CASE REPORT

Nagoya J. Med. Sci. **84**. 470–476, 2022
doi:10.18999/nagjms.84.2.470

Mantle cell lymphoma with aseptic meningitis mimicking hydrocephalus on brain imaging

Satoshi Samizo[1], Katsuya Furukawa[2] and Hiroyuki Umegaki[3]

[1]*Department of Community Healthcare and Geriatrics, Nagoya University Hospital, Nagoya, Japan*
[2]*Department of Hematology, Nagoya University Hospital, Nagoya, Japan*
[3]*Department of Community Healthcare and Geriatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan*

ABSTRACT

An 83-year-old man underwent head computed tomography (CT) to investigate cognitive decline and gait disturbance and was admitted to undergo a cerebrospinal fluid (CSF) tap test for suspected idiopathic normal-pressure hydrocephalus. He had a history of chemotherapy for mantle cell lymphoma (MCL), but CT on admission showed no evidence of recurrence. After admission, his level of consciousness rapidly deteriorated and CSF examination suggested infiltration of MCL into the central nervous system (CNS). Although CNS involvement in MCL is rare, this case demonstrates that even if recurrence of MCL is not suspected based on CT findings.

Keywords: mantle cell lymphoma, hydrocephalus, aseptic meningitis, meningeal infiltration, dementia

INTRODUCTION

Mantle cell lymphoma (MCL) is a malignant non-Hodgkin's lymphoma derived from B cell lymphocytes in the mantle zone of lymphoid follicles. It is an independent disease entity with immunohistology characterized by CD5, cyclin D1, and SOX11 positivity and molecular genetics characterized by a BCL-1 (CCND1) gene rearrangement associated with chromosomal translocation t(11; 14) (q13; q32). In older patients, chemo-immunotherapy followed by maintenance rituximab is the current standard of care. Initial therapy can be deferred in the patients who present with the more indolent course without adversely affecting survival.[1] MCL often involves extranodal organs, particularly the bone marrow and gastrointestinal tract, but central nervous system (CNS) involvement occurs in only around 5% patients with MCL.[2]

Idiopathic normal-pressure hydrocephalus (NPH) is a condition caused by impaired cerebrospinal fluid absorption with primary symptoms of gait disturbance, cognitive impairment, and urinary incontinence in the absence of preceding diseases such as subarachnoid hemorrhage

Received: July 28, 2021; accepted: August 24, 2021
Corresponding Author: Satoshi Samizo, MD
Department of Community Healthcare and Geriatrics, Nagoya University Hospital, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8560, Japan
Tel: +81-52-744-2364, Fax: +81-52-744-2371, E-mail: s.samizo@med.nagoya-u.ac.jp

and meningitis. In Japan, the prevalence of idiopathic NPH is estimated to be 0.2%–3.7%, its incidence is estimated to be about 1.2/1000 per year, and it is a relatively common disease in older adults.[3,4] Computed tomography (CT) and magnetic resonance imaging (MRI) show enlargement of the ventricles, and the Evans Index (ie, the ratio of the maximum width of the frontal horns of the lateral ventricle to the maximal internal diameter of the skull at the same level) is usually used for assessing ventricular enlargement. According to Japanese guidelines,[4] NPH patients usually have an Evans index of ≥0.3, but the value is <0.3 in a small number of patients. The subarachnoid space expands at the Sylvian fissure and below and narrows at the area of high convexity. At least 80% of patients with properly diagnosed NPH show clinical improvement after ventricular shunt placement. The standard diagnostic procedure is the tap test, in which motor and cognitive evaluations are performed after cerebrospinal fluid (CSF) drainage by large-volume lumbar puncture or placement of an external lumbar drain. Improvement after drainage of a large volume of CSF (30–50 mL) by lumbar puncture has a high positive predictive value for improvement after ventriculoperitoneal shunting.[5]

We present a case in which aseptic meningitis due to meningeal infiltration of MCL found on analysis of CSF collected in a tap test for suspected NPH.

