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Jin-Lei Wang Editor-in-Chief
World Journal of Clinical Cases

Dear Editors:

We wish to re-submit the manuscript titled “Percutaneous Balloon Venoplasty Successfully Treats Disdialysis Syndrome Caused by Pacemaker Leads-Related Superior Vena Cava Syndrome with Chylothorax after Bacteremia.” The manuscript ID is 87717.

We thank you and the reviewer for your thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions. I look forward to working with you and the reviewer to move this manuscript closer to publication in the *World Journal of Clinical Cases*.

The manuscript has been rechecked and the necessary changes have been made in accordance with the reviewer’s suggestions. These changes are indicated by text in the yellow line at the last of this letter. The responses to all comments have been prepared and attached herewith.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,
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Response to Reviewer:#1

The authors are thankful to this reviewer for their insightful and constructive comments. The reviewer clearly has high levels of both expertise and experience in the field, and their insights for improving this manuscript are greatly appreciated.

1. This case report offers a detailed account of a rare clinical presentation of superior vena cava (SVC) syndrome leading to chylothorax and dialysis insufficiency in an elderly patient with a pacemaker. While intriguing, it does not present any original findings or propose new hypotheses about the pathogenesis, diagnosis, or management of this condition. As a single case study, it serves primarily to document an unusual constellation of clinical findings, not to report new discoveries that advance scientific understanding. The authors leverage existing knowledge to diagnose and treat their patient's condition. However, they do not conduct experiments or propose novel theories. While valuable for its clinical description, this report does not include major new insights or innovations.

Response: Thank you for your important comments. We believe that our case is novel because to the best of our knowledge, no case of an 'acute' SVC syndrome resulting in disdialysis in a patient on maintenance haemodialysis after pacemaker implantation has been reported. Furthermore, it is noteworthy that no recurrence occurred after treatment with percutaneous old balloon angioplasty (POBA) alone (i.e., without pacemaker removal, reimplantation, or stenting) during the 1 year of traceable follow-up in our case. The SVC syndrome has been reported to have developed slowly in several patients on dialysis; however, in our case, it interestingly developed rapidly with disdialysis difficulties. Furthermore, in some previously reported cases, invasive surgery was required when improvement was difficult with antimicrobial agents and anticoagulant therapy. Although endovascular treatment has been pursued in some recent cases, the pacemaker had to be removed prior to stent placement in the occluded area and be reimplanted thereafter. Compared with POBA, this procedure carries a higher risk and exerts a greater burden on older adult patients. In the present case, we performed POBA and minimized the procedural invasiveness as well as medical costs. Our patient was able to undergo stable dialysis without recurrence for approximately one years, during which she only required monitoring.. Accordingly, through our case, we would like to emphasize the following: 1) acute-onset SVC syndrome should be considered when acute disdialysis is encountered in patients with pacemakers who are on dialysis and 2) treatment with POBA alone seems

effective for a relatively long time. The following sentences have been added to page 5, lines 12–15, to clarify this: "Compared with the previously reported more invasive approach of PM removal, subsequent stenting, and PM reimplantation, treatment with POBA alone was less invasive and more successful in achieving a good prognosis during the traceable follow-up period."

2. This case report highlights an interesting clinical scenario that has not been frequently described. However, it does not contain major new concepts, techniques, findings, or solutions that significantly advance the field. The authors utilize standard diagnostic tools and conventional therapies to manage their patient. While they competently summarize their clinical approach and outcomes, the conclusions do not propose breakthroughs or major advances beyond what is currently established. As a single case study, this report necessarily has limited scope and impact. It provides a detailed account of an uncommon clinical presentation, but does not present discoveries or innovations that solve pressing problems or provide unique insights into SVC syndrome pathophysiology and care.

Response: Thank you very much for your important comment. We agree that our report may not have detailed any innovations aimed at addressing the pathophysiology of and care for the SVC syndrome. However, we believe that it is important to highlight the possibility that POBA alone can achieve a very good acute response and that older patients with an imminent deterioration of the respiratory status due to disdialysis can be maintained for a relatively longer period of time in the future .This may be more favourable not only in terms of a reduced invasiveness, but also in terms of reduced medical costs. The following sentences have been added to page 5, lines 19–22, to highlight this. "This report details a single case; nonetheless, our observations indicate that POBA alone may not only be less invasive, but may also lead to a reduction in the medical costs. Acute SVC occlusion after PM implantation has been rarely reported, and its long-term outcomes are currently unknown."

