

Dear editor Lian-Sheng Ma,

Response for the reviewer comments:

Reviewer #1:

1. This article reports that vegetation shedding occurs in patients, but there is only imaging evidence. If the patient undergoes autopsy, it is expected to provide the corresponding evidence.

(Answer) That is an important point. Unfortunately, the patient did not undergo an autopsy or surgery because he had several comorbidities, including elderly, chronically ill, fragility, end-stage renal disease, and chronic obstructive pulmonary disease. It is a limitation that there is no evidence other than imaging findings to diagnose infective endocarditis. However, infection signs, such as fever and leukocytosis, are less common in patients with end-stage renal disease, probably due to uremia-related impaired cellular host defenses (Eur Heart J 28;2307-2312). Furthermore, frequent administration of empirical antibiotics in hemodialysis patients may increase the likelihood of no microbial growth. We described them as challenges to the diagnosis and treatment of hemodialysis patients in the discussion section (on page 9, line 18-21). Nevertheless, it is no doubt that the patient had sepsis, judging by his metabolic acidosis, hemodynamic collapse, delayed leukocytosis and pneumonic infiltration. In fact, it could be problematic to apply strictly the Duke criteria for diagnosing infective

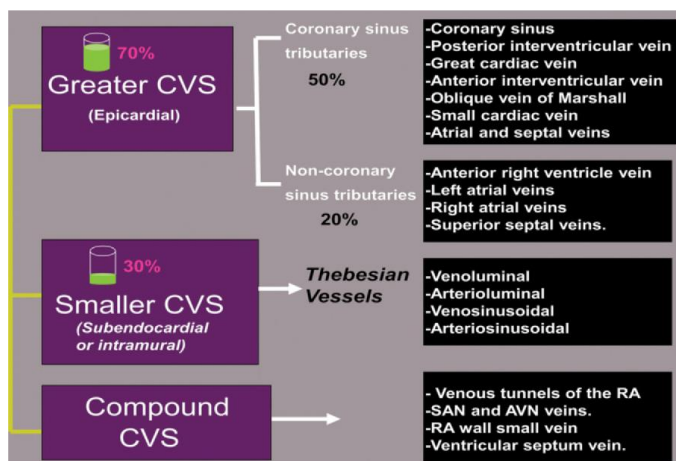
endocarditis in patients with end-stage renal disease. This might also be why imaging modalities for early detection of infective endocarditis are needed more in immunocompromised patients than in the general population. In addition, several previous cases have been diagnosed as infective endocarditis without pathologic confirmation [in Table (manuscript), Kumar, Gill, Theodoropoulos, Kwan, and Fournet's cases were diagnosed with infective endocarditis based on blood culture results].

2. As a case report and literature review, when summarizing this disease, the description of the diagnosis and treatment of this disease is not complete enough, and it is expected to be further modified.

(Answer) We further described the differences in diagnosis and treatment between vegetation and thrombosis of the CS, as your comment (on page 7, line 25 – page 8, line 21). In addition, we detailed the patient's clinical course (on page 7, line 1-9).

3. 90% of the venous blood of the heart drains into the right atrium through the coronary sinus, while it is described in this paper as The CS (Coronary Sinus) is a structure that receives approximately 60% of the total cardiac venous supply and drains into the right atrium.

(Answer) Masood et al. [StatPearls Pub: Treasure Island (FL), 2020; PMID, 29939583] and Ramsaran et al. (South Med J 1996; 89: 531-3) explained that the venous drainage of the heart mainly consists of two systems: coronary sinus (60%) and anterior cardiac veins (40%), and both systems are anatomically connected. They also described that there is a third minor system the thebesian vessels that drain directly into all chambers of the heart; thebesian vessels sometimes drain up to 50% of the total cardiac venous return (J Exp Med 1927;47:293). Saremi et al. (Radiographics 2012;32:E1-E32) dictated that the cardiac veins are divided into two groups: tributaries of the greater coronary venous system [70%; coronary sinus (50%) and non-coronary sinus tributaries (20%)] and tributaries of the lesser coronary venous system (30%; consists of the thebesian vessels). Based on these reports, we described that the CS is a structure that receives approximately 60% of the total cardiac venous supply.



Reviewer #2:

1 The patient was on regular hemodialysis, therefore, the level of renal function and immune system should be shown when he was transferred to the authors' hospital.

(Answer) We appreciate your recommendation. The laboratory findings were added to the manuscript (on page 5, line14-15).

(revised) *Laboratory tests revealed a white blood cell count of 8780 / μ L (neutrophils: 78%), C-reactive protein level of 1.6 mg/dL (normal range <0.5 mg/dL), procalcitonin level of 0.571 μ g/L (normal range <0.046 μ g/L), **creatinine level of 5.6 mg/dL (glomerular filtration rate by the modification of diet in renal disease study equation = 10 ml/min/1.73m²), and brain natriuretic peptide level of 124 ng/L (normal range <100 ng/L).***

At the time of admission in our hospital, vital signs of the patient were unstable (blood pressure of 85/40 mmHg, and heart rate of 110/min), his mental state was confused, and severe metabolic acidosis was observed. Nevertheless, there were no significant infectious signs, such as fever (body temperature, 36.5 °C) and leukocytosis (white blood cell count, 8780 / μ L). Leukocytosis occurred several days after treatment began. We estimated that these clinical findings might be caused by compromised cellular host defenses.

2 The chest radiography of the patient revealed a large right pleural effusion, so when a chest tube was inserted at the site of pleural effusion, the culture of pleural effusion was necessary and the culture result might be helpful to the treatment.

(Answer) The culture of pleural effusion was negative. We added the finding in the case presentation section as your recommendation (on page 6, line 1-2).

(revised) There was no growth of microorganisms on pleural fluid culture.

LANGUAGE QUALITY

(Answer) We revised the manuscript according to the reviewers' comments, and then edited it again through the English language editing company *Editage*.

CERTIFICATE OF ENGLISH EDITING

This document certifies that the paper listed below has been edited to ensure that the language is clear and free of errors. The edit was performed by professional editors at Editage, a division of Cactus Communications. The intent of the author's message was not altered in any way during the editing process. The quality of the edit has been guaranteed, with the assumption that our suggested changes have been accepted and have not been further altered without the knowledge of our editors.

TITLE OF THE PAPER

Coronary Sinus Endocarditis in a Hemodialysis Patient: A Case Report and Review of the Literature

AUTHORS

HUIJEONG HWANG

JOB CODE

KHNMC_269_2



Signature

Vikas Narang

Vikas Narang,
Chief Operating Officer,
Editage

Date of Issue
February 23, 2021

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Worldwide request@editage.com +1 (833) 979-0081 www.editage.com	Japan submissions@editage.com +81 0120-50-2967 www.editage.jp	Korea submit- korea@editage.com 02-3479-4396 www.editage.co.kr	China tblao@editage.cn 400-005-6056 www.editage.cn	Brazil contact@editage.com +55 (0) 200474773 www.editage.com.br	Taiwan submit@editage.com 02 2657 0096 www.editage.com.tw
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EDITORIAL OFFICE'S COMMENTS

The authors need to provide the written informed consent signed by the patient.

(Answer) A written informed consent form signed by the patient's legal guardian has been sent to you.