

[CASE REPORT]

Monomorphic Epitheliotropic Intestinal T-cell Lymphoma Involving the Lung and Brain: A Rare Case Study

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Abstract:

Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) is a primary intestinal T-cell lymphoma and other organ involvement is very rare. A rare case of MEITL involving the lung and brain is herein reported. The patient developed panperitonitis with a small intestinal perforation, and emergency surgery was performed. The pathological findings from the surgical specimens demonstrated atypical lymphoid cells which were positive for CD3, CD8, and CD56. Moreover, the pathological findings of lung specimens taken by bronchoscopy were consistent with those of the small intestine. It is therefore important to include the possibility of MEITL in the differential diagnosis of cancer patients.

Key words: monomorphic epitheliotropic intestinal T-cell lymphoma, lung, brain, metastasis, lactate dehydrogenase

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Introduction

Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), previously subclassified as enteropathy-associated T-cell lymphoma (EATL) type 2, is a rare primarily gastrointestinal type of peripheral T-cell lymphoma (1). The clinical course of MEITL is very aggressive, and its prognosis is generally poor (2). Most MEITL lesions involve the small intestine, and the involvement of other organs, such as the lung, brain, skin, and soft tissue, is very rare (2). A previous study reported cases of MEITL/EATL in which the serum lactate dehydrogenase (LDH) level was not elevated (2).

No case of MEITL involving the lung and brain has been previously reported. We herein report a very rare case of MEITL with lung and brain lesions not accompanied with an elevated serum LDH level. The current report calls atten-

tion to the importance of an early diagnosis of MEITL.

Case Report

A 74-year-old man was admitted to our hospital due to an acute onset of left hemiparesis. He had also complained of diarrhea over the previous 3 months. However, lower gastrointestinal endoscopy performed 3 months before admission revealed no abnormal findings. He had a past history of smoking, with 81 pack-years. There was no known history of allergy, brain, respiratory or digestive disorders. There were no crackles on auscultation with oxygen saturation of 95% on room air, no fever, and no abdominal pain despite the patient's diarrhea. A neurological examination showed mild left hemiparesis and aphasia.

As shown in the Table, laboratory examinations demonstrated a white blood cell count of 14,800/ μ L without atypi-

Table. Laboratory Data on Admission.

Hematology		Blood chemistry		Immunologic test	
White blood cell	14,800 / μ L	Total protein	5.8 g/dL	IgG	1,387 mg/dL
Neutrophils	77 %	Albumin	2.3 g/dL	IgA	312 mg/dL
Lymphocytes	10 %	AST	18 U/L	IgM	41 mg/dL
Monocytes	11 %	ALT	18 U/L	ANA	\times 640
Eosinophil	1 %	LDH	134 U/L	anti-ds-DNA IgG	0.7 IU/mL
Red blood cell	391 $\times 10^4$ / μ L	ALP	257 U/L	anti-U1-RNP	<5.0 U/mL
Hemoglobin	12.2 g/dL	Total bilirubin	0.7 mg/dL	anti-Sm	0.9 U/mL
Hematocrit	37.1 %	BUN	12 mg/dL	anti-SSA	<0.5 U/mL
Platelet	44.9 $\times 10^4$ / μ L	Creatinine	0.58 mg/dL	anti-SSB	<0.5 U/mL
Coagulation test		Na	130 mEq/L	anti-Scl70	<0.5 U/mL
PT	83.9 s	K	4.4 mEq/L	anti-Jo1	<0.5 U/mL
PT-INR	1.06	Cl	97 mEq/L	MPO-ANCA	<1.0 U/mL
APTT	27 s	CRP	2.51 mg/dL	PR3-ANCA	<1.0 U/mL
Fibrinogen	92 mg/dL	s-IL2R	4,680 U/mL		
FDP	6.4 μ g/mL	Biological test			
D-dimer	2.0 μ g/mL	β -D glucan	<6.0 pg/mL		
		Aspergillus antigen	0.7		
		T-SPOT (IGRAs)	(-)		

