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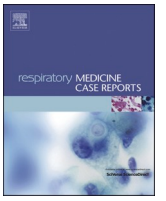

Case Report

A case of pulmonary mucosa-associated lymphoid tissue lymphoma diagnosed by detecting t(11;18)(q21;q21) in bronchial lavage fluid

Yusuke Nakamura [a], Akihiro Takemasa [a,d,*], Yuki Ohoka [a], Nobuhiko Tsukada [a], Azusa Tsukada [a], Yoshimasa Nakazato [b], Kinuko Mitani [c], Akihiko Toyoda [e], Yasuo Shimizu [a,d], Seiji Niho [a]

[a] Department of Pulmonary Medicine and Clinical Immunology, Dokkyo Medical University School of Medicine, 880 Kitakobayashi, Mibu, Tochigi, 321-0293, Japan
[b] Department of Pathology, International University of Health and Welfare, 2600-1 Kitakanemaru, Otawara City, Tochigi, 324-8501, Japan
[c] Department of Hematology and Oncology, Dokkyo Medical University School of Medicine, 880 Kitakobayashi, Mibu, Tochigi, 321-0293, Japan
[d] Respiratory endoscopy center, Dokkyo Medical University Hospital, 880 Kitakobayashi, Mibu, Tochigi, 321-0293, Japan
[e] Department of Pathology, Kamitsuga General Hospital, 1-1033 Shimotamachi, Kanuma, Tochigi, 322-8550, Japan

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ABSTRACT

A 76-year-old woman was diagnosed with mucosa-associated lymphoid tissue (MALT) lymphoma by upper gastrointestinal endoscopy. She underwent further investigation for concomitant bilateral pleural effusions and right pulmonary consolidation. MALT lymphoma with the t(11; 18)(q21; q21) translocation and *API2-MALT1* were detected in pleural fluid. Lymphoma was not histopathologically diagnosed by lung biopsies, but the same translocation was identified in bronchial lavage. MALT lymphoma is often difficult to diagnose by bronchoscopy because of only mild dysplasia. However, present report on using chromosomal translocation analysis from bronchial lavage indicates that such testing may serve as a useful diagnostic adjunct in MALT lymphoma with lung involvement.

1. Introduction

Mucosa-associated lymphoid tissue (MALT) lymphoma is a low-grade B-cell lymphoma that most commonly arises in the gastrointestinal tract (68 % of cases) but can also occur in the lungs (9 % of cases) [1]. Approximately 16–34 % of patients with MALT lymphoma have stage III/IV disease [2,3]. Because the neoplastic cells do not show marked atypia, it sometimes is difficult to diagnose MALT lymphoma by histopathological examination of a small specimen obtained by transbronchial lung biopsy.

2. Case report

A 76-year-old woman with exertional dyspnea presented to a local hospital. She was a nonsmoker with an unremarkable medical

* Corresponding author. Department of Pulmonary Medicine and Clinical Immunology, Dokkyo Medical University School of Medicine, 880 Kitakobayashi, Mibu, Tochigi, 321-0293, Japan.
E-mail address: takemasa@dokkyomed.ac.jp (A. Takemasa).

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history and no family or psychosocial history. Computed tomography showed bilateral pleural effusions, pulmonary consolidation with partial calcification in the right middle lobe, and thickening of the gastric wall but no mediastinal lymphadenopathy. The gastric lesion was diagnosed as MALT lymphoma by gastrointestinal endoscopy. A rapid urease test performed concurrently with endoscopy was negative, ruling out *Helicobacter pylori* infection.

The patient was referred to our hospital for management of the gastric MALT lymphoma and diagnosis of the pulmonary lesions and bilateral pleural effusion. Laboratory tests revealed no hepatic or renal dysfunction. Hemoglobin was slightly decreased to 11.3 g/dL; C-reactive protein was 2.19 mg/dL; and soluble interleukin-2 receptor was 859 U/mL.

A positron emission tomography–computed tomography scan showed mildly increased fluorodeoxyglucose (FDG) uptake (maximum standardized uptake value [SUV_{max}], 3.4) in the fundus and corpus of the stomach and abnormally increased FDG uptake (SUV_{max}, 5.5) in the upper and middle lobes of the right lung (Fig. 1). Bronchoscopy revealed edema of the airway mucosa and easy bleeding. The right peripheral bronchi were narrowed as a result of extramural compression due to pleural effusion. Lung biopsies of the right upper lobe (B3b) were performed using endobronchial ultrasound, followed by bronchial lavage with 20 mL of saline.