CASE PRESENTATION

An 83-year-old man had been diagnosed with MCL in December 2013 in the Department of Hematology and Oncology at our hospital. The primary lesion was the colon, the lesion was widespread in the mesenteric lymph nodes and colon, and staging was stage IV. He was treated with R-CHOP, with the last dose administered in May 2014. After treatment, he was followed up with observation due to the indolent course. However, in February 2019, fluorodeoxyglucose positron emission tomography (PET) showed extensive lesions in the terminal ileum (Fig. 1), and tumor cells appeared in the peripheral blood. Therefore, treatment with ibrutinib was started in March 2019 by hematologists. A PET-CT scan in January 2021 showed accumulation in the spleen and systemic lymph nodes, but the lesions in the terminal ileum had disappeared (Fig. 2). Combination therapy with bendamustine plus rituximab (BR) was started in January 2021, but drug eruptions and cognitive decline occurred after the second administration of bendamustine

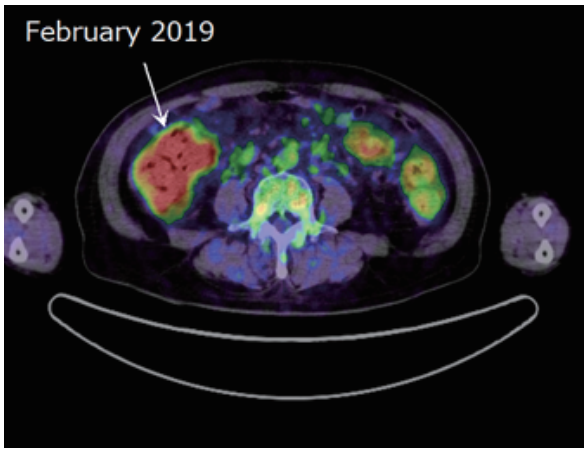

Fig. 1 Fluorodeoxyglucose positron emission tomography showing extensive lesions (arrow) in the colon in February 2019

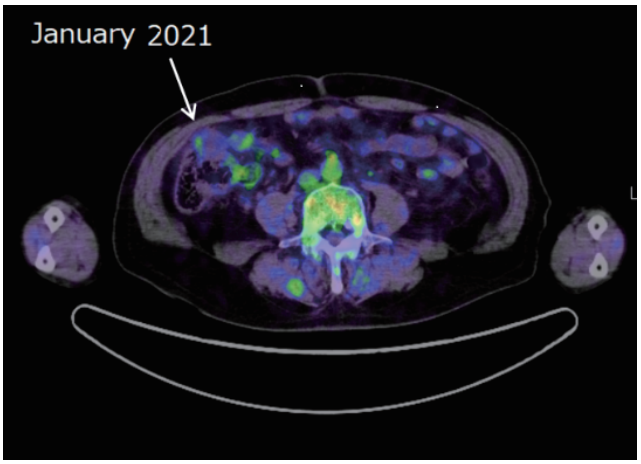

Fig. 2 Fluorodeoxyglucose positron emission tomography showing disappearance of the lesions (arrow) in the terminal ileum in January 2021

the following month, which the hematologists judged to be intolerable adverse effects of bendamustine. The patient gradually became less interested in his hobbies. He stumbled on steps and fell frequently. He developed urinary incontinence and began to wear diapers.

The patient visited the Department of Geriatrics in April 2021 to investigate the cause of cognitive decline and repeated falls. A head CT scan was performed, which showed marked lateral ventricle enlargement, Sylvian fissure enlargement, and a steep callosal angle. These findings were consistent with typical imaging findings of NPH and were not observed on past CT images (Fig. 3).[6,7] The Evans index was 0.29, but we suspected NPH based on the clinical symptoms that were consistent with NPH.

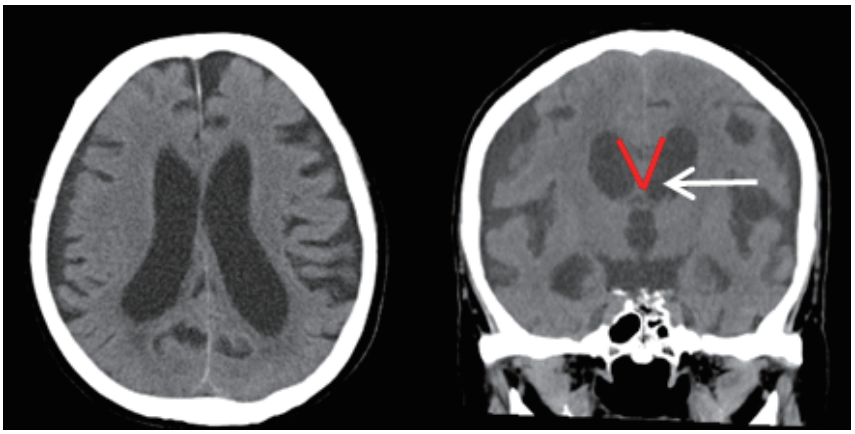

Fig. 3 Computed tomography images showing narrowing of the brain groove at the area of high convexity, with a steep callosal angle of 52.5° (arrow) and mild enlargement of the sylvian fissure

