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Case report

Inhaled vancomycin-induced allergic reaction in decontamination of respiratory tracts for allogeneic bone marrow transplantation

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Summary:

A 34-year-old male suffered from an allergic reaction after inhalation of decontaminating drugs for BMT. Clinical challenge tests were undertaken to determine the causal drug. It was found that vancomycin hydrochloride (VCM) repeatedly induced dyspnea, fever, hypoxia, eosinophilia, and elevation of CRP. Therefore, clindamycin (CLDM) was used instead of VCM for decontamination of patient respiratory tract. Although complete decontamination of the respiratory tract was not achieved during the leukocytopenic period, BMT was successful, and there were no life-threatening infectious complications. Although inhaled VCM-induced allergic reaction may be a very rare complication in the BMT setting, careful clinical attention should be paid to such patients.

Keywords: vancomycin; inhaled allergic reaction; chronic myelogenous leukemia; bone marrow transplantation; decontamination

Vancomycin hydrocloride (VCM) is widely used for decontamination during bone marrow transplantation (BMT) in Japan. We encountered a patient with chronic myelogeneous leukemia who suffered from an inhaled VCM-induced allergic reaction in the above setting. Such an allergic reaction is thought to be very rare, and there have been no previous reports of such a case. We finally diagnosed his VCM-induced allergic reaction by an inhalation challenge test. Although this complication may be very rare, more attention should be paid to clinical symptoms and signs in such cases.

Case report

A 34-year-old male was found to have chronic myelogenous leukemia in June 1994. He received 1500 mg of hydroxycarbamide and 3×10^6 units of interferon α daily. In October 1995, he was admitted for allogeneic BMT from an HLA-identical donor from the Japan Marrow Donor Program. Decontamination for BMT started from 11 days before BMT, using tobramycin (TOB), VCM and amphotericin B (AMPH-B) for the respiratory tract, and VCM and fluconazole for the gastrointestinal tract. Four days after the start of decontamination, he complained of dyspnea, nonproductive cough and high fever. CRP levels and leukocyte counts were elevated. Hypoxia (PaO_2 = 46.0 mmHg) was also detected on arterial blood gas analysis (Figure 1). Respiratory function tests were normal although these were not examined on 30 October 1995 and 14 January 1996 because of severe clinical symptoms. Chest roentgenography also showed normal findings on frequent examinations. Initially, the diagnosis was thought to be an early-phase interstitial pneumonitis due to opportunistic infection. Therefore, decontamination was stopped and the BMT was postponed. High-dose methyl-prednisolone pulse therapy (1000 mg for 3 days) was started; his symptoms cleared and the hypoxia recovered to 82.0 mmHg. After the patient had completely recovered decontamination was restarted from 12 days before BMT, using the same drugs as previously. Two days after restarting decontamination, the same symptoms reappeared, and arterial blood gas analysis revealed severe hypoxia of 59.3 mmHg. These symptoms completely disappeared 4 days after administration of antibiotics and methyl-prednisolone pulse therapy.

The possibility of a drug-induced allergic reaction was suggested by the fact that both of the episodes occurred about 30 min after inhalation of the decontamination drugs and the fact that eosinophilia was observed on both occasions. Intracutaneous reactions and drug-induced lymphocyte stimulation tests for the three inhaled drugs showed no positive results. Therefore, with the informed consent of the patient, inhalation challenge tests were performed. Two VCM inhalation tests were performed, and notable hypoxia, eosinophilia and elevation of CRP were observed each time, although these symptoms and signs disappeared soon after cessation of inhalation (Figure 2). Inhalation of TOB and AMPH-B, however, did not induce such adverse effects with the exception of a slight increase in eosinophils after the TOB challenge. These results suggested that VCM was the causal drug in the inhaled allergic reaction. Therefore, VCM inhalation was changed to CLDM, which has a similar antibiotic spectrum to that of VCM. VCM orally was also changed to tosufloxacin. The third decontami-

