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Analysis of Host Factor related to Patient's Mortality due to Viridans Streptococcal Bacteremia

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In their study entitled "Factors associated with infective endocarditis and predictors of three-month mortality in patients with Viridans streptococcal bacteremia" [1], Suh et al. suggest that underlying valvular heart disease and persistent bacteremia are independently associated with viridans streptococcal infective endocarditis (VSIE). The authors recommend routine echocardiography in patients who have these conditions. Previous steroid use and immunosuppressive therapy have both been shown to be associated with poor prognosis in patients with viridans streptococcal bacteremia (VSB) [1]. Many studies have shown that viridans streptococci cause various and severe infections [2-4] and play an important role in the etiology of primary bacteremia following immunosuppressive therapy [5]. In light of these findings, there is growing interest among clinicians about viridans streptococci and their role in infection.

Suh et al. reported that previous steroid use and immunosuppressive therapy are independently associated with mortality due to VSB. However, it is difficult to ascertain which specific host comorbidities are linked with increased mortality in VSB because Suh et al. did not specifically identify underlying conditions in patients with a history of steroid use and immunosuppressive therapy. Therefore, the aim of this study was to analyze the relationship between underlying disease, steroid use, chemotherapy, malignancy, infective endocarditis, and comorbidity in patients who died of VSB and compare our results with those of Suh et al.

In this study, of 259 patients diagnosed with VSB between October 2002 and December 2012 in a university-affiliated hospital, 106 patients younger than 18 years were excluded, leaving 153 patients for final analysis. Of these, 19 patients (12.4%) died before the end of the study (Table 1). Of the 19 patients, three (15.8%) had VSIE and two had a history of heart disease (one mitral valvuloplasty and one hypertrophic cardiomyopathy). Of the 19 patients who died of VSB, six (31.6%) took immunosuppressive therapy and, three (15.8%) also took steroids. None of the patients received steroid monotherapy. Of the six patients (31.6%) who had undergone immunosuppressive therapy, four were diagnosed with hematological malignancy and two were diagnosed with solid tumors (one lung cancer and one pancreatic cancer). Four of the 19 patients who died (21.1%) were diagnosed with diabe-

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Table 1. The mortality cases of viridans streptococcal bacteremia in a tertiary university hospital

Case No	Age	Sex	Underlying disease	IE	Steroid	ChemoTx agents	Co–infection
1	57	F	MS, MVR, DM	MV	–	–	Cholecystitis
2	46	M	MR, MVR, ICH	–	–	–	–
3	65	M	MS, MVR, CHF		–	–	–
4	59	M	HCMP, HTN	MV,AV	–	–	–
5	69	F	Atrial fibrillation, ICH	–	–	–	–
6	72	F	DM, HTN, RA	–	–	–	–
7	33	M	MDS, allo–BMT (2MA)	–	Yes[a]	Busulfan, methotrexate, cyclophosphamide	
8	70	M	Plasma cell leukemia	–	Yes[a]	Thalidomide	Pneumonia
9	37	F	Multiple myeloma, auto-PBSCT (10MA), DM	–	–	Fludarabine, melphalan	–
10	50	F	Relapsed AML (M1), allo-BMT (11MA)	–	–	Mitoxantrone, etoposide, ara–C	Bed sore
11	60	F	Cervical cancer	AV	–	–	Brain abscess
12	59	F	Lung cancer, DM	–	Yes[a]	Docetaxel	–
13	23	M	Pancreatic cancer	–	–	Gemcitabine	–
14	62	M	Klatskin tumor	–	–	–	Pneumonia
15	47	M	Alcoholic liver cirrhosis	–	–	–	–
16	78	M	CKD, stroke, abdominal aortic aneurysmal rupture	–	–	–	–
17	57	M	ICH	–	–	–	–
18	89	M	None	–	–	–	Pneumonia
19	25	M	None	–	–	–	Brain abscess

AML, acute myeloid leukemia; AV, aortic valve; BMT, Bone marrow transplantation; CHF, congestive heart failure; CKD, chronic kidney disease; DM, diabetes mellitus; HCMP, hypertrophic cardiomyopathy; HTN, hypertension; ICH, intracranial hemorrhage; IE, infective endocarditis; MA, months ago; MDS, myelodysplastic syndrome; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; MVR, mitral valve replacement; PBSCT, peripheral blood stem cell transplantation; RA, rheumatoid arthritis.
[a]Previous steroid use defined as ≥ prednisolone 15 mg/d for more than one week.

tes mellitus, two (10.5%) had cerebral hemorrhage, and two (10.5%) had no underlying disease.

In this study, the proportion of patients with VSIE to patients who died from VSB is higher than that reported by Suh et al. (15.8% vs. 8.3%). Because two of the three patients diagnosed with VSIE in the present study had underlying heart disease, echocardiography was required to evaluate the presence of infective endocarditis. Mortality due to VSB was high among the immunocompromised patients who received chemotherapy for hematological malignancies or solid tumors. Therefore, extensive assessment and early diagnosis of VSB are necessary in these patients. Unlike the study by Suh et al., 13 (68.4%) of 19 patients in our study who had not received steroid or immunosuppressive therapy died of VSB. Therefore, it is important to note that mortality is still high in immunocompetent patients.

