infectivity in the lesions, while the data in the PML assay are supposed to represent the productivity of replication-competent viruses derived from monocytes/macrophages infected in vivo. If this is the case, the dissociation between the antigenemia/viral loads and the PML assay may suggest that HCMV infected in vivo does not necessarily replicate with similar efficiency between PBMCs and the lesions.

The dissociation was particularly prominent in the sequence-proven GCV-resistant virus #hsct-22, which showed very low numbers of progeny viruses despite extremely high antigenemia or viral loads. Interestingly, slow replication in PBMCs was reproduced by in vitro experiments using simultaneously obtained blood culture isolates. Although virus tropism to leucocytes and/or endothelial cells can be affected by mutation of the genes encoding UL128–UL131A during in vitro culture [Akter et al., 2003; Hahn et al., 2004; Sinzger et al., 2008], a genomic sequence analysis revealed that the isolated virus at the fifth passage had no apparent mutations that led to amino acid substitutions or deletions in the UL128–UL131A genes compared with those of the blood sample (data not shown). To overcome the issues for these non-responsive samples, a detailed characterization of the virus is now being undertaken, including analyses of the genomic sequences of other genes and the clinical background information of the patients.

In most of the specimens tested in this study, direct phenotypic susceptibility testing under the conditions used appeared to be feasible, although further improvements are required. It is notable that some of the "apparent low-sensitivity" samples showed relatively high numbers of PML-positive cells, in contrast to the low numbers of PML-positive cells for the sequence-proven GCV mutants. Since the pathogenesis of HCMV infection is related to a number of interactions between HCMV and the host immune response, the host factors that can affect the numbers of PML-positive cells remain to be elucidated. However, a preliminary study revealed that several reported risk factors that impacts on HCMV infection had no bias for low GCV susceptibility, including the donor HCMV serostatus before transplantation, acute GVHD and relapse of antigenemia (data not shown). Further studies on the molecular basis of the cell type-specific preferential propagation of clinical strains may provide insights for better understanding of HCMV infection and disease.

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Rapidly progressive fatal hemorrhagic pneumonia caused by *Stenotrophomonas maltophilia* in hematologic malignancy

H. Araoka, T. Fujii, K. Izutsu, M. Kimura, A. Nishida, K. Ishiwata, N. Nakano, M. Tsuji, H. Yamamoto, Y. Asano-Mori, N. Uchida, A. Wake, S. Taniguchi, A. Yoneyama. Rapidly progressive fatal hemorrhagic pneumonia caused by *Stenotrophomonas maltophilia* in hematologic malignancy. Transpl Infect Dis 2012: 14: 355–363.

Abstract: *Background.* Pneumonia caused by *Stenotrophomonas maltophilia* is rare, but can be lethal in severely immunocompromised patients. However, its clinical course remains unclear.
Patients and methods. Patients with pneumonia caused by *S. maltophilia* in Toranomon Hospital (890 beds, Tokyo, Japan) were reviewed retrospectively between April 2006 and March 2010.
Results. During the study period, 10 cases of *S. maltophilia* pneumonia were identified. Seven patients had acute myeloid leukemia, 2 had myelodysplastic syndrome, and 1 had malignant lymphoma. All patients developed symptoms after allogeneic hematopoietic stem cell transplantation (HSCT). Five patients received first cord blood transplantation (CBT), 4 patients received second CBT, and 1 patient received first peripheral blood stem cell transplantation (PBSCT). The overall incidence of *S. maltophilia* pneumonia among 508 patients who received HSCT during the period was 2.0%. The incidence was 0% (0/95) in patients after bone marrow transplantation, 0.8% (1/133) after PBSCT, and 3.2% (9/279) after CBT. Pneumonia developed a median of 13.5 days (range, 6–40) after transplantation. At onset, the median white blood cell count was 10/μL (range, 10–1900), and the median neutrophil count was 0/μL (range, 0–1720). In all patients, *S. maltophilia* bacteremia developed with bloody sputum or hemoptysis. The 28-day mortality rate was 100%; the median survival after onset of pneumonia was 2 days (range, 1–10).
Conclusions. Hemorrhagic *S. maltophilia* pneumonia rapidly progresses and is fatal in patients with hematologic malignancy. Attention should be particularly paid to the neutropenic phase early after HSCT or prolonged neutropenia due to engraftment failure. A prompt trimethoprim-sulfamethoxazole-based multidrug combination regimen should be considered to rescue suspected cases of *S. maltophilia* pneumonia in these severely immunosuppressed patients.

