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LETTER TO THE EDITOR

Successful treatment of monomorphic epitheliotropic intestinal T cell lymphoma with pralatrexate

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Dear Editor,

A 72-year-old male was admitted to our hospital because of ileum perforation, and emergency surgery was performed. He was diagnosed with type II enteropathy-associated T cell lymphoma (EATL; Fig. 1a–f); he underwent chemotherapy and achieved complete remission (CR). However, the lymphoma recurred with bowel obstruction after 21 months. Operative resection of the intestinal tumor and chemotherapy were performed, following which second CR was achieved.

However, 11 months later, the patient developed severe constipation. Laboratory investigations revealed elevated C-reactive protein (CRP, 11.9 mg/dl) and sIL-2R (1529 U/ml) levels. Computed tomography (CT) and ^{18}F-fluorodeoxyglucose-PET/CT (Fig. 1g–i) examination revealed lymphoma recurrence. Although chemotherapy was performed, the patient's general condition progressively exacerbated with persistent fever, consciousness disturbance, severe peripheral edema, ascites, and pleural effusion with performance status 4. A reduced dose (20 mg/m^2/week) of pralatrexate was administered for 2–3 weeks, followed by a gap of 1 week (3- or 4-week cycle) because of moderate renal insufficiency and thrombocytopenia, although usually pralatrexate is administered at 30 mg/m^2/week for 6 weeks, followed by a gap of 1 week (7-week cycle) [1]. After the initiation of pralatrexate therapy, the patient's general condition promptly improved with reduced CRP and sIL-2R levels. Currently, he is in the third CR (Fig. 1j) 9 months after the initiation of pralatrexate therapy and 52 months after diagnosis (Fig. 1k).

EATL is an aggressive intestinal lymphoma with very poor prognosis [2–6] compared with B cell intestinal lymphoma [7]. The standard treatment for EATL is yet to be established. Primary debulking resection followed by chemotherapy is usually performed owing to the high risk of perforation and/or occlusion. However, many patients relapse with very high mortality, and the median overall survival was found to be 7 months [2, 5].

In the present case, the first and second courses of anthracycline-containing chemotherapy were effective, and the patient remained in CR for 21 and 11 months, respectively. However, at the second relapse, his condition progressively worsened after receiving anthracycline-containing chemotherapy, which suggested a more aggressive course. Increased CRP level is a predictor of adverse survival outcome [4]. Although the patient's general condition was very poor, rapid improvement in his condition was observed with the administration of pralatrexate therapy. Pralatrexate may have anti-inflammatory effects by the reduction of some cytokines, similar to other folate antagonists like methotrexate, a known anchor drug for rheumatoid arthritis [8, 9].

EATL accounts for only 5.4% of peripheral T cell lymphomas (PTCL). Although type II EATL is a minor subtype in Western countries, it is predominant in Asia [5, 6]. Neoplastic cells are derived from intestinal intra-epithelial lymphocytes. They are heterogeneous, and approximately half of them exhibit the CD8$^+$CD56$^+$ cytotoxic phenotype [5]. According to the WHO classification (2017) [10], type II EATL was reclassified as monomorphic epitheliotropic intestinal T cell lymphoma (MEITL). Although new agents for relapsed/refractory PTCL have been made available in recent years, effective agents for refractory MEITL have not been reported. The present case demonstrates the possible rescue from aggressive MEITL by pralatrexate therapy. Further evidence for effective treatment of this rare lymphoma is desired.