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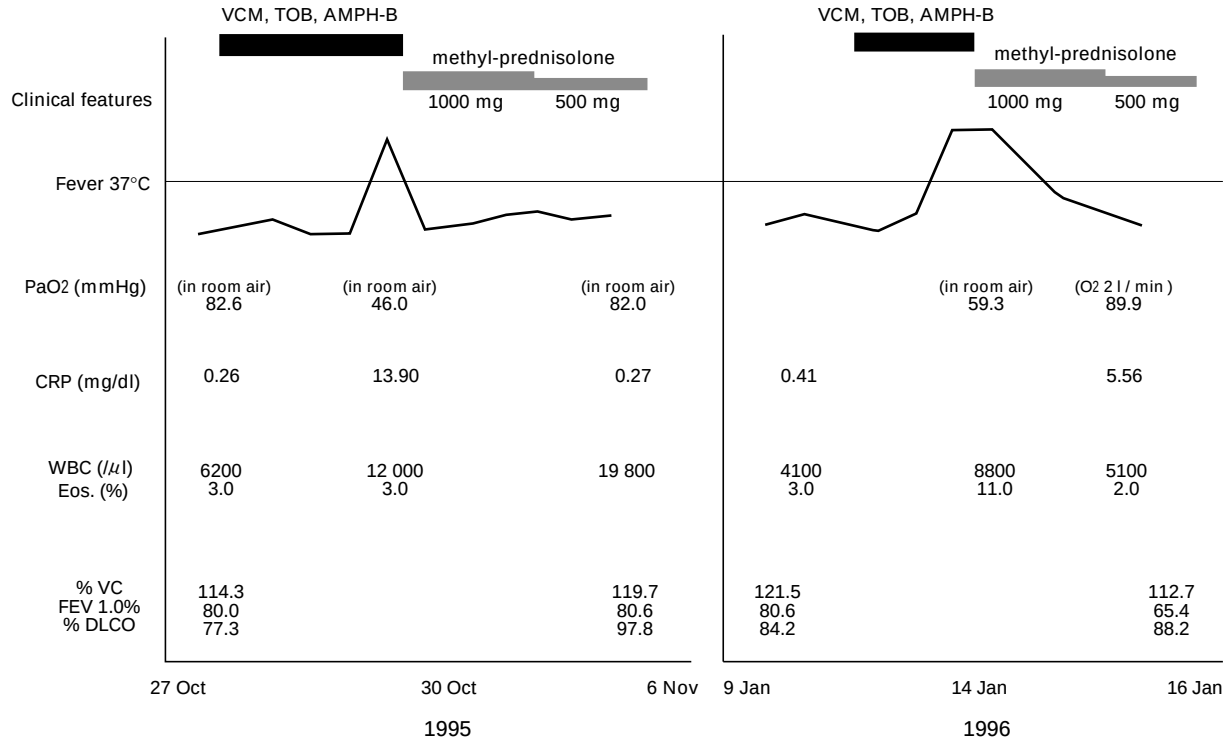

Figure 1 Clinical course of inhaled drug-induced allergic reaction.