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Key words: *Stenotrophomonas maltophilia*; pneumonia; incidence; neutropenia; hematologic malignancy; hematopoietic stem cell transplantation

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Stenotrophomonas maltophilia is a low-virulent non-fermenting gram-negative bacillus that can be isolated from diverse environments such as an aquatic environment and soil, and it rarely causes respiratory infections in the healthy population. When *S. maltophilia* is detected on culture of an airway sample, it usually represents colonization or a carrier state. However, it has recently been recognized as a

pathogen of hemorrhagic pneumonia in severely immunocompromised patients (1–5). Once respiratory infections caused by *S. maltophilia* develop, the prognosis is considered to be poor because of the severe immunodeficiency of these patients. However, the clinical features of *S. maltophilia* pneumonia have not been fully clarified, and only a few case series of *S. maltophilia* pneumonia have been published. In this study, we summarize the clinical features of 10 patients with a definitive diagnosis of *S. maltophilia* hemorrhagic pneumonia.

Patients and methods

Medical records of patients with pneumonia caused by *S. maltophilia* in Toranomon Hospital (890 beds, Tokyo, Japan) between April 2006 and March 2010 (4 years) were retrospectively reviewed. *S. maltophilia* pneumonia was defined when all of the following 4 criteria were met: 1) Clinical symptoms of cough, sputum production, and fever; 2) dominant thin gram-negative bacilli were detected on Gram staining of a lower respiratory airway sample obtained from sputum, tracheobronchial aspirate or bronchoscopy; 3) *S. maltophilia* was cultured from a lower respiratory airway sample; and 4) a new shadow appeared on chest x-ray. The onset of *S. maltophilia* pneumonia was defined when both the clinical symptoms and the new shadow on chest x-ray were demonstrated.

Vitek system (bioMérieux, Marcy l'Etiole, France), Vitek2 system (bioMérieux), and MicroScan WalkAway 96 SI (Siemens Healthcare, Deerfield, Illinois, USA) were used for bacterial identification and drug sensitivity tests.

Immunohistochemical study was performed using the MACH-2 multiplex staining system (Biocare Medical, Concord, California, USA) according to manufacturer's instructions. A rabbit polyclonal anti-*S. maltophilia* antibody (AB-T065; Advanced Targeting Systems, San Diego, California, USA) was used at a 1/50 dilution. Anti-cytokeratin CAM5.2 antibody (Becton Dickinson Biosciences, San Jose, California, USA) was used to highlight epithelial cells.

Results

All 10 patients were diagnosed as having *S. maltophilia* pneumonia. There was no apparent outbreak of *S. maltophilia* infection throughout the study period. The clinical characteristics of the 10 patients are shown in Tables 1 and 2.

There were 6 men and 4 women, with a median age of 58 years (range, 36–62). Underlying diseases were acute myeloid leukemia in 7 patients, myelodysplastic syndrome in 2 patients, and diffuse large B-cell lymphoma in 1 patient. All patients had already undergone allogeneic hematopoietic stem cell transplantation (HSCT). Five patients received first cord blood transplantation (CBT), 4 patients received second CBT, and 1 patient received first peripheral blood stem cell transplantation (PBSCT) (Table 1). All patients underwent transplantation in a non-remission state. During the study period, HSCT was performed in 508 patients (bone marrow transplantation [BMT]: 95, PBSCT: 133, CBT: 279, PBSCT + BMT: 1, and first HSCT: 366, second HSCT: 112, ≥ third HSCT: 30), and the overall incidence of *S. maltophilia* pneumonia was 2.0%. The incidence was 0% (0/95) in patients after BMT, 0.8% (1/133) after PBSCT, and 3.2% (9/279) with CBT. *S. maltophilia* pneumonia developed only in the HSCT setting, and no case of *S. maltophilia* pneumonia occurred among patients without hematologic disorders.