In conclusion, we recommend appropriate care for VSB patients who have underlying heart disease and immunosuppressed patients (especially after chemotherapy for hematological malignancy or solid tumors) who are currently taking steroids. Moreover, we must keep in mind that VSB occurs in various hosts.

This was a small, single-center, retrospective study and therefore had limitations. Collection of data on a national level, possibly including analyses of large administrative datasets or prospective comparisons, should be performed to confirm these observations.

References

1. Suh YS, Kim MK, Huh JH, Cho OH, Kim JR, Kim S, Bae IG. Factors associated with infective endocarditis and predictors of 3-month mortality of patients with viridans streptococcal bacteremia. Infect Chemother 2012;44:419-25.Bochud PY, Calandra T, Francioli P. Bacteremia due to

viridians streptococci in neutropenic patients : a review. Am J Med 1994;97:256-64.
2. Singh KP, Morris A, Lang SD, MacCulloch DM, Bremner DA. Clinically significant *Streptococcus anginosus* (*Streptococcus melleri*) infections: a review of 186 cases. N Z Med J 1988;101:813-6.
3. Wilson WR, Karchmer AW, Dajani AS, Taubert KA, Bayer A, Kaye D, Bisno AL, Ferrieri P, Shulman ST, Durack DT. Antibiotic treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HACEK microorganisms. American Heart Association. JAMA 1995;274:1706-13.
4. Tunkel AR, Sepkowitz KA. Infections caused by viridians streptococci in patients with neutropenia. Clin Infect Dis 2002;34:1524-9.
5. Shenep JL. Viridans-group streptococcal infections in immunocompromised hosts. Int J Antimicrob Agents 2000;14:129-35.

Reply to Song et al.

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Dear Editor,

We appreciate the comments of Dr. Song et al. [1] related to the underlying conditions associated with mortality in patients with viridians streptococcal bacteremia (VSB). In our original paper, we reported that previous steroid usage and immunosuppressive therapy were independently associated with 3-month mortality in patients with VSB [2]. Dr. Song et al. investigated underlying disease among patients with VSB to analyze the risk factors associated with mortality and to compare the results with our data [1]. In their study, of the 19 died patients due to VSB, six (31.6%) also underwent immunosuppressive therapy, three of those also took steroids. All of the patients who had previously undergone immunosuppressive therapy had either hematological malignancy (four patients) or solid tumors (two patients).

In our analysis, the three-month mortality rate was 21.7% (36 patients) in the patients with VSB. Of these patients who died, 15 (41.7%) had previously undergone immunosuppressive therapy and four patients also used steroids. All the 15 patients had either solid tumors (12 patients) or hematological malignancy (3 patients).

We evaluated the underlying conditions of previous immunosuppressive therapy and steroid usage, instead of underlying diseases (including solid and hematological malignancies) to analyze the predictors of 3-month mortality in patients with VSB. That's because all the patients in our cohort who had undergone immunosuppressive therapy or used steroids also had underlying solid or hematological malignancies. The previous immunosuppressive therapy and steroid usage were more powerful variable than solid and hematological malignancies in the statistical analysis. It has previously been reported that underlying solid tumors were significantly associated with higher 30-day mortality in VSB patients [3]. However, we suggested that high mortality among cancer patients was more likely to be related to immunosuppressive therapy, including antineoplastic chemotherapy, than cancer itself. This is due to the fact that VSB usually occurs in association with mucositis and profound neutropenia due to antineoplastic chemotherapy-related toxicity [4].

Even though VSB occurred in patients with various underlying diseases, including solid tumors, hematological malignancy, and valvular heart disease, we conclude that mortality in patients with VSB is more likely to be associated with underlying conditions such as previous immunosuppressive therapy and steroid usage than underlying disease.

References

1. Song SK, Hwang JH, Chung KM, Lee CS. Infect Chemother 2013;45:462-4.
2. Suh YS, Kim MK, Huh JH, Cho OH, Kim JR, Kim S, Bae IG. Factors associated with infective endocarditis and predictors of 3-month mortality of patients with viridans streptococcal bacteremia. Infect Chemother 2012;44:419-25.
3. Mrazova M, Docze A, Buckova E, Bucko L, Kacmarikova M, Grey E, Korcova J, Koprnova J, Saboova Z, Beno P, Karvaj M, Svetlansky I, Ondrus A, Benca J, Taziarova M, Rudinsky B, Krcmery V Jr. Prospective national survey of viridans streptococcal bacteraemia risk factors, antibacterial susceptibility and outcome of 120 episodes. Scand J Infect Dis 2005;37:637-41.
4. Shenep JL. Viridans-group streptococcal infections in immunocompromised hosts. Int J Antimicrob Agents 2000;14:129-35.