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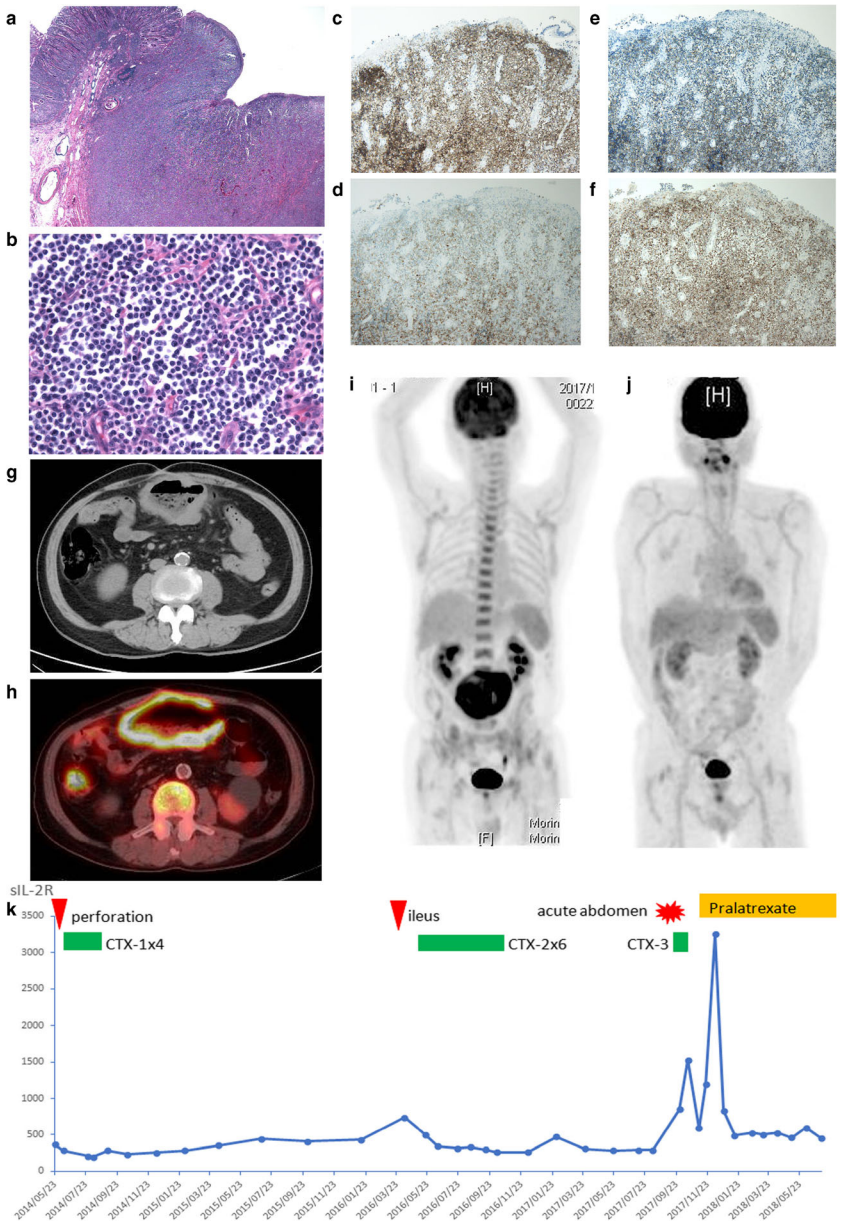

Fig. 1 Histological and immunohistochemical analysis of the tumor, imaging findings, and clinical course of the patient. **a**–**f** Histological and immunohistochemical examination of the resected ileum at the first admission. **a** Analysis of the intestinal mass exhibiting diffuse transmural infiltration of lymphoma cells (hematoxylin and eosin staining). **b** High-power view showing small- to medium-sized cells with clear cytoplasm. **c**–**f** Immunohistological examination showing positive reactivity for CD3 (**c**), CD8 (**d**), CD56 (**e**), and granzyme B (**f**). **g**–**j** Imaging examination. Computed tomography (CT; **g**) and ^{18}F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT (**h**, **i**) findings at the second relapse reveal irregular wall thickness and aneurysmal dilatation of the intestine with very strong accumulation of FDG [standardized uptake value $(SUV)_{max} = 11.7$] in the dilated intestinal wall. **j** The repetitive PET/CT findings reveal no abnormal findings, compatible with the third CR after the 20th administration of pralatrexate therapy (7 months after the initiation of pralatrexate therapy). **k** Clinical course of the patient. Administration of four courses of CHOP-like chemotherapy (CTX-1; 65 mg of doxorubicin hydrochloride, 1000 mg of cyclophosphamide, and 30 mg of prednisolone for 5 days) was followed by complete remission (CR). Twenty-one months later, the lymphoma recurred with bowel obstruction. Operative resection of the intestinal tumor and six courses of CHOP-like chemotherapy (CTX-2; 50 mg of pirarubicin, 1.0 mg of vincristine sulfate, 800 mg of cyclophosphamide, and 30 mg of prednisolone for 5 days) were performed, followed by second CR. However, 11 months later, the patient demonstrated second recurrence. CHOP-like chemotherapy (CTX-3; 65 mg of doxorubicin hydrochloride, 1000 mg of cyclophosphamide, and 30 mg of prednisolone for 5 days) was not effective. Subsequently, pralatrexate (20 mg/m^2) was administered on days 1 and 8 every 3 weeks or on days 1, 8, and 15 every 4 weeks. After the third administration of pralatrexate therapy, the patient's general condition showed rapid improvement with reduction in sIL-2R levels, and he achieved the third CR

Compliance with ethical standards

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

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