The patient was hospitalized in May 2021 for a CSF tap test. Body temperature was 36.9°C, heart rate was 68 beats per minute, blood pressure was 88/60 mm Hg, body mass index was 23.8 kg/m^2, and oxygen saturation was 98% on room air. The patient responded slowly when his name

was called, but his response was loud and clear. Chest and abdominal CT at admission showed that the lymph node lesions and spleen had shrunk, so recurrence of MCL was not immediately suspected. Blood test results (Table 1) showed hypernatremia (Na 153 mmol/L). Since the patient had not eaten before admission, dehydration was diagnosed as the cause of hypernatremia, and intravenous fluid replacement was started. A head MRI scan was stopped because the patient could not remain still, but no tumor formation was observed. On single-photon emission CT, cerebral blood flow showed a convexity apparent hyperperfusion sign (Fig. 4).[8]

Table 1 Blood test results showing hypernatremia and dehydration but no increased inflammatory response

WBC	5300	/μL	Na	153	mmol/L
RBC	4.05	$X10^6$/μL	Cl	116	mmol/L
Hb	12.8	g/dL	K	3.9	mmol/L
Total protein	6.0	g/dL	AST	33	U/L
albumin	4.1	g/dL	ALT	29	U/L
glucose	101	mg/dL	LDH	265	U/L
BUN	19.5	mg/dL	CRP	0.35	mg/dL
Cre	1.52	mg/dL	Osmotic pressure	304	mOsm/L
eGFR	34.5	ml/min/1.73m^2	HbA1c	5.2	%

ALT: alanine aminotransferase
AST: aspartate transaminase
BUN: blood urea nitrogen
Cre: creatinine
CRP: C-reactive protein
eGFR: estimated glomerular filtration rate
Hb: hemoglobin
HbA1c: glycated hemoglobin
LDH: lactate dehydrogenase
RBC: red blood cell
WBC: white blood cell

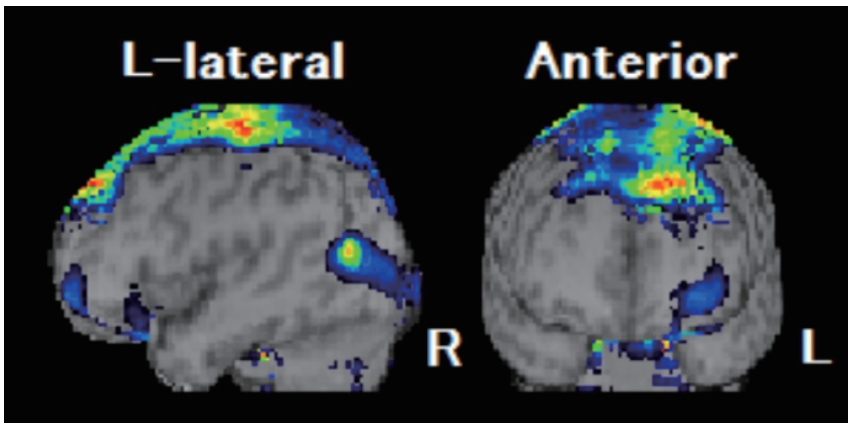

Fig. 4 Single-photon emission computed tomography showing relatively elevated blood flow in the area of high convexity

The hypernatremia tended to improve with fluid replacement, but his level of consciousness continued to decline. We decided to perform lumbar puncture. The findings of CSF analysis revealed aseptic meningitis. The initial CSF pressure was 135 mm H_2O, and the final pressure was 40 mm H_2O. The cell count was 432/3 visual fields, cerebrospinal fluid protein was 1.98 g/L, cerebrospinal fluid glucose was 0.19 g/L, and cerebrospinal fluid IgG was 5 mg/L (Table 2). CSF cytology revealed a large number of atypical lymphocytes (Fig. 5). The results suggested infiltration of MCL into the CNS, and we requested that the Department of Hematology and Oncology perform flow cytometry of the CSF. The results were CD5+, CD20+, and CD19+, with light chain restriction, leading to a diagnosis of aseptic meningitis due to infiltration of MCL into the CNS (Fig. 6).

