Diffuse Large B-cell Lymphoma Arising Primarily at the Stoma After Bladder Reconstruction Using Ileal Conduit

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Abstract

A 76-year-old man suffered from swelling stoma for several weeks. A biopsy sample revealed the diffuse infiltration of large lymphoid cells which were positive for CD20, bcl-6, and MUM1. The patient was diagnosed with diffuse large B-cell lymphoma, with a non-germinal center B-cell pattern. A whole-body PET-CT scan revealed that the lymphoma was restricted to the stomal site. Bladder reconstruction was undertaken using the ileal conduit: this is the first reported case of lymphoma that developed primarily at the stoma. During the long-term maintenance after bladder reconstruction, clinicians should consider the possibility of lymphoma at the stomal site.

Key words: diffuse large B-cell lymphoma, stoma, bladder reconstruction

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Introduction

The gastrointestinal tract is one of the most frequent sites of lymphoma (1). As a surgical treatment for inflammatory bowel disease, the ileum is used to form a reservoir for stools or a stoma after colonectomy. Even under such circumstances, lymphomas can arise primarily in the ileal pouch or stoma (2-6). Concerning bladder reconstruction using an ileal conduit, this is the first reported case of lymphoma that developed primarily at the stoma. In this report, we collected case reports relevant to primary lymphoma at the stoma or ileal pouch for investigation of the characteristics.

Case Report

A 76-year-old man who suffered from a swollen stoma and experienced several episodes of bleeding was admitted to Matsuyama Red-Cross Hospital. He had a history of invasive bladder cancer, and had received curative cystectomy and bladder reconstruction using an ileal conduit in 1999. He had underlying chronic hepatitis C. He had neither a past history of inflammatory bowel disease nor medication of immunosuppressant. In 2011, the mucosal surface of the stoma was gradually enlarged over several weeks. The surface of the stoma became red without pain but it was still functioning. At presentation, examination confirmed that the stoma extended to 5 cm from the surface of the abdominal wall (Fig. 1). It was an elastic, hard tumor with a diameter of 6 cm. The ECOG performance status was score 0. The serum LDH level was 332 U/L (119-229), and the sIL-2R level was 382 U/mL. A whole-body positron emission tomography (PET)-CT scan revealed a hyper metabolic mass (diameter, 5 cm), restricted to the stomal site on the abdominal wall (Fig. 1B, C). A biopsied sample revealed that the background was intestinal epithelium without atypia of columnar cells, and large lymphoid cells infiltrated diffusely in the lamina propria surrounding the glandular ducts (Fig. 2A). The large lymphoid cells were positive for CD20, bcl-6, and MUM1 (Fig. 2B, C), while they were negative for CD10 and bcl-2 by immunological staining. The MIB-1-positive cells exceeded 90% of large lymphoid cells. Epstein-Barr virus (EBV)-encoded RNA 1 (EBER1) signals

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Figure 1. A photo of the stoma site shows that the stoma was markedly enlarged (A). Maximum-intensity projection PET (B) and a trans-axial PET/CT image (C) show localized 18F-FDG accumulation in the abdominal wall (arrows).

Figure 2. Morphologic and immunophenotypic features of the biopsied specimen of the stoma. (A) Hematoxylin and Eosin staining shows the diffuse proliferation of large lymphoid cells among the enteric gland structures (original magnification ×100). (B) The cell membranes of infiltrating large lymphoid cells are positive for CD20 (immunoperoxidase stain, original magnification ×200). (C) The large lymphoid cells are positive for bcl-6. (immunoperoxidase stain, original magnification ×200). (D) MUM1 staining predominantly highlights the nucleus of the large lymphoid cells (original magnification ×200).
were negative on RNA in situ hybridization. The patient was diagnosed with diffuse large B-cell lymphoma, with a non-germinal center B-cell (non-GCB) pattern. Bone marrow examination revealed no invasion of lymphoma cells. According to the international prognostic score of DLBCL, we scored the patient with 2 points (LDH level and age). After 6 courses of rituximab with cyclophosphamide, pirarubicin, vincristine and prednisolone (THP-COP), he achieved complete remission.

**Discussion**

Accumulated case reports from PubMed/Medline are summarized in Table 1. All patients were male. The affected sites tended to be localized. The intervals between surgical interventions and the diagnosis of lymphoma were decades in 4 of the 6 patients including the present patient. A B-cell phenotype was apparent using an immunohistological study. Notably, all of the reported patients had underlying inflammatory bowel disease. In general, the occurrence of lymphoma is sometimes associated with chronic inflammations (7). The long term use of azathioprine or 6-MP also contributes to the risk of lymphoma (8): one patient with EBV-positive lymphoma at the ileal pouch received 6-MP for decades (3). Another patient was infected with human immunodeficiency virus (6). Congenital or acquired immunodeficiencies are also likely to be complicated with lymphoma (9). Therefore, we speculate that the long-term inflammation or immunodeficiencies might be the background factor of these lymphomas.

Pathologically, the lymphoma cells in the present patient show overexpression of the MUM1 protein, which is a new factor of these lymphomas. Accumulated case reports from PubMed/Medline are summarized in Table 1. All patients were male. The affected sites tended to be localized. The intervals between surgical interventions and the diagnosis of lymphoma were decades in 4 of the 6 patients including the present patient. A B-cell phenotype was apparent using an immunohistological study. Notably, all of the reported patients had underlying inflammatory bowel disease. In general, the occurrence of lymphoma is sometimes associated with chronic inflammations (7). The long term use of azathioprine or 6-MP also contributes to the risk of lymphoma (8): one patient with EBV-positive lymphoma at the ileal pouch received 6-MP for decades (3). Another patient was infected with human immunodeficiency virus (6). Congenital or acquired immunodeficiencies are also likely to be complicated with lymphoma (9). Therefore, we speculate that the long-term inflammation or immunodeficiencies might be the background factor of these lymphomas.

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