PT: prothrombin time, PT-INR: prothrombin time-international normalized ratio, APTT: activated partial thromboplastin time, FDP: fibrinogen degradation products, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, BUN: blood urea nitrogen, CRP: C-reactive protein, s-IL2R: soluble interleukin-2 receptor, IGRAs: interferon-gamma release assays, ANA: antinuclear antibody, anti-dsDNA IgG: anti-double-stranded DNA IgG antibody, MPO-ANCA: myeloperoxidase-anti neutrophil cytoplasmic antibody, PR3-ANCA: proteinase 3-anti neutrophil cytoplasmic antibody

cal lymphocytes, and elevated soluble interleukin-2 receptor (s-IL2R) of 4,680 U/mL (normal range, <466 U/mL) and C-reactive protein (CRP) of 2.51 mg/dL (normal range, <0.3 mg/dL), slightly decreased hemoglobin of 12.2 g/dL, normal LDH of 134 U/L (normal range, 119-229 U/L), and a normal serum β -D glucan level. Serum Aspergillus antigen was 0.7 (normal range, <0.5), and T-SPOT, which are interferon-gamma release assays (IGRAs), was negative. Antinuclear antibody was positive (640-fold with a centromere pattern), but no other autoantibodies were detected. Gadolinium-enhanced magnetic resonance imaging (MRI) of the brain showed a ring-enhanced lesion and edema in the right cerebral hemisphere (Fig. 1A). Whole body contrast CT demonstrated multiple nodules with cavitation and thick-walled cysts in the bilateral lungs and a mass in the pelvic cavity Fig. 1B-C. There was right hilar lymphadenopathy without calcification. Positron emission tomography (PET)-MRI revealed high 18 F-fluorodeoxyglucose (FDG) accumulation in the right cerebral hemisphere [standard uptake value (SUV) maximum of 8.3], bilateral lungs (SUV maximum of 11), mediastinal lymph nodes (SUV maximum of 8.6) and pelvic cavity (SUV maximum of 12.9) (Fig. 1D-F).

Bronchoscopy for the right lower lobe lesion was conducted. However, no malignancy or vasculitis was found. A culture of bronchial washing specimens revealed no microorganisms, including fungi or tuberculosis. In addition, upper gastrointestinal endoscopy revealed no specific findings suggestive of a definite diagnosis. At this point, we planned to perform lower gastrointestinal endoscopy, but the patient suddenly developed panperitonitis with an intestinal perfora-

tion, and emergency surgery instead had to be performed. During surgery, intraoperative exploration revealed a pelvic abscess which adhered to the small intestine, and a small intestine dilatation on the oral side. The patient was considered to have a pelvic abscess and panperitonitis due to the small intestinal perforation. Approximately 60 cm of the small intestine, including the perforated site, was removed, and sigmoid colostomy was performed.

A histopathological examination of the resected small intestine demonstrated the infiltration of monomorphic medium-sized atypical lymphocytes in the superficial layer of the mucous membrane (Fig. 2A). Immunohistochemically, the atypical lymphoid cells were positive for CD3, CD8, CD56, TIA-1, and were negative for CD4, CD5, CD20, TCR β (Fig. 2B-I). The atypical lymphoid cells were negative for Epstein-Barr virus-encoded small RNA *in situ* hybridization (EBER-ISH), which indicated that our case was different from extranodal NK/T-cell lymphoma, nasal type. Therefore, we re-evaluated the pathology of the lung lesion previously taken by bronchoscopy. As a result, a histopathological examination of the lung lesion revealed the interstitial infiltration of medium-sized atypical lymphoid cells (Fig. 3A), and an immunohistochemical examination also revealed that the lesion was positive for CD3, CD8, CD56, and negative for CD20 (Fig. 3B-E). Finally, based on the abovementioned findings, we made a diagnosis of MEITL of the small intestine, involving the lung and brain.

Unfortunately, the patient could not undergo chemotherapy due to his poor performance status, and he was transferred to our outpatient clinic for palliative care.