Table 2 Cerebrospinal fluid test results showing an increased cell count and suspected aseptic meningitis

xanthochromia	(+)	
pH	7.2	
specific gravity	1.006	
Cell count	432	/3 VF
mononucleocytes	432	/3 VF
polymorphonuclear	0	/3 VF
protein	1.98	g/L
glucose	0.19	g/L
albumin	1185	mg/dL
IgG	25	mg/dL

VF: visual field

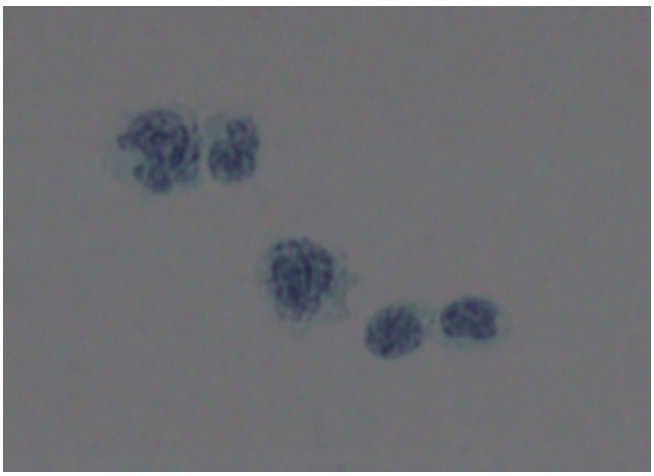

Fig. 5 Cytology showing many atypical lymphocytes in the cerebrospinal fluid (400× image)

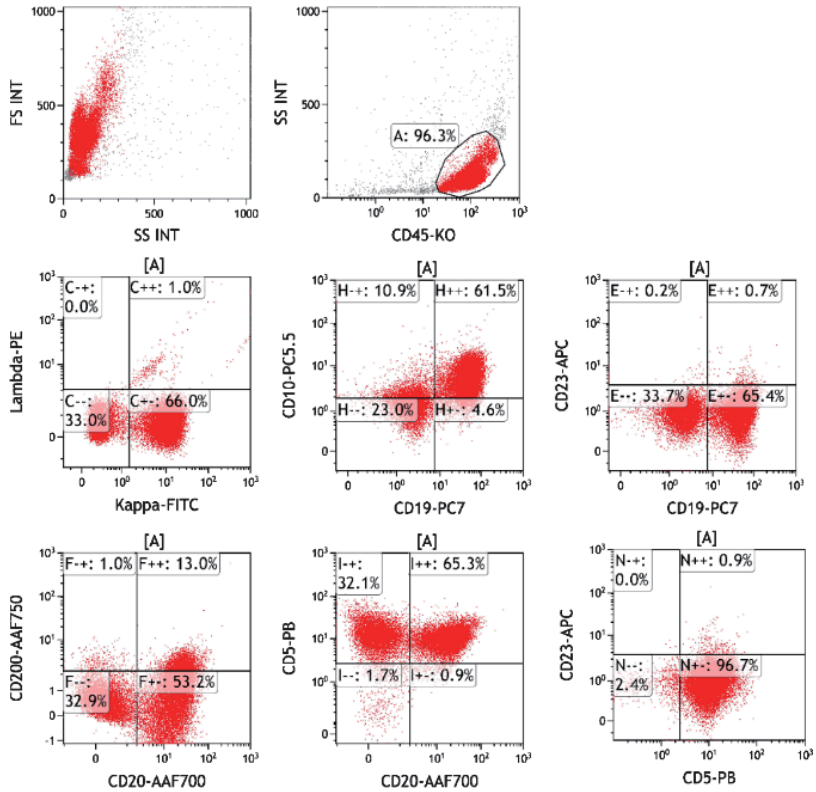

Fig. 6 Flow cytometry results showing CD5+, CD20+, and CD19+, with light chain restriction

Given that the patient had a recurrence after ibrutinib therapy, was intolerant of RB, and was bedridden and unable to communicate, with the consent of his family, he was provided best supportive care. He died a week later.

