

—Report on Experiments and Clinical Cases—

Usefulness of Bronchoalveolar Lavage for the Diagnosis and Treatment of Refractory Pneumonia in a Patient with Kostmann Syndrome, a Severe Congenital Neutropenia

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Abstract

An 11-year-old girl with Kostmann syndrome developed refractory pneumonia. Culture of oral discharge, throat-swab specimens, and blood could not identify the causative organism, and systemic antimicrobial therapy failed to achieve improvement. We then performed diagnostic bronchoalveolar lavage (BAL) and culture of BAL fluid (BALF) yielded *Pseudomonas aeruginosa*. Therapeutic BAL using gentamicin produced a striking improvement of her pneumonia.

Conclusion: In immunocompromised children with pneumonia, BAL helps to identify the causative organism. If the patient is unresponsive to systemic antimicrobial therapy, BAL using antimicrobial agents is also worth trying. (J Nippon Med Sch 2001; 68: 340—343)

Key words: Bronchoalveolar lavage (BAL), Kostmann syndrome

Introduction

In immunocompromised children with pneumonia, identification of the causative organism using bronchoalveolar lavage (BAL) can be important for providing appropriate treatment. We performed BAL in an 11-year-old girl with Kostmann syndrome who had refractory pneumonia. The causative organism was determined and therapeutic lavage using gentamicin was carried out, resulting in striking improvement of her pneumonia.

Case Report

The patient was an 11-year-old girl who had been followed up at our department since infancy because

of frequent bacterial infections, including stomatitis, otitis media, cervical lymphadenitis, furunculosis, acute bronchitis, pneumonia, and pulmonary abscess due to Kostmann syndrome. She developed fever, cough, and gingivostomatitis, and was admitted for treatment of pneumonia diagnosed from a chest X-ray film (**Fig. 1**).

On admission, the temperature was 38.0°C, and she had labial and oral ulcers as well as a reddened pharynx.

Auscultation revealed coarse crackles posteriorly in the upper to middle right lung field. Laboratory findings were as follows. The peripheral leukocyte count was 10,000/μl, with 0/μl of neutrophils, 150/μl of eosinophils, 3,100/μl of lymphocytes, and 6,750/μl of monocytes, indicating a compensatory increase of monocytes. C-reactive protein (CRP) was increased

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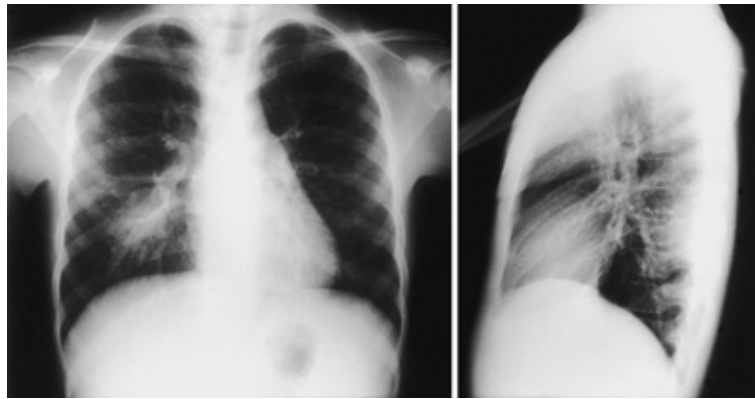


Fig. 1 Chest radiography on admission: Consolidation was observed in the right S⁶ and S¹⁰ segments, and band opacity was seen in the left S⁸ segment.

to 16.3 mg/dl, and because of her frequent infections, the immunoglobulin levels might be high (IgG, 3,360 mg/dl; IgA, 551 mg/dl; and IgM, 485 mg/dl). Microbiological examination of oral secretions, throat-swab specimens, and blood was negative.

After admission, the patient received daily treatment with granulocyte colony-stimulating factor, but neutrophils did not increase in either the peripheral blood or bone marrow. Following the intravenous administration of amikacin, panipenem plus betamipron, and fluconazole, her fever subsided and the CRP level decreased. When treatment was discontinued, however, her fever recurred and CRP increased. Chest X-ray films showed repeated improvement and exacerbation of pneumonia in parallel with the inflammatory response. Since opacities on chest X-ray film persisted even after the CRP level was normalized, BAL was performed at two months after admission for investigation of the causative organism and treatment.

Examination of the airways with a fiberoptic bronchoscope (Olympus BF 3 C 20) under general anesthesia revealed no evidence of inflammation such as redness of the bronchial mucosa or increase of secretions. There was also no pus due to the absence of neutrophils. To perform BAL, the tip of the bronchoscope was wedged into the entrance of the right B⁶ bronchus, and 18 ml (0.7 ml/kg) of physiological saline was injected, followed by immediate aspiration to collect BAL fluid (BALF). After this procedure was repeated three times, 20 ml of physiological saline containing 24 mg of gentamicin was injected and aspirated immediately. The right B¹⁰ bronchus was treated similarly.

Table 1 shows the BALF findings. The BALF was watery and slightly turbid, and the recovery rate was markedly lower for the right B⁸ bronchus. Cultures of BALF samples yielded *Pseudomonas aeruginosa*. Cytologic examination showed lymphocytosis and a neutrophil count of 0%, as in the peripheral blood. The level of IgG, IgA, and IgM were all increased. Transient infiltrates at the sites of lavage and fever were the only complications of BAL. There was subsequent rapid improvement of the chest X-ray findings and the patient could be discharged (**Fig. 2**).