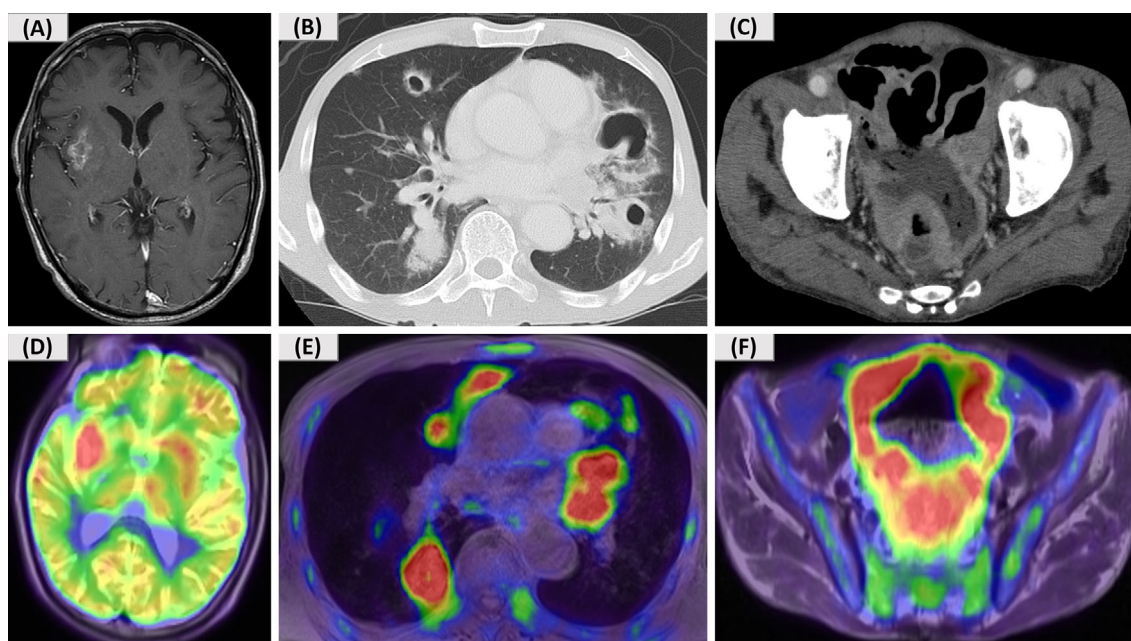


Figure 1. Gadolinium-enhanced -brain MRI, whole body contrast CT scans and trans-axial PET-MRI images. (A) Brain MRI showed a ring-enhanced lesion and edema in the right cerebral hemisphere. (B, C) Whole body contrast CT demonstrated multiple cavities and thick-walled cysts in the bilateral lungs, and a mass in the pelvic cavity. (D, E, F) PET-MRI revealed high FDG accumulation in the right cerebral hemisphere, bilateral lungs, mediastinal lymph nodes and pelvic cavity. MRI: magnetic resonance imaging, CT: computed tomography, PET-MRI: positron emission tomography-magnetic resonance imaging, FDG: ^{18}F -fluorodeoxyglucose

Discussion

To the best of our knowledge, to date there has been no report describing MEITL of the small intestine involving the lung and brain.

MEITL is a primary T-cell lymphoma derived from intestinal epithelial T-cells. Previously, primary intestinal T-cell lymphomas were divided mainly into two types according to the World Health Organization (WHO) 2008 classification; EATL type 1, which is associated with celiac disease, and EATL type 2, which is not associated with enteropathy. These disease names were changed in the WHO 2016 revised classification; EATL type 1 to EATL and EATL type 2 to MEILT (1). MEITL and EATL are rare, with an incidence of 0.25% of all malignant lymphomas and <5% of all digestive tract malignant lymphomas (2, 3). MEITL is usually positive for CD3, CD8 and CD56, but negative for CD 30, CD103, with small to medium-sized cells (1, 4).

Delabie et al. reported that the small intestine was the most commonly involved site (90% of cases) in EATL and MEITL patients (2). In their study, a total of 62 cases of EATL and MEITL were evaluated, with only three cases involving the lung (5%). Furthermore, to the best of our knowledge, no cases involving both the lung and the brain have yet been reported.

The most common primary non-Hodgkin lymphoma in the lung is marginal zone B-cell lymphoma of mucosa-

associated lymphoid tissue type, and primary T-cell lymphoma in the lung is rare (5). A previous study reported that pulmonary manifestations of non-Hodgkin lymphoma are multiple, such as nodules, consolidation, ground-glass opacities, and cavitation (6). MEITL is often associated with necrosis (7). To date, there has only been one report of a case of MEITL (EATL type 2) involving the lung, in which chest CT demonstrated multiple nodules without cavitation (8). In the present case, the chest CT findings demonstrated multiple nodules with cavitation in the bilateral lungs, which were compatible with lymphoma, and suggested necrotic lesions.

