Pseudomonas aeruginosa Endocarditis in a Patient with Acute Leukemia: Probable Etiologic Role of Central Line-Induced Endocardial Damage

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Introduction

Right-sided endocarditis due to *Pseudomonas aeruginosa* is almost exclusively a disease of intravenous drug abusers¹⁻⁴⁾. Recently, however, we have experienced a case of acute septic right-sided infective endocarditis caused by *P. aeruginosa* in a patient with acute leukemia who had a distant infected site with associated bacteremia.

Case Report

A 29-year-old woman was admitted to the Kanazawa University Hospital on July 16, 1986, with a three-week history of malaise and low-grade fever (Fig. 1). Physical examination disclosed a temperature of 38.4°C, scattered petechiae over the extremities and trunk, generalized lymphadenopathy, and a grade II-III/VI systolic ejection murmur at the base of the heart. The electrocardiogram showed sinus tachycardia. Laboratory values included a hematocrit of 29%, a leukocyte count of 18100/mm³ (46% lymphocytes and 54% blast forms), a platelet count of 25000/mm³, and serum lactate dehydrogenase (LDH) of 8241 IU/l. Bone marrow biopsy and aspiration as well as lymphnode biopsy revealed predominance of blast cells, leading to the diagnosis of acute myelomonocytic leukemia.

Directly after admission, she was placed on cefmetazole and gentamicin, followed three days later by amphotericin B on an empirical basis. Prior to initiation of antileukemic therapy, she had a central venous catheter inserted via the right subclavian vein, with the tip resting in the right atrium, as seen on chest radiograph (Fig. 2). Her temperature returned toward normal, but fever related to the administration of amphotericin B occurred occasionally. On the third day of catheter insertion, continuing arrhythmia developed, and both supraventricular and ventricular premature contractions were noted on the electrocardiogram. Results of echocardiography were not contributory. Lidocaine and deslanoside in combination proved effective.

On August 2, she complained of pain in the external genitalia, with relapse of fever to 39.0°C. There was a tender, erythematous, edematous, subcutaneous nodule with a blackish central area of necrosis, which spontaneously sloughed, leaving a dark red base. *P. aeruginosa* (serogroup E) was isolated from the

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Fig. 1 Clinical course of a patient with acute leukemia who developed right-sided *Pseudomonas aeruginosa* endocarditis.

Abbreviations: AMMoL, acute myelomonocytic leukemia; CMZ, cefmetazole; GM, gentamicin; FOM, fosfomycin; AMK, amikacin; AMPH, amphotericin B; DNR, daunorubicin; NCS, neocarzinostatin; BH-AC, enocitabine; PDN, prednisolone; WBC, white blood cells; AGC, absolute granulocyte count; Plats, platelets; and LDH, lactate dehydrogenase (normal range, 205—415 IU/l).

lesion, and three days later from the peripheral blood. The antibacterial regimen was switched to fosfomycin and gentamicin, to which the isolate was sensitive. The leukocyte count was $200/\text{mm}^3$, with 100% lymphocytes. The local infectious process seemed to regress gradually with a favorable rise in her granulocyte count (the leukocyte count of $1200/\text{mm}^3$, with 89% granulocytes on August 18). The serum LDH level was also decreased to 459 IU/l. She continued, however, to develop temperature elevations as high as 39.5°C , and have multiple positive blood cultures, although fosfomycin was continued at an increased dose with substitution of amikacin for gentamicin. No apparent inflammation was observed at the exit site or along the subcutaneous tunnel of her central catheter. Her heart murmur seemed to change somewhat, but echocardiographic studies failed to reveal any abnormality. In the middle of August, bilateral facial nerve palsy, lumbago, and muscle weakness, followed by leukemia cutis, developed. The serum LDH level was gradually elevated, exceeding 1000 IU/l. On August 26, the second course of antileukemic therapy was initiated. Her condition rapidly deteriorated, and she died while in septic shock on September 2.

At autopsy, leukemic infiltrates were found in multiple organs. Examination of the heart showed right-sided cardiac vegetations (Fig. 3). Neither acquired valvular nor congenital heart lesions were observed. Many tiny vegetations were rather evenly distributed in the right atrium and ventricle and on the tricuspid valve, with small clusters found in some areas. On the other hand, vegetations on the pulmonic valve and in the main pulmonary artery were somewhat larger than those present in the former

Fig. 2 Chest X-ray on September 1 (taken in the supine position) showing the tip of a central venous catheter (arrows), which is located deep in the right atrium. Mild interstitial abnormalities throughout the lung fields can be seen with pleural effusions.