With respect to clinical characteristics that predisposed the patients to developing *S. maltophilia* pneumonia, they had been generally heavily pretreated before HSCT. Most patients had received >2 lines of chemotherapy before HSCT, and median length of hospital stay before HSCT was 123 days (range, 49–412). All patients had previously received broad-spectrum antimicrobial therapy including carbapenem and prophylactic fluoroquinolone in the 90 days before HSCT. Graft-versus-host disease (GVHD) prophylaxis consisted of tacrolimus and mycophenolate mofetil in 8 and tacrolimus alone in 2 patients. Corticosteroid had been used for GVHD or pre-engraftment immune reactions in 5 patients with a diagnosis of *S. maltophilia* pneumonia (Table 1). All patients had preparative regimen-related mucositis (grade ≥ 2 according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0). Similarly, 9/10 patients had diarrhea (grade ≥ 1) due to preparative regimen and/or GVHD at the diagnosis of *S. maltophilia* pneumonia. However, no patients had apparent *Clostridium difficile*-associated disease.

The median onset of *S. maltophilia* pneumonia was 13.5 days (range, 6–40) after transplantation, and the median white blood cell and neutrophil counts at the time of onset were 10/μL (range, 10–1900) and 0/μL (range, 0–1720), respectively (Table 1). Pneumonia developed during broad-spectrum antibiotic treatment including fluoroquinolones in all patients. *S. maltophilia* was detected in airway samples before pneumonia onset in 3 patients (Patients 3, 4, and 10) (Table 1).

Clinical characteristics of the 10 patients with *Stenotrophomonas maltophilia* pneumonia (background)

Patient No.	Age (years)	Gender	Diagnosis	Transplantation	GVHD prophylaxis	Corticosteroid	White blood cell count (/μL)	Neutrophil count (/μL)	Time of onset after transplantation (days)	Pretreatment with antibiotics	Carrier state
1	45	M	AML	2nd CBT	TAC+MMF	No	20	0	11	MEPM, VCM	No
2	62	M	AML	CBT	TAC+MMF	No	10	0	6	PIPC/TAZ, CPFX, VCM	No
3	57	M	AML	Allo-PBSCT	TAC+MMF	No	1900	1720	27	CPFX	Yes
4	36	M	AML	2nd CBT	TAC+MMF	No	10	0	7	PAPM/BP, VCM	Yes
5	59	M	NHL	CBT	TAC	Methylprednisolone 125 mg	150		16	PIPC/TAZ, AZT, VCM	No
6	60	M	AML	CBT	TAC+MMF	Hydrocortisone 150 mg	10	0	7	PAPM/BP, VCM	No
7	56	F	AML	2nd CBT	TAC+MMF	Methylprednisolone 20 mg	10	0	34	CFPM, VCM	No
8	42	F	MDS	CBT	TAC+MMF	Methylprednisolone 40 mg	10	0	7	MEPM, VCM	No
9	59	F	AML	2nd CBT	TAC	Methylprednisolone 40 mg	310	78	25	MEPM, CPFX, AMK, VCM	No
10	62	F	MDS	CBT	TAC+MMF	No	10	0	40	PIPC/TAZ, GM, VCM	Yes

GVHD, graft-versus-host disease; M, male; F, female; AML, acute myeloid leukemia; NHL, non-Hodgkin lymphoma; MDS, myelodysplastic syndrome; CBT, cord blood transplantation; Allo-PBSCT, allogeneic peripheral blood stem cell transplantation; TAC, tacrolimus; MMF, mycophenolate mofetil; MEPM, meropenem; VCM, vancomycin; PIPC/TAZ, piperacillin/tazobactam; CPFX, ciprofloxacin; PAPM/BP, panipenem/betamipron; AZT, aztreonam; CFPM, cefepime; AMK, amikacin; GM, gentamicin.