The diagnostic yield of bronchoscopy for malignant lymphoma with pulmonary lesions has been reported to be about 30% (9). In the present case, MEITL in the lung was confirmed using the bronchoscopy specimens, although we initially regarded the lesion as having no atypical lymphocytic infiltration. One of the reasons for this was due to the fact that the bronchoscopy specimens showed few lymphocytes.

MEITL is frequently complicated with intestinal perforations (10), which is what occurred in the present case. The prognosis of MEITL is generally poor. A previous study reported the median progression free survival of patients with MEITL/EATL to be 3 months, and the median overall survival is 7 months (11). One of the reasons for the late diagnosis of MEITL in the present case is probably mainly due to tumor development in the small intestine (2). Although

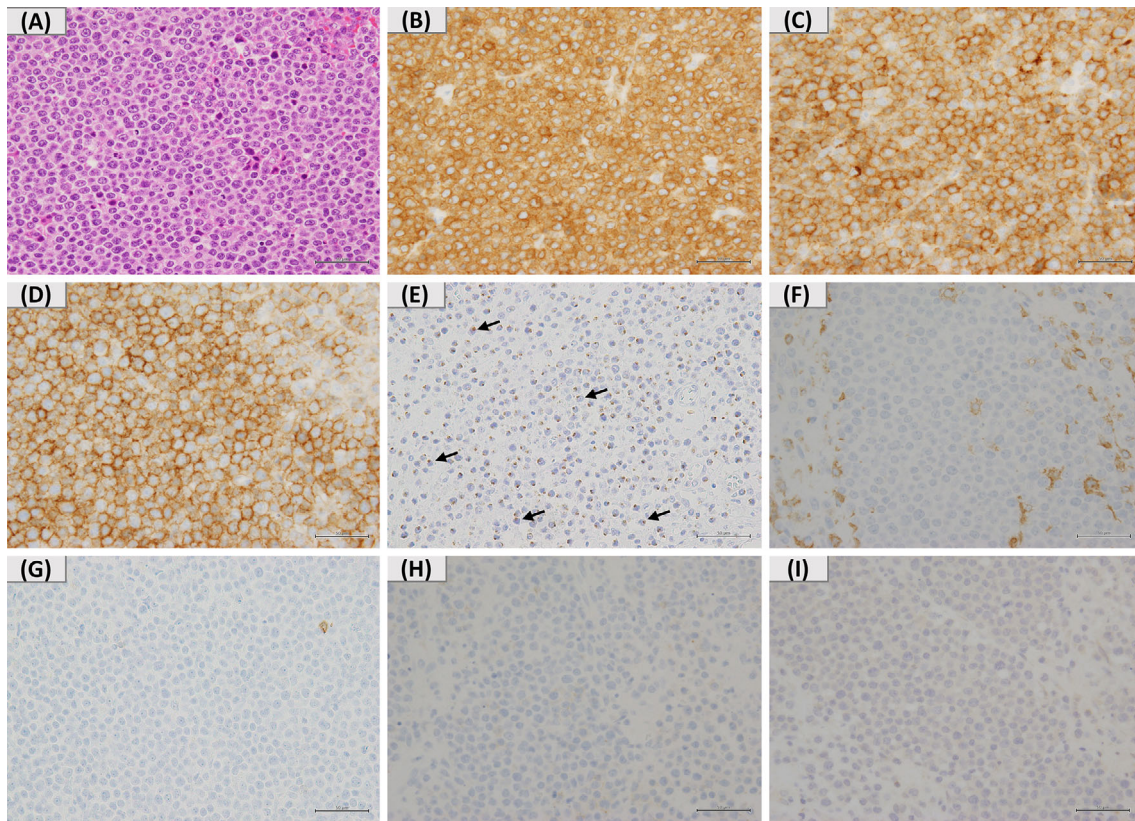


Figure 2. Histological and immunohistochemical findings obtained from the small intestine during surgery. (A) Microscopic evaluation following Hematoxylin and Eosin staining of the tumor tissue revealed the infiltration of monomorphic medium-sized atypical lymphocytes monomorphic in the superficial layer of the mucous membrane. (B, C, D) IHC examination revealed positive CD3, CD8 and CD56 expression, respectively, in the small intestine tumor. (E) Some of the cells show TIA-1 in their cytoplasm (arrows). (F, G, H, I) IHC examination revealed negative CD4, CD5, CD20 and TCR β expression, respectively in the small intestine tumor. All scale bars=50 μ m. IHC: immunohistochemical