DISCUSSION

MCL is a non-Hodgkin's lymphoma derived from B cell lymphocytes that is largely a disease of older adults, with a median age at diagnosis of 60–70 years. Most patients present with advanced disease, with multiple lymph node involvement and hepatosplenomegaly, which carries a poor prognosis. In some patients, MCL involves extranodal organs, particularly the bone marrow, peripheral blood, and gastrointestinal tract, making it challenging to perform initial staging and plan treatment.[9] Approximately 5% patients with MCL have CNS involvement, mostly presenting as leptomeningeal disease, but the incidence at presentation is less than 1%.[2]

The classic triad of gait instability, cognitive impairment, and urinary incontinence distinguishes idiopathic NPH from other disorders. Cognitive features of NPH include generalized slowing, which is usually more prominent than deficits in attention, concentration, and memory. Apathy that manifests as a lack of motivation is commonly identified as a psychiatric difficulty in patients with NPH. The development of apathy can cause NPH to mimic a depressive illness, leading to delayed diagnosis.[10]

In this case, NPH was suspected from this classic triad and head CT images. Thus, a CSF tap test was performed, which revealed a diagnosis of aseptic meningitis due to meningeal infiltration of MCL. Atypical lymphocytes may have caused abnormal circulation of cerebrospinal fluid, but the relationship between ventricular enlargement and infiltration of MCL is unknown. However, in this case, we diagnosed the cause of the rapid decrease in consciousness as aseptic meningitis due to meningeal infiltration of MCL.

CONCLUSION

CNS involvement of MCL is rare. In such case, even if no mass formation or lymphadenopathy is observed on CT and MRI, meningeal infiltration of MCL may occur. In addition, it is necessary to fully consider that the cause of ventricular expansion could be metastatic disease. Patients with ventricular expansion or a history of MCL who experience a rapid decline in consciousness should have a cerebrospinal fluid test immediately.

CONFLICT OF INTEREST

The authors no conflict of interest to declare.

REFERENCES

1 Maddocks K. Update on mantle cell lymphoma. *Blood*. 2018;132(16):1647–1656. doi:10.1182/blood-2018-03-791392.

2 Cheah CY, George A, Giné E, et al. Central nervous system involvement in mantle cell lymphoma: clinical features, prognostic factors and outcomes from the European Mantle Cell Lymphoma Network. *Ann Oncol*. 2013;24(8):2119–2123. doi:10.1093/annonc/mdt139.

3 Iseki C, Takahashi Y, Wada M, Kawanami T, Adachi M, Kato T. Incidence of idiopathic NPH (iNPH): a 10-year follow-up study of a rural community in Japan. *J Neurol Sci*. 2014;339(1–2):108–112. doi:10.1016/j.jns.2014.01.033.

4 The Japanese Society of NPH. *Idiopathic normal pressure hydrocephalus : iNPH* [in Japanese]. 3rd ed. Medical Review Co., Ltd; 2020.

5 Wu EM, El Ahmadieh TY, Kafka B, et al. Clinical outcomes of normal pressure hydrocephalus in 116 patients: objective versus subjective assessment. *J Neurosurg*. 2019;132(6):1757–1763. doi:10.3171/2019.1.JNS181598.

6 Ishii K, Kawaguchi T, Shimada K, et al. Voxel-based analysis of gray matter and CSF space in idiopathic NPH. *Dement Geriatr Cogn Disord*. 2008;25(4):329–335. doi:10.1159/000119521.

7 Yamashita F, Sasaki M, Takahashi S, et al. Detection of changes in cerebrospinal fluid space in idiopathic NPH using voxel-based morphometry. *Neuroradiology*. 2010;52(5):381–386. doi:10.1007/s00234-009-0610-z.

8 Ohmichi T, Kondo M, Itsukage M, et al. Usefulness of the convexity apparent hyperperfusion sign in 123I-iodoamphetamine brain perfusion SPECT for the diagnosis of idiopathic NPH. *J Neurosurg*. 2018;130(2):398–405. doi:10.3171/2017.9.JNS171100.

9 Shah BD, Martin P, Sotomayor EM. Mantle cell lymphoma: a clinically heterogeneous disease in need of tailored approaches. *Cancer Control*. 2012;19(3):227–235. doi:10.1177/107327481201900307.

10 Feyza M, McKinley G, Bryce W, William TC. Case 10-2021: A 70-Year-Old Man with Depressed Mood, Unsteady Gait, and Urinary Incontinence. *N Engl J Med*. 2021;384(14):1350–1358. doi:10.1056/NEJMcpc2027090.