Effect of Recombinant Human Granulocyte Colony-Stimulating Factor on Combination Therapy with Aztreonam and Clindamycin for Infections in Neutropenic Patients with Hematologic Diseases

Keisuke TOYAMA1), Makoto YAGUCHI1), Hideaki MIZOGUCHI2), Michihiko MASUDA2), Akio URABE3), Yasuo IKEDA4), Isao AOKI5), Takuro SHINBO6), Atsushi TOGAWA7), Kunitake HIRASHIMA8), Yasusada MIURA9), Shunichi HIROSE10), Nobuyoshi TSUROUKA11), Mitsuhiro OMINE12), Masahide KAMAKURA13), Tsunehiro SAITO14), Shigeru ARIMORI15), Nobuo AOKI16), Yasunobu KURAISHI17), Hisamaru HIRAI18), Shigetaka ASANO19), Mayumi MORI20), Tatsuo SHIRAI21), Yoshitomo MUTO22), Yasusuke ONOZAWA23), Takeo NOMURA24), Kenshi SUZUKI25), Toshiteru OSHIMA26), Kazuo MOTOYOSHI27) and Fumimaro TAKAKU28)

1)First Department of Internal Medicine, Tokyo Medical College  
2)Department of Hematology, Tokyo Women’s Medical College  
3)Department of Hematology, Kanto Teishin Hospital  
4)Department of Internal Medicine, School of Medicine, Keio University  
5)The Second Department of Internal Medicine, Kyorin University School of Medicine  
6)The Second Tokyo National Hospital  
7)Department of Internal Medicine, Division of Hematology, International Medical Center of Japan  
8)First Department of Internal Medicine, Saitama Medical School  
9)Department of Hematology, Jichi Medical School  
10)Department of Internal Medicine, Juntendo University School of Medicine  
11)Department of Hematology, Showa University School of Medicine  
12)Department of Hematology, Showa University Fujigaoka Hospital  
13)First Department of Internal Medicine, Teikyo University School of Medicine  
14)Third Department of Internal Medicine, Teikyo University School of Medicine  
15)Fourth Department of Internal Medicine, Tokai University School of Medicine  
16)First Department of Internal Medicine, Faculty of Medicine, Tokyo Medical and Dental University  
17)Third Department of Internal Medicine, Jikei University School of Medicine  
18)Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo  
19)Department of Internal Medicine, Tokyo University Institute of Medical Science  
20)Department of Hematology, Tokyo Metropolitan Geriatric Hospital  
21)First Department of Internal Medicine, Toho University  
22)Department of Hematology, Toranomon Hospital  
23)Department of Hematology, Tokyo Metropolitan Komagome Hospital

Correspondence to: Keisuke TOYAMA M.D.  
First Department of Internal Medicine, Tokyo Medical College, 6-7-1 Nishi-shinjuku, Shinjuku-ku, Tokyo 160, Japan.

感染症学雑誌 第70巻 第12号
Abstract

The present multicenter study was performed to evaluate the effect of recombinant human granulocyte-colony stimulating factor (rhG-CSF) on combination therapy using aztreonam (AZT) and clindamycin (CLDM) to treat severe infection in neutropenic patients with hematologic diseases. Forty-three neutropenic patients with infections (rhG-CSF group) were treated with AZT (2 g) and CLDM (600 mg) 2–3 times daily as well as rhG-CSF (Lenograstim or Filgrastim: 2–5 μg/kg/day). The clinical efficacy of this regimen was compared to that obtained in 44 febrile neutropenic patients, with hematologic diseases, who received only AZT and CLDM in a previous study (historical control group).

The overall efficacy rate was 69.8% (30/43) in the rhG-CSF group and 65.9% (29/44) in the historical control group. Although the neutrophil count was significantly increased and C-reactive protein tended to be lower in the rhG-CSF group, the daily maximum body temperature profiles of the 2 groups were nearly the same.

These results suggest that rhG-CSF is of little benefit in the treatment of single infectious episodes in neutropenic patients, and that appropriate antibiotic therapy is more important.

Introduction

In patients with hematologic malignancies, as exemplified by lymphoma and acute leukemia, life-threatening infections such as septicemia and pneumonia are not uncommon when severe neutropenia develops due to the underlying diseases or myelosuppression after chemotherapy or radiotherapy.