Table 1

Clinical characteristics of the 10 patients with *Stenotrophomonas maltophilia* pneumonia (diagnosis and treatment)

Patient No.	Blood culture	Mixed infection blood culture	Respiratory cultures except *S.maltophilia*	Time of death after onset (days)	Treatment		
					TMP-SMX (Dose of TMP)	CCr (mL/min)	Fluoroquinolone
1	Positive	No	–	1	–	30	–
2	Positive	No	–	3	320 mg after HD	HD	Yes
3	Positive	No	*Enterococcus faecalis, Enterococcus faecium, Elizabethkingia meningoseptica*	10	400 mg after HD	HD	Yes
4	Positive	*Enterococcus* species	–	2	–	41	Yes
5	Positive	No	–	1	–	HD	–
6	Positive	*Enterococcus faecium*	–	2	320 mg/day	77	Yes
7	Positive	*Enterococcus faecium*	–	1	–	55	–
8	Positive	No	*Aspergillus* species	4	320 mg/day	40	Yes
9	Positive	No	*Enterococcus faecalis, Enterococcus faecium*	3	320 mg/day	16	Yes
10	Positive	*Citrobacter freundii*	–	1	720 mg/day	92	Yes

TMP-SMX, trimethoprim-sulfamethoxazole; HD, hemodialysis; CCr, creatinine clearance.

Table 2

Three patients (Patients 2, 3, and 5) received treatment with mechanical ventilation when pneumonia developed.

All patients had *S. maltophilia* bacteremia. Bacteria other than *S. maltophilia* were simultaneously detected on blood culture in 4 patients: Enterococci in 3 (*Enterococcus faecium*: 2, *Enterococcus* species: 1) and *Citrobacter freundii* in 1 (Table 2).

Bloody sputum or hemoptysis was noted in all patients. As shown in Figure 1A, red blood cells and many thin gram-negative bacilli were present in airway samples in all patients. Seven of 10 patients had pure *S. maltophilia* pneumonia, and only *S. maltophilia* was cultured from respiratory secretions. In the other 3 patients, other bacteria were cultured, but these bacteria were not observed on Gram stain finding, suggesting bacterial colonization in the airway. Also, these bacteria had low pathogenicity, except *Aspergillus* species (Patient 8) (Table 2). Two patients had fungal infection (*Candida glabrata*, *Aspergillus* species). No patients had apparent viral infection.

Chest computed tomography findings in Patient 6 are shown in Figure 2. Infiltrating shadows rapidly progressed within a very short period. Autopsy was performed in Patient 6. The lungs (weight 1110/1450 g) were voluminous with hemorrhage and edema. Microscopically, the lungs showed diffuse alveolar hemorrhage with the alveolar spaces filled with abundant extravasated blood and fibrinous exudate; the alveolar epithelial cells were widely disrupted and detached from the alveolar septa. There were some areas showing focal collapse due to fibrosis with hemosiderosis. Arterial and capillary vascular structures were retained, and no evidence of vasculitis or capillaritis was noted. The presence of *S. maltophilia* was clearly demonstrated on immunohistochemistry as shown in Figure 1B–F.

The mortality rate from *S. maltophilia* pneumonia was 100%. Although empiric or Gram staining-guided preemptive higher doses of trimethoprim-sulfamethoxazole (TMP-SMX) and fluoroquinolones with multiple broad-spectrum antibiotics were administered in 6 of the 10 patients, all of these patients died within a very