Discussion

Kostmann syndrome is a condition with a poorly defined etiology in which there is failure of the normal maturation of promyelocytes or myelocytes in the bone marrow, causing susceptibility to fatal pyogenic infections from early infancy. Treatment of this syndrome with granulocyte colony-stimulating factor preparations has become common and can prolong survival, but the incidence of myelodysplastic syndrome and acute myelocytic leukemia is also believed to have increased¹. The present patient also developed acute myelocytic leukemia after discharge and is now undergoing chemotherapy. Although pneumonia has occurred again, no opacities have been seen at the sites treated by BAL for 9 months.

In the management of immunocompromised children with pneumonia, BAL is a safe and rapid first-line investigation that has probably reduced the need for open lung biopsy²⁻⁵. In the present patient,

Table 1 BALF findings

Segments lavaged : rS ⁶ , rS ¹⁰
Quantity recovered (ml)/injected (ml) : rS ⁶ ; 3.8/54.0 (7.0%), rS ¹⁰ ; 32.0/54.0 (59.3%)
Appearance : Watery and slightly turbid
Investigation for the causative organism * :
Bacterial cultures : <i>Pseudomonas aeruginosa</i> .
Fungal cultures : Negative.
Viral isolation and cultures : Negative
Cytologic investigation * :
Total number of cells : 14×10^4 /ml.
Differential cytology : Macrophages 61.0%, Lymphocytes 39.0%, Neutrophils 0.0%, Eosinophils 0.0%, Basophils 0.0%
Cytopathology * : class I, no malignancy, lymphocytic alveolitis suspected.
The morphology of lymphocytes is relatively stable and chronic-stage pneumonia is compatible.
Immunoglobulins * : IgG 296 μ g/ml, IgA 13 μ g/ml, secretory IgA 6.5 μ g/ml, IgM 3 μ g/ml, IgE < 5.0 IU/ml
Antibiotic injection : When the examination was completed, gentamicin 24mg/20ml (saline) was injected into each of the rS ⁶ and rS ¹⁰ segments, and then aspirated.

*The data are for the BALF recovered from the rS¹⁰ segment due to low recovery from the rS⁶ segment.

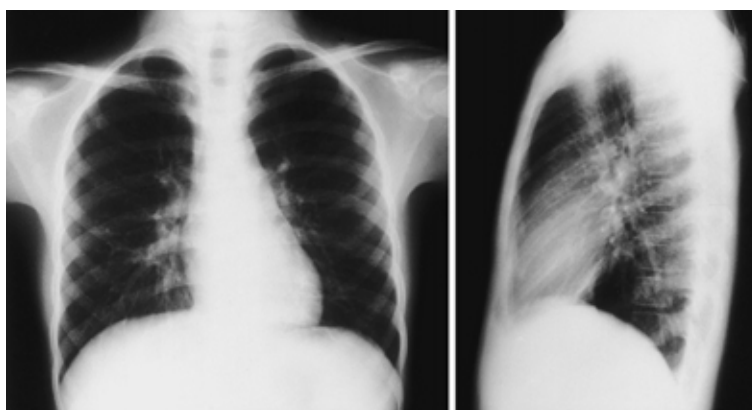


Fig. 2 Chest radiography one month after BAL: The consolidation in the right S⁶ and S¹⁰ segments almost disappeared. The band in the left S⁸ segment remained unchanged throughout the course before and after admission, suggesting the shadow was change caused by previous pneumonia and pulmonary abscess.

although microbiological examination of oral secretions, throat-swab specimens, and blood was negative, culture of BALF yielded *Pseudomonas aeruginosa*, showing the usefulness of BAL for identifying the causative organism. The very low rate of BALF recovery from the right B⁶ bronchus may have been related to the anatomy of this bronchus and possibly to trapping of the injected fluid in the peripheral damaged lung tissue. On cytologic examination of BALF, the percentage of neutrophils was 0% due to the presence of Kostmann syndrome, while the percentage of lymphocytes were increased above normal for chil-

dren⁶, suggesting the influence of infection. Regarding immunoglobulins, although no reference values for BALF in children are available, the IgG, IgA, and IgM levels were markedly higher than those reported in adults⁷, probably compensating for the lack of phagocytosis by neutrophils.

The indications for therapeutic BAL are limited and include the removal of proteinaceous substances in patients with pulmonary alveolar proteinosis and removal of mucous plugs in status asthmaticus⁸, but BAL using antifungal agents has also been reported in a child with cystic fibrosis complicated by pneumo-

nia⁹. Katoh et al. performed BAL using latamoxef in 14 adult patients with bacterial pneumonia, achieving cure in 12 patients without using any concomitant systemic antibiotics. They also stated that BAL using gentamicin and latamoxef cured three patients who had refractory pulmonary infections unresponsive to systemic antibiotics¹⁰. They suggested that lavage with antibiotics achieved much higher local concentrations than the minimum inhibitory concentration for the causative organism, and that the antibiotics exert an antibacterial effect on the lesions even after the drugs are transferred to the blood. In our patient, although we did not measure the sputum and blood concentrations of gentamicin after BAL, the marked improvement in the chest radiographic findings after lavage was presumed to be because the gentamicin in the fluid injected for BAL acted directly on pneumonic foci, causing the death of *Pseudomonas aeruginosa*. In the management of pneumonia in immunocompromised children, the identification of the causative organism using BAL is important, and patients unresponsive to systemic antimicrobial therapy as our patient worth undergoing therapeutic BAL using antimicrobial drugs.

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