Abstract

Purpose MEITL is a very rare and highly aggressive peripheral T cell lymphoma with poor prognosis and for which there is no standard treatment. Treatment options for patients with relapsed/refractory disease are scarce and the choice of an appropriate rescue still represents an unmet need.

Methods Here, we report the case of a 65-year-old woman affected by MEITL, progressing after initial treatment with an anthracycline-based chemotherapy and surgery, who received single-agent PEG-asparaginase salvage therapy at our institution.

Results PEG-asparaginase single-agent rescue proved to be rapidly effective in controlling the disease and its associated paraneoplastic features. Nevertheless, toxicity was high and the patient died due to a treatment-related complication.

Conclusion The case we described brings new evidences on the effectiveness of PEG-asparaginase therapy in MEITL patients. Whether PEG-asparaginase should be included in the treatment course of MEITL patients could be the subject of future studies.

Keywords Monomorphic epitheliotropic intestinal T cell lymphoma · T cell lymphomas · Gastrointestinal lymphomas · Extranodal lymphomas · PEG-asparaginase

Introduction

Monomorphic epitheliotropic intestinal T cell lymphoma (MEITL), previously known as type II enteropathy-associated T cell lymphoma [1], is a very rare and highly aggressive peripheral T cell lymphoma (PTCL). Prognosis is poor, with most studies reporting a median overall survival of less than 1 year [2–9]. There is no standard treatment for MEITL, and the patients often undergo combination therapies that include surgery and an anthracycline-based chemotherapy, with ASCT consolidation, usually reserved for chemo-sensitive young and fit patients [3, 10–12]. Nevertheless, relapse or refractoriness rates are high and disease progression still represents the main cause of mortality, with few effective treatment options. Here, we report the case of a patient with progressive disease after initial treatment, who received single-agent pegylated asparaginase (PEG-asparaginase) salvage therapy at our institution.

Case presentation

A 65-year-old woman presented to her general practitioner with a 2-month history of mild abdominal pain, change in bowel habits, and unintentional weight loss. She reported no nausea, fever, night sweats, or fatigue. Her past medical history was unremarkable, except for past hepatitis B virus infection. She was not taking any medication at that time.
Abdominal examination revealed mild tenderness, without signs of peritonitis. Laboratory studies were significant for mild microcytic anemia and elevated erythrocyte sedimentation rate. Computed tomography (CT) scan of the abdomen revealed the presence of a 13-cm duodenojejunal mass infiltrating adjacent organs (i.e., intestinal loops, adipose tissue, anterior wall of the abdominal aorta) and was surrounded by many enlarged lymph nodes. An endoscopic biopsy was made. On microscopic examination, the mass was composed of monomorphic small lymphocytes positive for CD3, CD8, and CD56 consistent with a diagnosis of MEITL (Fig. 2). Staging positron emission tomography (PET) scan revealed increased uptake in multiple abdominal lymph nodes, hepatic flexure, ascending colon, and spleen. Bone marrow biopsy showed no signs of disease.

Surgical resection was not performed, due to the aortic wall infiltration. The patient received an anthracycline-containing regimen, inspired to the SNLG protocol [3], achieving partial remission, allowing surgical resection of the residual mass by laparotomy. She was then considered for autologous stem cell transplant (ASCT) consolidation. Bone marrow biopsy showed no signs of disease. However, when relapse became overt, the use of single-agent PEG-asparaginase salvage therapy resulted in a rapid control of the disease and its paraneoplastic features; nonetheless, death occurred due to a treatment-related complication.

In the present case, we favored the use of PEG-asparaginase over its native Escherichia coli formulation (L-asparaginase) or the Erwinia-derived preparation due to its longer half-life, decreased immunogenicity and convenience despite demonstrated similar safety profile and efficacy [14–16]. However, even though schedules of administration were comparable between our patient and the one reported by Gentille and colleagues (Gentille C., personal communication), toxicities were significantly higher in the case we reported, possibly due to poorer general conditions and the more advanced stage of the disease.

Discussion

To the best of our knowledge, this is the second case described in the literature on the use of PEG-asparaginase in relapsed/refractory MEITL, following the first case report by Gentille and colleagues [13]. Our patient received high doses of steroids that might have helped controlling the disease and its paraneoplastic manifestations, first. However, when relapse became overt, the use of single-agent PEG-asparaginase salvage therapy resulted in a rapid control of the disease and its paraneoplastic features; nonetheless, death occurred due to a treatment-related complication.
Indeed, the effectiveness of asparaginase therapy in MEITL has also been reported by Tse and colleagues [5], with no apparent differences of outcomes compared to anthracycline-containing regimens, albeit asparaginase was administered in combination with other chemotherapeutic agents and at an earlier treatment phase. Interestingly, a few studies reported similarities between MEITL and other entities that may share a γδ T cell origin, especially extranodal NK-/T cell lymphoma nasal-type (ENKTCL) [17–19], where guidelines already recommend asparaginase-containing regimens as standard of care [11, 20], and some authors even suggested that these regimens might challenge the role of anthracycline-based regimens in the future of MEITL [7].

It is worth noting that few data on alternative therapies for relapsed/refractory MEITL have been published to date. Although novel agents have emerged in recent years for relapsed/refractory PTCL, data on their effectiveness in MEITL are still lacking. A few authors reported the use of pralatrexate and temozolomide, with favorable outcomes [21, 22] (Table 1). More recently, the Singapore Lymphoma Study Group has published pre-clinical data on the effectiveness of combination treatment with romidepsin and pimozide [23], but whether this treatment can translate into clinical benefit is still unknown.

In conclusion, treatment options for relapsed/refractory MEITL are scarce, and the choice of an appropriate...
rescue for patients with progressive disease still represents an unmet need. The present case adds to the list of studies reporting the effectiveness of asparaginase therapy in MEITL patients. Whether PEG-asparaginase should be included in the treatment course of MEITL and, possibly, considered during earlier treatment phases, is still unknown and should be tested in future studies.

**Author contribution** EB, SP, RG, LR, MM, LP, RM, LM, and GL treated the patient and wrote the manuscript. All the authors approved the manuscript.

**Declarations**

**Ethics approval** This study was conducted in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Consent to participate** The patient’s family provided informed consent for participation.

**Consent for publication** The patient’s family provided informed consent for publishing.

**Conflict of interest** The authors declare no competing interests.

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