Fig. 4 Section of vegetation on atrial surface. The vegetation is covered with a fibrin layer and contains fibrin and many masses of bacteria without associated inflammatory cell response. The underlying endocardium appears intact. Hematoxylin and eosin, original magnification, $\times 100$.

Fig. 3 Section of right heart showing vegetations (arrows). Vegetations diffusely found in the right side of the heart are smaller in the atrium and ventricle and on the tricuspid valve than in the main pulmonary artery and on the pulmonic valve. A, right atrium; B, tricuspid valve; C, right ventricle; D, pulmonic valve; and E, main pulmonary artery.

Fig. 5 Section of right middle lobe of lung showing a septic embolic infarct with hemorrhage. A: small artery, and E: embolus containing masses of bacteria. Hematoxylin and eosin, original magnification, $\times 100$.

regions. Microscopically, vegetations which contained many masses of microorganisms were covered with a fibrin layer (Fig. 4). Sections of the lungs revealed multiple small septic embolic infarcts (Fig. 5). Autopsy specimens were not cultured, nor was the catheter tip.

Discussion

Endocarditis is a rare complication of *P. aeruginosa* bacteremia, which most frequently occurs in

granulocytopenic patients with hematologic malignancies, especially acute leukemia³⁻⁹). Resolution of *P. aeruginosa* bacteremia in such patients depends largely upon a rise in the granulocyte count during therapy^{9,10}). It is therefore suggested that the clinician suspect endocarditis in any acute leukemia patient with *P. aeruginosa* bacteremia which persists despite a favorable rise in the granulocyte count, as seen in our patient.

Garrison and Freedman¹¹) showed that placement of a polyethylene catheter in the right side of the rabbit heart leads to the development of small sterile vegetations at points of contact between the catheter and endocardium. Furthermore, Durack and Beeson¹²) demonstrated that the sterile vegetations thus produced can easily be colonized by microorganisms injected intravenously, serving as the source of persistent bacteremia. On the other hand, Rowley *et al.*¹³), and Tsao and Katz¹⁴) reported that right-sided infective endocarditis may occur as a consequence of flow-directed pulmonary-artery catheter- or central venous catheter-induced endocardial damage with concurrent or subsequent bacteremia. This mechanism of pathogenesis may be regarded as the human analogue of the animal model just mentioned.

In our patient, the development of both supraventricular and ventricular arrhythmias soon after insertion of the central venous catheter suggested that, as seen on chest radiograph (Fig. 2), the catheter tip remained in a position just at the entrance to or within the right ventricle, leading to endocardial damage inducing susceptibility to infective endocarditis. This was also indicated by the fact that small clusters of vegetations were found in some parts which were considered to be the probable points of contact between the catheter and endocardium, although many tiny vegetations were rather evenly distributed on the surfaces of the right atrium and ventricle.

Indwelling central venous catheters are often used to facilitate the care of patients with cancer undergoing intensive chemotherapy^{15,16}). On the other hand, the frequency of *P. aeruginosa* bacteremia in patients with acute leukemia remains almost unchanged despite the introduction of potent antipseudomonal β -lactam antibiotics¹⁷). It should be kept in mind, therefore, that right-sided endocarditis due to *P. aeruginosa* may supervene with increasing frequency in granulocytopenic patients who have indwelling central venous catheters.

In conclusion, we described an unusual case of acute septic right-sided infective endocarditis caused by *P. aeruginosa* in a patient with acute leukemia who developed extracardiac gangrenous cellulitis with associated bacteremia. The risk of hematogenous seeding of the endocardium damaged by a central venous catheter was discussed.

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急性白血病症例にみられた緑膿菌による心内膜炎 —中心静脈カテーテルによる心内膜損傷の可能性—

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要 旨

29歳、女性の急性白血病患者に対する寛解導入療法中に、緑膿菌による右心系の心内膜炎が経験された。この発症に先駆けて、同一血清群の緑膿菌による菌血症をともなった外陰部の壊疽性蜂巣炎がみられた。中心静脈カテーテルの先端が右心房にまで挿入され、挿入後に不整脈が出現していた。それで、カテーテル先端による心内膜の損傷

部に血栓が形成され、このなかに流血中の菌が取り込まれて、心内膜炎の発症に至ったと推測された。剖検肺には、敗血症性塞栓による微小梗塞巣が多発していた。緑膿菌による心内膜炎は急性白血病症例に非常にまれであるが、顆粒球数の回復にもかかわらず菌血症が持続するときは本症を疑って精査が必要である。