All cell surface markers and chromosome or fusion gene detection tests were performed by an outsourced testing company (SRL Inc.). The gastric lesion diagnosed at the previous hospital showed an immunophenotype of CD20(+), bcl-2(+), CD10(−), cyclin D1 (−), and CD21(−). Lymphoepithelial lesions and plasmacytoid differentiation were observed, and MALT lymphoma was diagnosed. Cytological examination of bilateral pleural fluid showed that most cells were CD20(+), and plasmacytoid differentiation was reported. These findings, also noted in bilateral pleural effusions, were consistent with a diagnosis of MALT lymphoma. Biopsy specimens from the right upper lobe of the lung showed prominent interstitial hyaline degeneration, no CD20(+) cells, and no findings consistent with MALT lymphoma. However, chromosomal analysis of G-banding revealed the t(11; 18)(q21; q21) translocation in cells from bronchial lavage fluid; this translocation was also confirmed in both pleural effusions. Additionally, the *API2-MALT1* fusion gene, which is thought to be the causative gene aberration in MALT lymphoma, was confirmed by fluorescence in situ hybridization analysis from the right pleural effusion (Fig. 2). On the basis of these results, the patient was diagnosed with stage IV MALT lymphoma with multiple organ involvement, including the stomach, right lung, and bilateral pleura.

After 1 course of rituximab and bendamustine, the number of CD20 (+) cells in the pleural fluid decreased. However, the treatment was changed to rituximab, pirarubicin, cyclophosphamide, vincristine, and prednisolone (R-THP-COP regimen) because of adverse events observed with the initial treatment. After 6 courses of R-THP-COP therapy, a partial response was achieved, and treatment was continued.

3. Discussion

Treatment of *H. pylori*–negative MALT lymphoma typically requires radiation therapy and/or chemotherapy, depending on the lymphoma stage [4]. Regardless of whether *H. pylori* infection is present, MALT lymphomas with a t(11; 18) translocation are thought to be more likely to spread to regional lymph nodes or distal sites and to fail to respond to *H. pylori* eradication therapy [4].

Mutually exclusive chromosomal translocations detected in a study of MALT lymphoma cases included *API2-MALT1* t(11; 18)(q21; q21) (17 %), *IGH-MALT1* t(14; 18)(q32; q21) (5 %), *IGH*–unknown translocation partner (3 %), and *IGH-BCL10* (1 %) [5]. The same

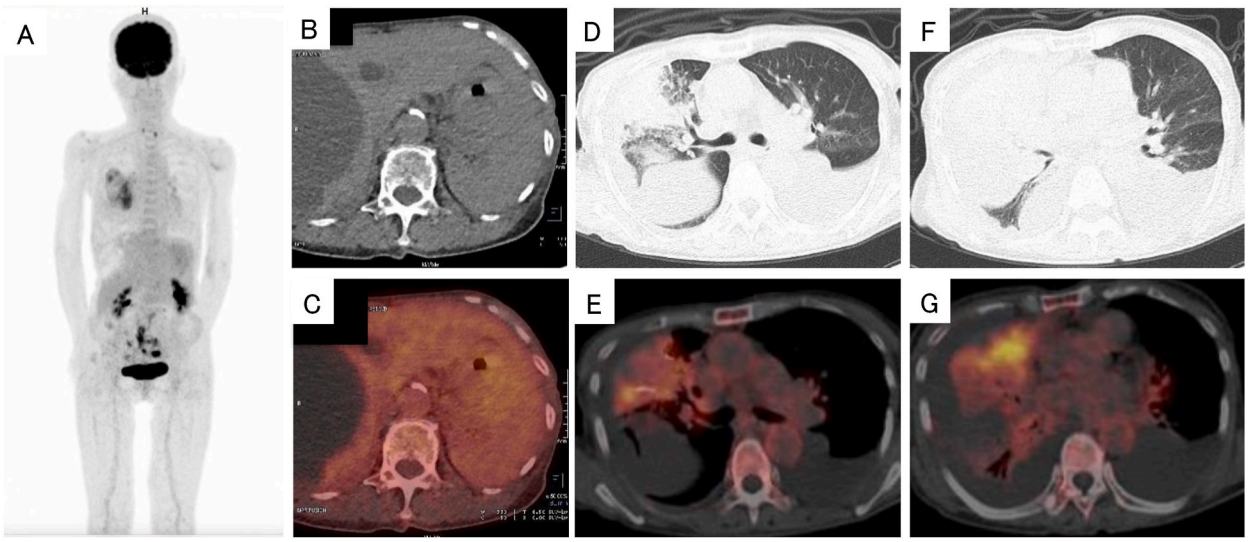

Fig. 1. PET-CT images.
PET images of a whole body scan (A), the stomach (B, C), and chest (D–G) showed increased FDG uptake in the right upper and middle lobes of the lungs (SUV_{max}, 5.5) and slightly increased FDG uptake in the fundus and body of the stomach (SUV_{max}, 3.4).
FDG, fluorodeoxyglucose; PET, positron emission tomography; PET-CT, positron emission tomography–computed tomography; SUV_{max}, maximum standardized uptake value.

