement bands that differed in size from those in primary DLBCL. Polymerase chain reaction amplification of IgH VDJ [3] revealed distinct rearranged bands and junctional sequences (Fig. 1g, h). Bortezomib and dexamethasone treatment brought about resolution of clinical symptoms and normalization of serum albumin and cholesterol levels.

Locally distributed ileal multicentric plasmacytomas have not been reported. Since the majority of bile acids are reabsorbed from the ileum, extremely low levels of serum cholesterol might reflect massive involvement of the ileum with EP. A subset of normal plasma cell precursor cells resides in the ileum and locally expands within the lamina propria of the small intestine [4, 5]. We speculate that the oncogenic process occurred in the ileum-resident plasma cell precursor cells, which led to locally distributed multicentric plasmacytomas. In addition to the rarity, absence of specific laboratory, endoscopic, and radiological findings limited the establishment of preoperative diagnosis.

The presence of clonally unrelated B-lineage neoplasms raises the possibility that the patient's B-precursor cells were susceptible to transformation. Studies have reported an increased risk of therapy-related B cell lymphomas in patients

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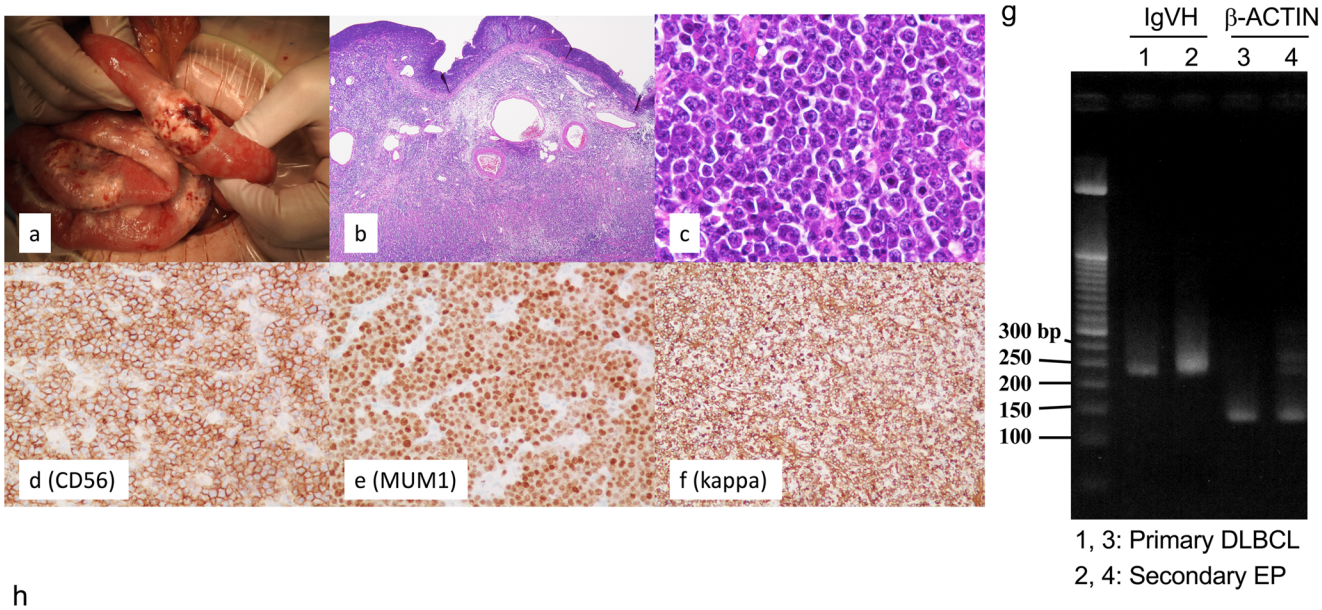

h

	V	N1	D	P	N2	J	
Primary DLBCL	V3-53 -TGTACG	TC	AGCAGTGTCTGGGAC		ATTTTCAAC	CTACTGG-	J4
Secondary EP	V3-7 -TGTGCGAGA	GT	GGGGAGAGCAGTGGCTGGTAC	G	GGGGCGTTT	AATTGGTTCGACCCCTGG-	J5

Fig. 1 **a**–**f** Extraosseous plasmacytomas of the ileum. **a** Intraoperative photograph demonstrating multiple extraosseous plasmacytomas (arrows) and a pinhole perforation (arrowhead) of the ileum. **b** Representative histological photograph of the resected ileal specimen. HE staining (×20) shows dense, diffuse infiltration of atypical lymphoid cells. **c** These lymphoid cells are medium-sized, showing strong nuclear atypia, and distinct nucleoli (HE, ×400). Some atypical cells display plasmacytoid features. The atypical lymphoid cells express CD56 (**d**), MUM1/IRF4 (**e**), and cytoplasmic kappa light chain (**f**). **g**, **h** PCR-based detection of a monoclonal IgH gene rearrangement shows different-sized monoclonal fragments (**g**) and junctional sequences (**h**) between tumors. DLBCL, diffuse large B cell lymphoma; EP, extraosseous plasmacytoma; HE, hematoxylin and eosin; PCR, polymerase chain reaction; IgH, immunoglobulin heavy chain

treated for Hodgkin lymphoma [6–8]. In chronic lymphocytic leukemia/small lymphocytic lymphoma, DLBCL developing in Richter's transformation has been clonally unrelated to preexisting clones in approximately 20% of cases [9, 10]. Non-DNA-damaging molecular therapeutic strategies that minimize second cancer risks may be attractive treatment options.

Funding This work was supported in part by grants from the Ministry of Education, Culture, Sports, Science, and Technology in Japan (17K09928 0001), the Yasuda Medical Foundation, the Foundation for Promotion of Cancer Research in Japan, the Project Mirai Cancer Research Grants, and Japan Leukaemia Research Fund.

Compliance with ethical standards

Written informed consent was obtained from the patients for publication.

Conflict of interest The authors declare that they have no conflict of interest.

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