Identification of the causative pathogens is often difficult in patients who have infections associated with neutropenia, and it is necessary for such infections to be treated empirically with broad-spectrum antimicrobial agents before identification of the causative organisms.

Aztreonam (AZT) is active against aerobic gram-negative bacteria, including *Pseudomonas aeruginosa*, while clindamycin (CLDM) is effective against aerobic gram-positive bacteria and anaerobic bacteria. Therefore, a broad spectrum of antibacterial activity can be provided by using these two drugs in combination, and excellent results have been obtained in patients with various infections.

The combination of AZT and CLDM has also been used to treat infections in patients with neutropenia due to hematologic malignancy. In 1990, we reported on the excellent efficacy of combination therapy with AZT and CLDM for severe infections in patients with hematologic diseases.

Recombinant human granulocyte colony-stimulating factor (rhG-CSF) not only increases the neutrophil count but also enhances leukocyte function. Accordingly, combination therapy with rhG-CSF and antimicrobial agents has been studied in neutropenic animal models and in patients with infections. However, the efficacy of rhG-CSF for treating infections in neutropenic
patients has not yet been confirmed. The present study was undertaken to evaluate the effect of adding rhG-CSF to combination therapy with AZT and CLDM for the treatment of infections in neutropenic patients with hematologic diseases, and the efficacy obtained was compared to that of combination therapy using only AZT and CLDM.

**Subjects**

The subjects of this study were patients with hematologic diseases who were admitted to 27 participating institutions in the 13-month period from March 1992 through April 1993 and met the following criteria.

Febrile neutropenic patients with hematologic diseases who were treated by combination therapy with AZT and CLDM between August 1988 and November 1989 at the same institutions severed as historical controls.

(1) **Inclusion criteria:**
- A temperature of $\geq 38^\circ$C due to septicemia (or suspected septicemia) or other overt signs of a severe infection, such as pneumonia.
(2) **Neutropenia with a neutrophil count $\leq 1,000/\mu l$**
(3) **Exclusion criteria:**
- Antimicrobial therapy within one week before the study.
- Simultaneous administration of anticancer drugs, steroids, gammaglobulin preparations, or other antibiotics (except oral antibiotics such as antifungal agents and sulfamethoxazole/trimethoprim).
- A history of hypersensitivity to AZT or CLDM.
- Severe hepatic or renal dysfunction, or a severe underlying disease indicating a poor prognosis.

AZT and CLDM were respectively administered at doses of 2 g and 600 mg by intravenous infusion twice or three times daily. The duration of treatment was at least 4 days. rhG-CSF (Lenograstim or Filgrastim) was administered at a dose of 2-5 μg/kg/day from the start of antimicrobial therapy.

The daily maximum body temperature, leukocyte count, neutrophil count, and CRP level were determined. The clinical and microbiological efficacies of treatment, as well as adverse reactions, were then evaluated by the Efficacy Evaluation Committee (K. Toyama, MD., M. Yaguchi, MD., H. Mizoguchi, MD., M. Masuda, MD., and I. Aoki, MD.)

Clinical efficacy was classified into the following 4 grades. In patients with pneumonia, changes in CRP and chest X-ray findings were also taken into consideration.

- **Excellent:** Body temperature $<37^\circ$C, and symptoms as well as the laboratory findings improved by the 4th day of treatment.
- **Good:** Body temperature $<37^\circ$C, and symptoms as well as the laboratory findings improved after more than 4 days of treatment.
- **Fair:** Fever improved, but body temperature was not $<37^\circ$C. Symptoms and laboratory findings improved after the initiation of treatment.
- **Poor:** Fever unchanged. Symptoms and laboratory findings also unchanged or aggravated, necessitating the initiation of new therapy.

Numerical data were analyzed by the $\chi^2$ test and metric data by Student’s $t$-test. Paired data were analyzed by the paired $t$-test. Values of $p<0.05$ were considered significant.

**Results**

1. Handing of the subjects
Combination therapy with AZT and CLDM plus rhG-CSF was performed in a total of 91 patients (rhG-CSF group).

However, 48 patients were excluded from this group because of protocol violations (e.g., prior administration of rhG-CSF or concomitant use of antifungal or anticancer agents), leaving 43 patients. Of the 250 patients in our previous study of AZT and CLDM therapy, 206 were excluded based on the same inclusion or exclusion criteria as applied to the rhG-CSF group, and the remaining 44 served as historical controls.