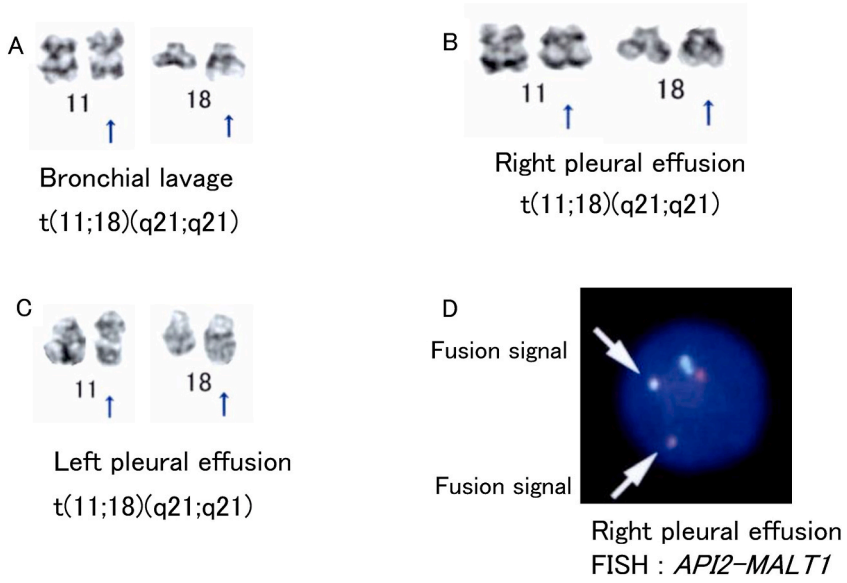

Fig. 2. G-banding chromosomal analysis and *API2-MALT1* fusion gene analysis.
The same t(11; 18)(q21; q21) translocation was detected in bronchial lavage fluid (A) as well as fluid samples from a right pleural effusion (B) and left pleural effusion (C). FISH analysis confirmed the presence of the *API2-MALT1* fusion gene in right pleural fluid (D).
FISH, fluorescence in situ hybridization.

study also found that chromosomal translocations have remarkable site specificity, with *API2-MALT1* showing a marked predilection for the lungs and intestines and *IGH-MALT1* and *IGH- BCL10* being detected almost exclusively in the lungs [5]. Additionally, the authors reported that 23 % of translocation-negative primary MALT lymphomas showed trisomy 18 [5].

The diagnostic yield of bronchoscopic biopsies for pulmonary MALT lymphoma is low (31 %) [6]. Bronchoalveolar lavage (BAL) and fine-needle aspiration also are possible methods of detecting pulmonary MALT lymphoma [7,8]. However, these approaches are diagnostic in only 30–50 % of cases, primarily as a result of the tiny samples obtained [8].

In the present case, the lung lesion involved a consolidation. Because of limited lung volume, it was thought that the lavage fluid did not reach the periphery and eventually overflow, becoming unrecoverable; consequently, bronchial lavage was performed instead of BAL. Other authors have reported diagnosing MALT lymphoma by using BAL to detect *API2-MALT1* [7]. This article reported that MALT1 translocation was useful in the diagnosis of MALT lymphoma. However, BAL uses a total of 150 mL of sterile saline, and a special assay kit is needed to detect *API2-MALT1*. Therefore, this method of diagnosis may not be feasible at all facilities. The chromosomal or genetic testing method used in the present case requires only a small amount of bronchial washing fluid from the lesion and successfully detected the chromosomal translocation using a standard test that is available to any facility via outsourcing. This suggests that our testing strategy could be a useful adjunct in diagnosing MALT lymphoma. Cryobiopsy has become more widespread in recent years and has greater potential for diagnosing MALT lymphoma in a pulmonary lesion; even if cryobiopsy were performed, however, not all cases of MALT lymphoma could be diagnosed by this method [9].

In conclusion, in patients with pulmonary lesions suspected to be MALT lymphoma, testing of small tissue samples obtained by transbronchial lung biopsy often does not yield a definitive diagnosis. The use of adjunct chromosomal translocation and fusion gene analysis is recommended as a means to improve diagnostic accuracy in this setting.

CRediT authorship contribution statement

Yusuke Nakamura: Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Akihiro Takemasa:** Writing – review & editing, Writing – original draft, Investigation. **Yuki Ohoka:** Investigation. **Nobuhiko Tsukada:** Investigation. **Azusa Tsukada:** Investigation. **Yoshimasa Nakazato:** Investigation. **Kinuko Mitani:** Writing – review & editing, Investigation. **Akihiko Toyoda:** Investigation. **Yasuo Shimizu:** Writing – review & editing, Investigation. **Seiji Niho:** Writing – review & editing, Writing – original draft, Project administration, Investigation, Funding acquisition, Conceptualization.

Informed consent statement

Written informed consent was obtained from the patient for publication of this case report, including any accompanying images.

Additional information

The authors declare no competing financial interests.

IRB information

IRB review is not required.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2024.102133.

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