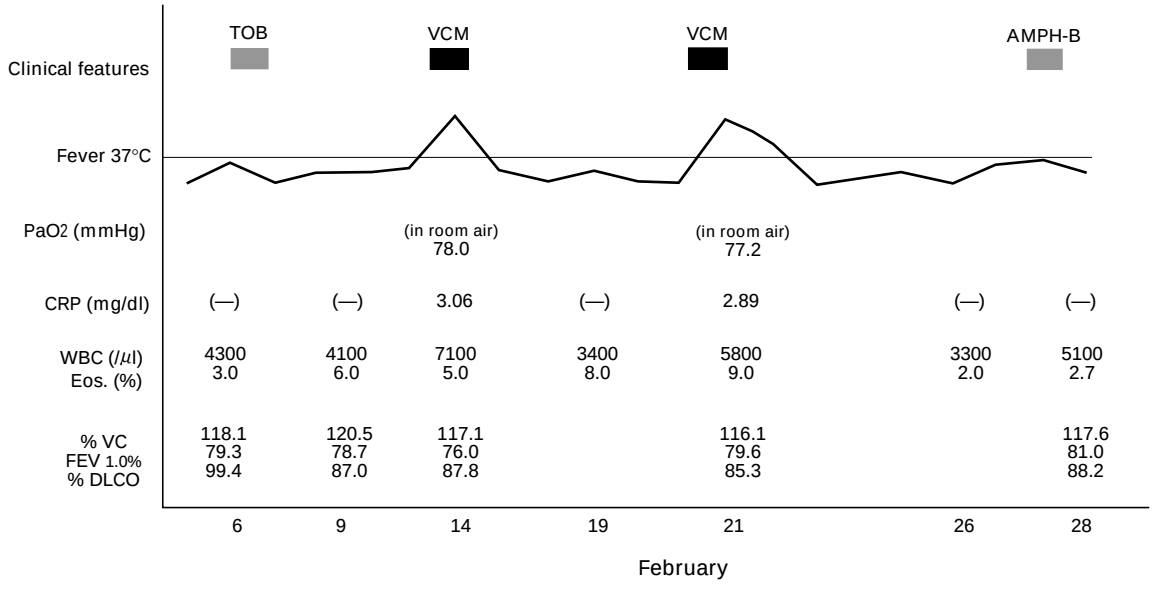

Figure 2 Results of challenge tests by tobramycin, vancomycin and amphotericin B.

nation was successfully performed with no adverse respiratory symptoms. Conditioning for BMT consisted of busulfan at 4 mg/kg orally in divided doses, daily for 4 days (total dose, 16 mg/kg) and cyclophosphamide at 60 mg/kg once daily i.v. for 2 days (total dose, 120 mg/kg). GVHD prophylaxis was with cyclosporin A at 3 mg/kg and short-term methotrexate. BMT was performed in March 1996. Leukocytes increased to 1000/μl day 16 after BMT. Although some normal flora were present in the respiratory tract during the neutropenic period, the patient showed no serious infectious complications in the respiratory tract. Hematopoietic recovery was good and he had no severe GVHD or infections.

Discussion

In Japan, VCM is widely used for decontamination of respiratory and gastrointestinal tracts during BMT and has a good antibiotic effect especially on anaerobic bacterias.[1]

Drug hypersensitivity eruptions and drug-induced fever with VCM are rare, even in cases of infusion-related side-effects.[1] In our hospital, VCM-containing decontamination methods are used for all BMT patients.[2] This inhaled VCM-induced allergic reaction was the first case in our hospital, and there is no report of such a complication in the literature. In this case, challenge tests for suspected drugs were found to be the most useful procedure for diagnosing the inhaled allergic reaction. Although inhalation challenge tests to determine the causative drugs in allergic reactions are generally thought to be dangerous, these tests are more reliable than intracutaneous tests or drug-induced lymphocyte stimulation tests.[1,3] Although the reason why inhaled VCM-induced allergic reaction in this patient is not clear, the high molecular weight of VCM (MW: approximately 1500 dalton), possibly antigenic itself, may be one of the factors.[4,5]

The change of decontamination drug from VCM to CLDM was beneficial in this case. CLDM, which has a similar anti-anaerobic potential to that of VCM was the most suitable candidate.[6] In the present case, although complete decontamination of the respiratory tract was not achieved, the patient did not suffer severe respiratory infections even during neutropenia. Recently, it has been shown that allogenic peripheral blood stem cell transplantation[7] or the administration of G-CSF accelerate leukocyte recovery and decrease the risk of severe infectious complications early after BMT. Therefore, it is conceivable that VCM will not be necessary for BMT decontamination in the near future.

We report a very rare case of a VCM-induced allergic reaction during decontamination for BMT, which was clearly shown by inhalation challenge tests. This study indicates that physicians should pay careful attention to respiratory symptoms and signs in the BMT setting.

References

1 Fink JN. Hypersensitivity pneumonitis. *J Allergy Clin Immunol* 1984; **74**: 1–9.
2 Ishikawa T, Hashino S, Toyoshima N *et al*. Decontaminations and early infection in bone marrow transplants (in Japanese). *J Germfree Life Gnotobiol* 1991; **1**: 111–116.
3 Richerson HB, Bernstein IL, Fink JN *et al*. Guidelines for the clinical evaluation of hypersensitivity pneumonitis. *J Allergy Clin Immunol* 1989; **84**: 839–844.
4 Davies PD. Drug-induced lung disease. *Br J Dis Chest* 1969; **63**: 59–70.
5 Wilhelm MP. Vancomycin. *Mayo Clin Proc* 1991; **66**: 1165–1170.
6 Kislak JW. The susceptability of *Bacteroides fragilis* to 24 antibiotics. *J Inf Dis* 1972; **125**: 295–299.
7 Tanaka J, Kasai M, Imamura M, Asaka M. Clinical application of allogeneic peripheral blood stem cell transplantation. *Ann Hematol* 1995; **71**: 265–269.