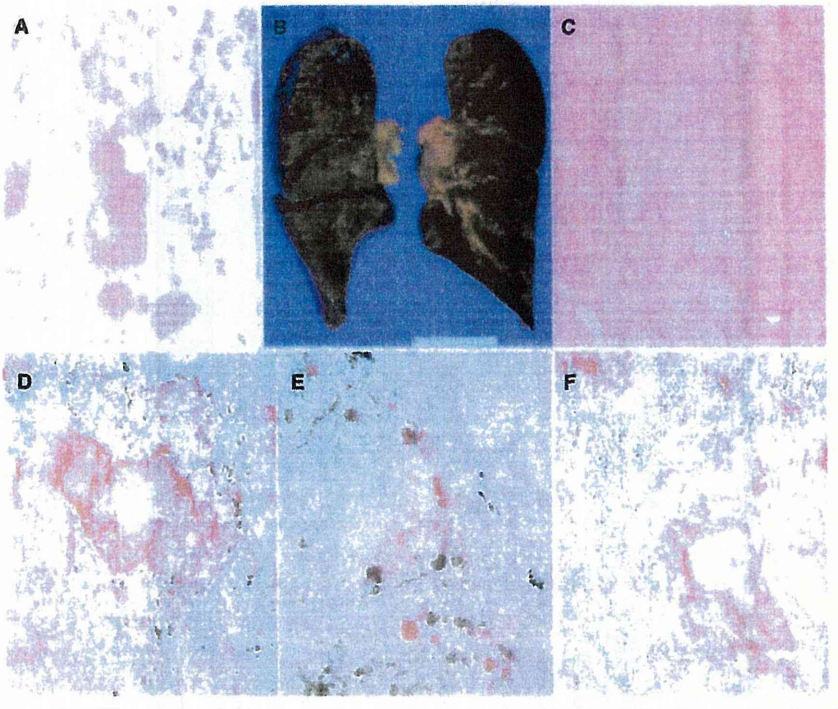

Fig. 1. Stenotrophomonas maltophilia pneumonia developed in a neutropenic state after cord blood transplantation. Bronchoalveolar lavage showed a red color, suggesting alveolar hemorrhage. Large amounts of red blood cells and thin gram-negative bacilli were found on Gram staining (A). Lungs obtained at autopsy demonstrated the presence of diffuse alveolar hemorrhage macroscopically (B) and histologically (C; hematoxylin-eosin, ×41) (Patient 6). Double immunohistochemical staining of the lung (D: ×83; E: ×165, F: ×41) showed the presence of *S. maltophilia* (red) located within/along the alveolar spaces filled with abundant extravasated blood/fibrinous exudate and widely disrupted alveolar epithelial cells (brown). In addition, the presence of macrophages phagocytizing *S. maltophilia* are noted.

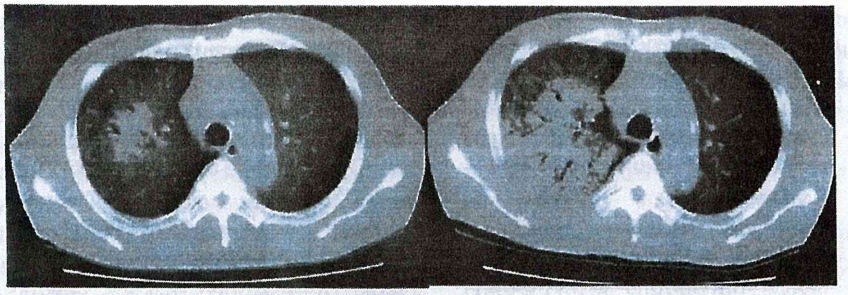

Fig. 2. Patient 6 underwent cord blood transplantation for acute leukemia. Pneumonia developed when the neutrophil count was 0/μL on day 7 after transplantation. Compared with chest computed tomography on day 7 after transplantation (left), consolidation accompanied by an air bronchogram showed rapid expansion in the right lung field on the following day (day 8) (right).

short time after pneumonia onset (median: 2 days; range, 1–10) (Table 2). Regarding drug sensitivity, *S. maltophilia* was susceptible to TMP-SMX in all patients excluding Patient 6. The susceptibility rates to levofloxacin, minocycline, and ceftazidime were 70%, 100%, and 20%, respectively.