2. Clinical characteristics (Table 1)

The mean ages of the rhG-CSF and historical control groups were 45.1 years and 52.6 years respectively. The mean durations of AZT administration were 8.5 and 8.8 days for the respective groups, and the daily doses were 3.9 and 4.9 g. There was a significant difference in daily dose between the rhG-CSF group and the historical control group (p < 0.01). The corresponding values for CLDM were 8.5 and 9.0 days, 1,861 and 2,009 mg.

Concerning the underlying diseases, lymphoma predominated in the rhG-CSF group while acute leukemia was more common in the historical control group (Table 1).

3. Clinical efficacy

Clinical efficacy was determined on the basis of the efficacy rate (the percentage of good or excellent responses).

The efficacy rates determined by the Evaluation Committee were 69.8% and 65.9% for the rhG-CSF and historical control groups, respectively. There was no significant difference between the two groups (Table 2).

Clinical efficacy in relation to the type of infection is presented in Table 3. Efficacy varied

---

### Table 1 Clinical characteristics of the subjects

<table>
<thead>
<tr>
<th></th>
<th>rhG-CSF group</th>
<th>Historical control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>13–75 (45.1±18.1)</td>
<td>16–81 (52.6±16.6)</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>17</td>
<td>28</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td><strong>AZT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of administration (days)</td>
<td>8.5±6.1</td>
<td>8.8±3.8</td>
</tr>
<tr>
<td>Daily dose (g)</td>
<td>3.9±1.3*</td>
<td>4.9±1.4</td>
</tr>
<tr>
<td><strong>CLDM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of administration (days)</td>
<td>8.5±6.3</td>
<td>9.0±3.8</td>
</tr>
<tr>
<td>Daily dose (mg)</td>
<td>1,861±547</td>
<td>2,009±482</td>
</tr>
</tbody>
</table>

p < 0.01

### Table 2 Clinical efficacy

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Response</th>
<th>Efficacy rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Excellent</td>
<td>Good</td>
</tr>
<tr>
<td>rhG-CSF group</td>
<td>43</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>Historical control group</td>
<td>44</td>
<td>11</td>
<td>18</td>
</tr>
</tbody>
</table>

Test: There was no significant difference between the 2 groups.
4. Microbiological efficacy

It is difficult to identify causative pathogens in neutropenic patients with hematologic malignancies, such that evaluation of microbiological efficacy is often impossible. Only patients with positive blood cultures were defined as having definite causative pathogens. Bacteria were eradicated from the blood in all cases, but clinical efficacy was recognized in 4/4 patients in the rhG-CSF group and 3/6 historical controls. Thus, AZT + CLDM appears to have a broad spectrum of activity against gram-positive cocci and bacilli as well as gram-negative bacilli (Table 4).

5. Clinical and laboratory findings

1) Daily maximum body temperature (Fig. 1)

The pretreatment daily maximum body temperature was 38.5 ± 0.6°C in the rhG-CSF group and 38.9 ± 0.7 in the historical control group, showing a significant difference on day 1 of treatment (p < 0.05). The average body temperature was 37.6 ± 0.9 on day 4 and 37.0 ± 0.9°C on day 7 in the rhG-CSF group. In the historical control group, the corresponding values were 37.7 ± 0.9 and 37.2 ± 1.0°C. Body temperature at the end of treatment were 37.3 ± 1.1°C and 37.4 ± 1.3°C, respectively, and there was no significant difference between the rhG-CSF and historical control groups. The body temperature profiles of the two groups were nearly the same.

2) Neutrophil count (Fig. 2)

The pretreatment neutrophil count was 180.3 ± 202.2/μl in the rhG-CSF group and 223.9 ±
rhG-CSF, AZT and CLDM Therapy for Neutropenic Patients

Fig. 1 Comparison of Daily Maximum Body Temperature between rhG-CSF and Historical Control Groups
Daily maximum body temperature in the rhG-CSF group (○) and the historical control group (●). The body temperature was significantly higher in the historical control group on the 1st day of treatment, but there was no difference between the two groups thereafter.

