

# Impact of Synchronous Multiple Primary Malignant Tumors on Newly Diagnosed Hematologic Malignancies

Satoshi Nishiwaki,<sup>1,2</sup> Shingo Okuno,<sup>1</sup> Kotaro Suzuki,<sup>1</sup>  
Shingo Kurahashi,<sup>1</sup> Isamu Sugiura<sup>1</sup>

## Abstract

**The existence of synchronous multiple primary malignant tumors was not a significant risk factor for patients with newly diagnosed hematologic malignancies. It is important to provide adequate treatment to both hematologic malignancies and solid tumors appropriately.**

**Background:** Hematologic malignancies are occasionally observed with synchronous multiple primary malignant tumors (sMPMTs) at diagnosis. We aimed to clarify the effect of sMPMTs on newly diagnosed hematologic malignancies and determine the optimal treatment strategies. **Patients and Methods:** We analyzed the outcomes of 649 patients with hematologic malignancies, including 19 patients with sMPMTs (2.9%), and compared the outcomes between patients with and without sMPMTs. **Results:** The overall survival (OS) and disease-free survival (DFS) rates for patients with sMPMTs were 77% and 70%, respectively, at 2 years; these rates were not statistically different from those for patients without sMPMTs ( $P = .17$  and  $P = .64$ , respectively). Multivariate analysis showed that the presence of sMPMTs was not a significant prognostic factor for OS, DFS, or relapse (hazard ratio [HR] 1.48, 95% confidence interval [CI] 0.65-3.38,  $P = .35$ ; HR 0.97, 95% CI 0.46-2.10,  $P = .97$ ; and HR 0.79, 95% CI 0.29-2.14,  $P = .65$ ). In patients with sMPMTs, the order of treatment was not a significant prognostic factor. However, discontinuation of treatment was a marginally favorable factor and might reflect a selection bias. **Conclusion:** The presence of sMPMTs was not a significant risk factor for patients with newly diagnosed hematologic malignancies. It is important to provide adequate treatment for both hematologic malignancies and solid tumors at the physician's discretion.

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## Introduction

Synchronous multiple primary malignant tumors (sMPMTs) are occasionally diagnosed during screening tests of patients with newly diagnosed malignant neoplasms.<sup>1,2</sup> Although it has been reported that special attention should be given to MPMTs, especially for head and neck cancer and urinary tumors,<sup>1</sup> their prevalence is generally very low. Only sporadic cases have been reported concerning hematologic malignancies with sMPMTs.<sup>3-5</sup>

Because multiple cycles of combination chemotherapy are standard, at least several months are necessary for the treatment of newly diagnosed hematologic malignancies, such as acute leukemia, malignant lymphoma, and multiple myeloma.<sup>6-10</sup> Therefore, deciding when to treat the sMPMTs can be difficult. Physicians must balance the risk of re-exacerbating the hematologic disease by insufficient treatment with the risk of exacerbating the untreated sMPMTs. No optimized treatment policy exists for hematologic malignancies presenting with sMPMTs.

In the present study, we analyzed the prognostic effect of sMPMTs on patients with hematologic malignancies. We also assessed the effect of different treatment strategies on the outcomes.

## Patients and Methods

### Patients

sMPMTs were found in 19 patients with newly diagnosed hematologic malignancies at Toyohashi Municipal Hospital from 2009 to 2015. The hematologic diseases diagnosed in the 19 patients were

<sup>1</sup>Division of Hematology and Oncology, Toyohashi Municipal Hospital, Toyohashi, Japan

<sup>2</sup>Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, Nagoya, Japan

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Address for correspondence: Satoshi Nishiwaki, MD, PhD, Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, 65 Tusukami-cho Showa-ku, Nagoya 4668560, Japan  
E-mail contact: n-3104@tf7.so-net.ne.jp

## Impact of sMPMTs on Hematologic Tumors

**Table 1** Characteristics of Patients With Newly Diagnosed Hematologic Malignancies Stratified by the Presence of sMPMTs

| Characteristic         | sMPMTs |       | P Value | Total |
|------------------------|--------|-------|---------|-------|
|                        | No     | Yes   |         |       |
| Patients               | 630    | 19    |         | 649   |
| Age at diagnosis (y)   |        |       | .40     |       |
| Median                 | 69     | 69    |         | 69    |
| Range                  | 20-99  | 60-86 |         | 20-99 |
| Sex                    |        |       | .51     |       |
| Male                   | 347    | 9     |         | 356   |
| Female                 | 283    | 10    |         | 293   |
| Diagnosis              |        |       | .94     |       |
| FL                     | 73     | 5     |         | 78    |
| MALT                   | 21     | 0     |         | 21    |
| MZL                    | 14     | 0     |         | 14    |
| HCL                    | 1      | 0     |         | 1     |
| DLBCL                  | 310    | 10    |         | 320   |
| AITL                   | 17     | 1     |         | 18    |
| PTCL                   | 12     | 0     |         | 12    |
| MCL                    | 8      | 0     |         | 8     |
| BL                     | 6      | 0     |         | 6     |
| Extranodal NK/T        | 5      | 0     |         | 5     |
| EBV-LPD                | 4      | 0     |         | 4     |
| Plasmablastic lymphoma | 4      | 0     |         | 4     |
| Other B-cell lymphoma  | 10     | 0     |         | 10    |
| Other T-cell lymphoma  | 4      | 0     |         | 4     |
| MM                     | 141    | 3     |         | 144   |
| Lymphoma grade         |        |       | .40     |       |
| Indolent               | 109    | 5     |         | 114   |
| Aggressive             | 380    | 11    |         | 391   |
| IPI                    |        |       | .52     |       |
| Low                    | 173    | 4     |         | 177   |
| Low to intermediate    | 139    | 4     |         | 143   |
| Intermediate to high   | 107    | 6     |         | 113   |
| High                   | 69     | 2     |         | 71    |
| Missing                | 1      | 0     |         | 1     |
| ISS                    |        |       | .86     |       |
| I                      | 28     | 1     |         | 29    |
| II                     | 53     | 1     |         | 54    |
| III                    | 56     | 1     |         | 57    |
| Missing                | 4      | 0     |         | 4     |
| Risk                   |        |       | .52     |       |
| Low                    | 312    | 8     |         | 320   |
| High                   | 317    | 11    |         | 328   |
| Missing                | 1      | 0     |         | 1     |

Abbreviations: AITL = angioimmunoblastic T-cell lymphoma; BL = Burkitt lymphoma; DLBCL = diffuse large B-cell lymphoma; EBV-LPD = Epstein-Barr virus-associated lymphoproliferative disease; FL = follicular lymphoma; HCL = hairy cell leukemia; IPI = international prognostic index; ISS = international staging system; MALT = mucosa-associated lymphoid tissue; MCL = mantle cell lymphoma; MZL = marginal zone lymphoma; PTCL = peripheral T-cell lymphoma; sMPMTs = synchronous multiple primary malignant tumors.

non-Hodgkin lymphoma (NHL) and multiple myeloma (MM); therefore, 649 patients with a diagnosis of NHL or MM during the same period were included in the present study. The therapeutic strategies for patients with sMPMTs were determined by physician preference. The hospital's institutional review board approved the present study.

### Definitions

sMPMTs were defined as solid tumors within 6 months of the diagnosis of hematologic disease.<sup>11</sup> Indolent NHL was defined, in reference to previous classifications,<sup>12,13</sup> as follicular lymphoma, mucosa-associated lymphoid tissue lymphoma,

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