Discussion

Low-virulent multidrug-resistant *S. maltophilia* with low pathogenicity has been increasingly isolated with the development of immunosuppressive anti-cancer treatment including HSCT. Safdar and Rolston (6) reported that the ratio of gram-negative bacteria isolated from cancer patients was 2% in 1986, but accounted for 7% in 2002. However, it remains unclear whether the isolation frequency has steadily increased, because the isolation rate depends on local factors at each hospital (7). *S. maltophilia* has low virulence in healthy populations, but it is pathogenic in profoundly immunosuppressed patients. In general, *S. maltophilia* cultured from lower respiratory airway samples comprise mostly bacteria that have colonized the airway. When *S. maltophilia* is isolated from lower respiratory airway samples, it is difficult to differentiate infection from colonization. To diagnose *S. maltophilia* pneumonia, quantitative culture of bronchoalveolar lavage may be useful, but it has a limitation (8). To date, there has been limited literature describing the epidemiology of *S. maltophilia* pneumonia. A previous report showed that *S. maltophilia* accounted for 4.5% of hospital-acquired pneumonia cases and 6% of ventilator-associated pneumonia (9). Also, Jones (10) reported that *S. maltophilia* was isolated from 3.1% of patients hospitalized with pneumonia in the last 5 years of the SENTRY Antimicrobial Surveillance Program. However, the true incidence of *S. maltophilia* pneumonia could be much lower because that report included cases demonstrating colonization of *S. maltophilia* in the respiratory tract. We consider that Gram staining of lower respiratory airway samples is important. When dominant thin gram-negative bacilli are observed under a microscope and *S. maltophilia* is detected in culture, it is likely to be a true pathogen. We incorporated Gram stain findings into the diagnostic criteria of *S. maltophilia* pneumonia to exclude the cases of *S. maltophilia* colonization and improve the accuracy of diagnosis. However, it is possible that severe cases were selected, whereas mild to moderate cases that could be cured with antimicrobial therapy were excluded by these criteria.

This is the first report, to our knowledge, describing the incidence of *S. maltophilia* pneumonia in HSCT recipients. The majority of the patient population was CBT recipients, and the incidence of *S. maltophilia* pneumonia in CBT recipients tended to be higher compared with that in BMT and PBSCT recipients. The retrospective nature of this study is a limitation, as in other studies, and our study did not sufficiently exclude *S. maltophilia* cross-transmission. Thus, the true incidence of *S. maltophilia* pneumonia still remains unknown. However, no apparent outbreak occurred during the study period.

Regarding risk factors for *S. maltophilia* pneumonia, various studies mainly reported the following factors: 1) neutropenia; 2) hematologic malignancy, such as leukemia and malignant lymphoma; 3) patients treated with broad-spectrum antibiotics (carbapenems, broad-spectrum cephalosporins, and fluoroquinolones); 4) prolonged mechanical ventilation for 7 days or longer, or tracheotomy; and 5) anatomic abnormality in the trachea or lung, such as cystic fibrosis and chronic obstructive pulmonary disease (3, 6, 11).

Hemorrhagic pneumonia in patients with hematologic malignancy accompanied by neutropenia is a

characteristic pathological condition of *S. maltophilia* pneumonia, and it has been reported to cause alveolar hemorrhage and rapidly result in death (1–5). In our study, the disease developed with severe neutropenia in 9 of 10 patients, and occurred during the early phase after HSCT or prolonged neutropenia due to engraftment failure. Many of these patients had bloody sputum or hemoptysis. Clinicians should not overlook these clinical signs, although they may be lacking in the early stage of pneumonia, which should receive attention. In our series, 4 patients did not receive TMP-SMX-based multidrug combination treatment for *S. maltophilia,* because it was diagnosed after death. In these 4 patients, the median time of death after onset was only 1 day (range, 1–2). Reportedly, bacterial colonization is observed in the airway before the development of pneumonia in many cases, but in the presence of neutropenia, it may rapidly develop in the absence of confirming colonization. Indeed, colonization had been detected in only 3 of the 10 patients before the onset of *S. maltophilia* pneumonia.

Reportedly, images of *S. maltophilia* pneumonia did not show any characteristic feature compared with those of common bacterial pneumonia. It may show a uni- or bilateral pattern, but is rarely accompanied by pleural effusion (3, 11). Cavernous lesions are also rare. In patients with hematologic malignancy accompanied by neutropenia, particularly patients after HSCT, it may show rapid progression accompanied by hemorrhagic pneumonia. On imaging, early changes are minute in many cases, requiring careful observation. The detailed mechanism of alveolar hemorrhage has not been clarified, and further studies are necessary.