* p<0.05

Fig. 2 Comparison of Neutrophil Counts between rhG-CSF and Historical Control Groups
Neutrophil count in the rhG-CSF group (●) and the historical control group (●). The neutrophil count was significantly higher in the rhG-CSF group than in the historical control group on the 7th day of treatment (3684.0 ± 3815.3 vs 442.4 ± 971.0/μl, ***p<0.001; inter-group t-test), as well as on completion of therapy (3231.8 ± 3490.3 vs 587.8 ± 1087.4/μl).

+ p<0.1
*** p<0.001

310.5/μl in the historical control group. In the rhG-CSF group, the neutrophil count had increased to 902.2 ± 1896.3 by day 4 and to 3684.0 ± 3815.3/μl by day 7 of treatment. In the historical control

平成8年12月20日
gorup, the corresponding values were 370.8 ± 843.8/μl and 442.4 ± 971.0/μl. Neutrophil counts at the end of treatment were 3231.8 ± 3490.3/μl and 587.8 ± 1087.4/μl, respectively, in the rhG-CSF and historical control groups.

There was a significant difference in neutrophil count between the rhG-CSF and historical control groups on day 7 of treatment and at the end of treatment (p<0.01).

3) The mean durations of fever in patients showing a response were 4.27 ± 1.90 days, in the rhG-CSF group, and 4.27 ± 1.89 days, in the historical control group.

4) Efficacy in patients with a ≥20% increase in the neutrophil count (Table 5)

The efficacy rates in patients with a post-treatment neutrophil count increase of ≥20% were 92.9% (26/28) and 82.6% (19/23) in the rhG-CSF and historical control groups, respectively. The corresponding values for the patients with a post-treatment increase of <20% were 25.0% (3/12) and 42.1% (8/19). In both groups, patients with a ≥20% neutrophil count increase showed a significantly higher efficacy rate than patients with a <20% increase (p<0.01). However, the number of patients with a ≥20% increase in neutrophils did not differ significantly between the rhG-CSF and historical control groups.

5) Changes in CRP (Fig. 3)

CRP tended to increase in both groups after 4 days of treatment, but was lower in the rhG-CSF

<table>
<thead>
<tr>
<th>Neutrophil increase</th>
<th>rhG-CSF group</th>
<th>Historical control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>≥ “Good”</td>
</tr>
<tr>
<td>≥20%</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>&lt;20%</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>29</td>
</tr>
</tbody>
</table>

Fig. 3 Comparison of CRP Levels between rhG-CSF and Historical Control Groups
C-reactive protein (CRP) level in the rhG-CSF group (●——●) and the historical control group (●——●). The CRP level on the 4th day tended to be lower (+p<0.1: inter-group t-test) in the rhG-CSF group than in the historical control group, suggesting that the inflammatory process was promptly suppressed by rhG-CSF therapy.
group than in the historical control group on day 4 (8.7 ± 9.2 vs 10.1 ± 6.2) and on day 7 (3.2 ± 3.0 vs 6.1 ± 5.2) of treatment and at the end of treatment (6.5 ± 8.9 vs 6.6 ± 6.4). However, the difference did not reach statistical significance.

6) Influence of rhG-CSF dose on efficacy. The efficacy rate was 78.3% (18/23) in patients receiving rhG-CSF at doses < 120 μg/day and 60.0% (12/20) in those receiving doses ≥120 μg/day. The difference was not significant.

6. Adverse reactions and abnormal laboratory tests

No adverse reactions occurred in the rhG-CSF group. In the historical control group, a skin rash developing in one patient was suspected of being treatment related.

Abnormal liver functions, including elevated GOT, GPT, γ-GTP and serum alkaline phosphatase (ALP), were noted in 3 patients from the rhG-CSF group and 2 from the historical control group. Increases in serum creatinine and BUN were recognized in one patient in the historical control group. All abnormalities showed rapid resolution regardless of whether treatment was continued or discontinued, except in one patient from the rhG-CSF group who showed a persistently high ALP level during treatment. It was generally unclear which agent caused laboratory abnormalities, as 2 or 3 drugs were being administered concurrently. No increases in the leukemic cell count were seen in any of the patients after rhG-CSF administration.