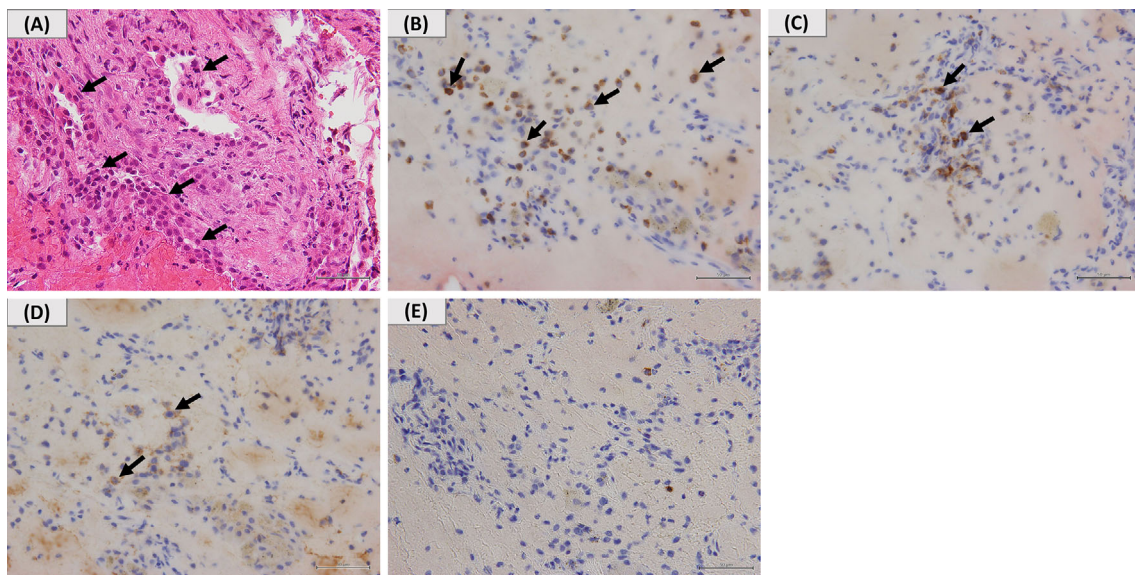


Figure 3. Histological and immunohistochemical findings obtained from bronchoscopy. (A) A microscopic evaluation following Hematoxylin and Eosin staining of the tissue revealed interstitial infiltration of medium-sized atypical lymphoid cells (arrows). (B, C, D) IHC examination revealed positive CD3, CD8 and CD56 expression, respectively in the interstitium of lung tissue (arrows). (E) An IHC examination revealed a negative CD20 expression in the interstitium of lung tissue. All scale bars=50 μ m. IHC: immunohistochemical

there were no abnormal findings of the large intestine in lower gastrointestinal endoscopy at 3 months before admission, the tumor of the small intestine may have already been present. Since the clinical course of MEITL is very aggressive, it is important to consider the possibility of MEITL from the viewpoint of symptoms, radiological findings and laboratory data. An early diagnosis of MEITL may contribute to the prevention of perforation and implementation of successful chemotherapy.

A previous study reported that elevated serum LDH and CRP levels are risk factors associated with a worse overall survival and failure-free survival in MEITL/EATL patients (2). High serum LDH and CRP levels may reflect a high tumor burden and extensive tissue damage, which may explain the adverse prognosis. The above-mentioned study demonstrated that 65% (37/57) of MEITL/EATL cases did not have an elevated LDH level (2). In the current case, laboratory examinations showed a slightly elevated CRP and normal LDH at admission to our hospital, in spite of widespread lesions including lung and brain metastasis. Consequently, the possibility of malignant lymphoma including MEITL and the high risk of intestinal perforation should be considered, even in cases with low serum LDH and CRP levels.

In conclusion, we herein described a case of MEITL involving the lung and brain. The radiographic findings of multiple nodules with cavitation in the lung may warrant consideration of a diagnosis of malignant lymphoma including MEITL. We should pay particular attention to the possibility of MEITL from the viewpoint of radiological findings and make an effort to diagnose this as soon as possible.

The authors state that they have no Conflict of Interest (COI).

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