The mortality rate from *S. maltophilia* pneumonia is high, being reported to be 23–77% (12), and further increases in cases accompanied by *S. maltophilia* bacteremia (13). The blood culture positivity rate rises in the presence of neutropenia, and the mortality rate of such cases is very high. In severely immunocompromised patients who have profound neutropenia, mucositis, or presence of a catheter, multiple pathogens are often present, and the prognosis is poor (13). For such cases, blood culture to determine pathogens is very important. We also noted combined bacteremia in 4 of the 10 patients. It was reported that early catheter removal led to a better prognosis in the case of catheter-related *S. maltophilia* bacteremia (13).

In our study, the mortality rate of *S. maltophilia* pneumonia was higher than that in previous reports. This could have been due to the fact that 9 of the 10 patients received CBT and had prolonged severe neutropenia; furthermore, all 10 patients underwent transplantation in a non-remission state. It may be difficult to rescue patients when bacteria are shown in lower respiratory airway samples on Gram staining despite prompt treatment with TMP-SMX alone or TMP-SMX-based multidrug regimen, as observed in our cases. Patient 3, who received PBSCT and had a relatively shorter neutropenic period, had longer survival, indicating the essential role of neutrophils to manage *S. maltophilia* pneumonia. The prevention and early diagnosis of disease development need to be investigated.

S. maltophilia exhibits intrinsic resistance to a wide variety of antibiotics. It is resistant to most β-lactams including carbapenems by producing the L1- (class B metallo β-lactamase) and L2-type (class A) β-lactamases (14, 15); fluoroquinolones through a drug efflux pump, or reducing the outer membrane permeability to drugs (16, 17); and aminoglycosides by producing an aminoglycoside-modifying enzyme and through a drug efflux pump (6, 18–20). In previous reports, sensitivity to TMP-SMX and minocycline was high, but sensitivity to other drugs varied among reports (6). Treatment with TMP-SMX alone or TMP-SMX-based multidrug regimen (combination with ticarcillin clavulanate and/or fluoroquinolones) is considered the first choice (21–24). Treatment with TMP-SMX and fluoroquinolones is the only treatment option for *S. maltophilia* pneumonia in severely immunocompromised patients, as ticarcillin clavulanate has not been approved, and is not commercially available in Japan. However, treatment of *S. maltophilia* pneumonia without ticarcillin clavulanate would be disadvantageous because many patients at risk are likely to have fluoroquinolone prophylaxis, predisposing patients to fluoroquinolone-resistant *S. maltophilia* infection.

Regarding the dose of TMP-SMX, no clear data are available. As its action on *S. maltophilia* is considered bacteriostatic (25), higher dose may be recommended, as is the case for *Pneumocystis* pneumonia (15 mg/kg/day of trimethoprim) (26), but no prospective study data are available.

As most patients had not achieved neutrophil engraftment, none of them received prophylactic administration of TMP-SMX. A negative influence of TMP-SMX is a concern of clinicians engaged in HSCT because the prophylactic administration of TMP-SMX inhibits engraftment of hematopoietic stem cells. Prophylactic oral TMP-SMX administration between the transplantation day and neutrophil engraftment is not incorporated into common practice (27). It remains unclear whether TMP-SMX can prevent

S. maltophilia pneumonia and sepsis at the oral prophylactic dose for *Pneumocystis* pneumonia. Moreover, it remains unclear whether high-dose TMP-SMX negatively influences neutrophil engraftment when *S. maltophilia* pneumonia or sepsis develops before engraftment. However, a prompt TMP-SMX-based multidrug combination regimen should be considered to rescue suspected cases of *S. maltophilia* pneumonia in severely immunocompromised patients after HSCT. Further investigation is needed regarding the adequacy of the prophylactic administration of TMP-SMX before neutrophil engraftment after HSCT, particularly CBT, for which the incidence was the highest.

Conclusion

Hemorrhagic *S. maltophilia* pneumonia is rapidly progressive and associated with a high mortality rate in patients with hematologic malignancy. Attention should be particularly paid to the neutropenic phase early after HSCT or prolonged neutropenia due to engraftment failure. A prompt TMP-SMX-based multidrug combination regimen should be considered to rescue suspected cases of *S. maltophilia* pneumonia in these severely immunosuppressed patients. Considering the early mortality of our cohort, the prevention and early diagnosis of hemorrhagic *S. maltophilia* pneumonia will require further investigation.

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