Discussion

Patients with hematologic malignancies, such as lymphoma and acute leukemia, suffer not only from impaired immunity attributable to the disease itself but also have weakened defense mechanisms due to chemotherapy and radiotherapy. In patients with aplastic anemia, neutropenia results from the disease itself and infections such as septicemia are common. Infections arising from neutropenia have a sudden onset and are apt to become severe. In patients with hematologic diseases, the prevention and treatment of infection is thus an important consideration.

Causative pathogens cannot be identified in many patients with infections supervening upon blood dyscrasias, but aerobic gram-negative bacteria, such as P. aeruginosa, Klebsiella sp., and Escherichia coli, are generally regarded as being responsible. On the other hand, aerobic gram-positive bacteria (Staphylococcus sp. and Streptococcus sp.) and fungi have increasingly been detected as causative pathogens in neutropenic patients.

In the treatment of infections complicating hematologic diseases, antimicrobial agents with a broad spectrum of activity against anaerobic bacteria as well as against aerobic gram-negative and gram-positive bacteria are essential, because these patients are prone to rapid deterioration. AZT is active against aerobic gram-negative bacteria, such as P. aeruginosa and E. coli, while CLDM is effective against aerobic gram-positive bacteria, such as Staphylococcus aureus, as well as against anaerobic bacteria. A large amount of information is available concerning combination therapy with these two drugs for infections in patients with various underlying diseases.

rhG-CSF acts specifically on neutrophilic cells to enhance their functions and to stimulate the proliferation and differentiation of myeloid progenitors. It is highly effective for correcting neutropenia, but its clinical value for treating infections has yet to be established. In patients with hematologic diseases, rhG-CSF may reduce the frequency of infection by shortening the duration of neutropenia. It can also decrease the number of patients in whom severe infections necessitate postponement of treatment. When rh-G-CSF is used with antimicrobial agents for the treatment of infections in neutropenic patients, it may increase the efficacy of antimicrobial therapy by enhancing neutrophil function. To evaluate this possibility, we treated patients with infections secondary to hematologic diseases using AZT and CLDM plus rhG-CSF, and the efficacy of this regimen was
compared to that of AZT and CLDM without rhG-CSF obtained in our previous study.

There was no difference in the efficacy rate between the rhG-CSF group and the historical control group. However, when only excellent responses were assessed, the efficacy rate was higher in the rhG-CSF group than in the historical control group (44.2% vs. 25.0%), although the difference did not reach statistical significance. The efficacy rate was higher for patients with increased neutrophil counts than for those without such an increase regardless of the concomitant use of rhG-CSF, and the number of patients with a ≥20% increase in the neutrophil count did not differ significantly between the two groups. Although rhG-CSF had produced a neutrophil count increase by day 7 of treatment, there was little difference in either average body temperature profile or the overall efficacy rate (excellent + good responses/all responses) between the two groups. It is possible that the rhG-CSF group was actually composed of 2 subgroups, one showing a marked response to rhG-CSF exceeding that to antibiotics alone and another showing no response to rhG-CSF or even a worse response than that to antibiotics alone. Since the average of 2 such subgroups was defined as the response of the rhG-CSF group in this study, differences in body temperature profile, duration of fever, and overall efficacy between the rhG-CSF and historical control groups would be minimal. The slight difference between the two groups might be attributable to the mean daily dose of AZT being significantly lower in the rhG-CSF group than in the historical control group. However, an Australian study (a double blind, placebocontrolled trial) of rhG-CSF therapy in 218 patients with chemotherapy-induced febrile neutropenia showed that rhG-CSF reduced the median duration of neutropenia and the time to resolution of febrile neutropenia, but not the duration of fever. Their results are consistent with our present data. It was also recently reported that G-CSF produced no significant difference in septicemia-related mortality in children with leukemia and neutropenia caused by chemotherapy.

Combination therapy with AZT and CLDM is effective in patients with neutropenia. In the present study, the efficacy rates for patients with severe neutropenia (initial neutrophil count <500/μl) were 68.4% (26/38) and 63.9% (23/36) in the rhG-CSF and historical control groups, respectively, and the corresponding values in those with an initial neutrophil count <200/μl were 72.0% (18/25) and 64.3% (18/28). These data indicate that AZT and CLDM used in combination are highly effective even in patients with profound neutropenia.

It appears that there was a time lag between the initiation of rhG-CSF therapy after the onset of infection and the observed increases in neutrophil counts, which depended on the degree of bone marrow impairment. Provided that the antimicrobial agents administered during this period were appropriate, the infection resolves despite neutropenia. Thus, administration of rhG-CSF would not necessarily be worthwhile during single infectious episodes. However, because neutropenia showed early recovery after rhG-CSF administration, it is reasonable to assume that such therapy effectively prevents the recurrence of infection.

Our results suggest that rhG-CSF should be given prophylactically to neutropenic patients with aim of preventing infection.

Conclusions

1. Investigation of treatment responses in single infectious episodes in neutropenic patients with hematologic diseases revealed the efficacy rate to be no higher in the group receiving aztreonam and clindamycin plus rhG-CSF than in the group receiving only the two antimicrobial agents.

2. rhG-CSF produced marked increases in the neutrophil counts of patients with severe infection secondary to neutropenia, though the efficacy rate in patients receiving aztreonam and clindamycin plus rhG-CSF did not exceed that in those receiving antibiotics alone, perhaps because
recovery from neutropenia took several days or did not occur in some patients receiving rhG-CSF.

3. It appears that selection of appropriate antimicrobial agents is important in treating the infectious complications of hematologic diseases, and that aztreonam and clindamycin are effective for this purpose whether or not rhG-CSF is concomitantly administered.

References

血液疾患に併発した好中球減少性感染症に対するAztreonamと
Clindamycin併用療法におけるG-CSF併用効果

東京医科歯科大学・第一内科
外山 千助2) 矢口 唐雄3)
東京女子医科大学・血液内科
満口 秀昭2) 増田 道彦3)
関東通信病院・血液内科
浦部 晶夫2)
慶應義塾大学・内科
池田 康夫2)
杏林大学医学部・第二内科
青木 功3)
国立東京第二病院
新保 卓郎
国立国際医療センター・内科
戸川 敦
埼玉医科大学・第一内科
平嶋 邦猛
自治医科大学・血液科
三浦 恭定
順天堂大学・内科
藤瀬 俊一
昭和大学・血液内科
鶴岡 延熹
昭和大学第三内科
長谷川 薫江
帝京大学医学部・第一内科
鎌倉 正英
帝京大学医学部・第三内科
齋藤 恒博
東海大学・第四内科
有森 茂

東京都歯科大学・第一内科
青木 延雄
東京慈恵会医科大学・第三内科
倉石 安庸
東京大学医・第三内科
平井 久丸
東京大学医学研究所・内科
浅野 茂隆
東京老人医療センター・血液内科
森 映由美
東邦大学・第一内科
白井 達男
虎ノ門病院・血液内科
武藤 良知
都立駒込病院・内科
小野沢康輔
日本医科大学・第三内科
野村 武夫
日本赤十字医療センター・血液内科
鈴木 憲史
日本大学板橋病院・第一内科
大島 年照
防衛医科大学校・第三内科
元吉 和夫
国立国際医療センター・総長
高久 史磨

1)代表世話人, 2)世話人, 3)判定委員

要 旨
本多施設試験では血液疾患を有し、感染症を併発した好中球減少疾患患者を対象として、Aztreonam, Clindamycin併用療法におけるrecombinant human granulocyte colony-stimulating factor (rhG-CSF)の効果を検討した。感染症を併発した好中球減少症患者43例にaztreonam (2g)および clindamycin (600mg)を1日2〜3回投与し、同時にrhG-CSF (LenograstimまたはFilgrastim;2〜5μg/kg/day)を投与した。この療法がもたらす臨床効果を、以前の試験で2種類の抗生物質のみによる治療を受けた血液疾患に伴う熱性好中球減少症患者44例に認められた臨床効果 (rhG-CSF非投与群)と比較した。全
体としての有効率は rhG-CSF 投与群が 69.8% (30/43)，rhG-CSF 非投与群が 65.9% (29/44) であった。rhG-CSF 群では投与 7 日目に好中球数が有意に増加し，また CRP がより低い値を示す傾向が見られたものの，平均最高体温の推移に関し
ては 2 群間でほとんど差を認めなかった。
以上の結果から，好中球減少症患者に発生した感染の 1 エピソードの治療には，rhG-CSF はそれほど有効とは言えず，適切な抗生物質療法のほうがより重要と考えられた。