3. A key limitation of this report is the lack of long-term follow up, making the lasting outcomes unknown. Further research is needed to better characterize the long-term prognosis and risk of recurrence in patients with pacemaker-associated SVC syndrome after endovascular treatment.

Response: Thank you for this insightful comment. We agree that our report only details a single case with a relatively short-term follow-up of one year. Further research is certainly required to determine the long-term prognosis and risk of recurrence after endovascular treatment in patients with pacemaker-associated SVC syndrome. Accordingly, we have addressed this as a limitation of our report by adding the following sentences to page 5, lines 26-29: "The limitation of this report is that it details both a single case and one year is too short to determine the outcomes. Further cases and long-term follow-up data are needed to evaluate outcomes with POBA alone for PM-associated SVC syndrome."

Response to ***Science editor:***

The manuscript has been peer-reviewed, and it is ready for the first decision.

Response: We greatly appreciate the time and effort devoted to peer reviewing this manuscript.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, please provide and upload the following important documents: Signed Consent for Treatment Form(s) or Document(s), the primary version (PDF) of the consent for treatment that has been signed by the patients in the study, prepared in the official language of the authors' country to the system; CARE Checklist-2016, an important document related to case report writing. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's

authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Response: We greatly appreciate the time and effort devoted to the detailed review of our manuscript and are very thankful for the insightful comments provided for its improvement. We have revised the text and figures as instructed and have also uploaded the necessary documents separately. Please let us know if anything else is required; we will endeavour to address it to the best of our ability.

CasePresentation

Chief complaints:*

The patient complained of malaise and dyspnoea.

History of present illness:

A 96-year-old woman was referred to our hospital for malaise and dyspnoea during dialysis which had otherwise continued smoothly until then.

History of past illness:

She was implanted with a dual-chamber pacemaker (PM) due to the sick sinus syndrome eight years ago. The right ventricular (RV) lead was dislodged on the day after implantation. Fortunately, the patient lived without symptoms in the AAI mode. Three years ago, she was referred for dialysis treatment for end-stage renal failure of an unknown aetiology. A shunt was created in the right upper extremity by anastomosing the brachial artery and the median mesodermal vein.

Personal and family history:*

No family history was available.

Physical examination:*

The body temperature was elevated to 37.5 ° C, and her SpO2 was 94% (oxygen consumption: 5 L/min). No murmurs or lung rales were noted during auscultation, and the breath sounds decreased on the right dorsal side. Visual inspection revealed no oedema of the extremities.

Laboratory examinations:*

An infection was suspected because of the slightly elevated white blood cell count (11400/ μ L) and C-reactive protein level (1.4 mg/dL). Thoracentesis further revealed a foul-smelling, cloudy pleural effusion. Extended-spectrum beta-lactamase-producing *Escherichia coli* (ESBL *E. coli*) were detected in both the pleural effusion and blood cultures. The patient was diagnosed with pyothorax and bacteraemia caused by ESBL *E. coli*; both were successfully treated by placement of a chest drainage tube and by administration of intravenous meropenem and clindamycin for 11 days. The pleural effusion decreased gradually, and a negative blood culture of ESBL E. coli was confirmed.

Imaging examinations:*

Chest radiography and computed tomography (CT) revealed a massive right pleural effusion (Figure. 1). Echocardiography revealed an ejection fraction of 66.3% without asynergy, a trans-tricuspid valve regurgitant pressure gradient of 11.3 mmHg, no significant valvular disease, and no vegetation. Thus, acute heart failure and infectious endocarditis were ruled out.

Progress during hospitalization

On day 4 of admission, despite the course of the treatment, the pleural effusion increased rapidly again and the respiratory condition worsened. A milky-white pleural effusion without any foul odour was observed through the chest drainage tube (Figure. 2). Moreover, the blood pressure dropped excessively during dialysis. This made the patient unbearably fatigued during every dialysis session, although dialysis was attempted by regulating the slow ultrafiltration rate or by catecholamine administration. We decided to increase the dry weight (DW) from 36.5 kg to 38–39 kg due to the disdialysis syndrome. Interestingly, even under this condition, leg oedema was not observed and the brain natriuretic peptide (BNP) level decreased from 202 pg/mL upon admission to 139 pg/mL. Contrarily, the upper body oedema worsened (Figure. 3). Due to the localised oedema and the course of the BNP level, the superior vena cava (SVC) syndrome was suspected. Contrast-enhanced CT (CECT)

revealed severe stenosis of the SVC and a highly developed collateral circulation in the abdominal wall vein (Figure. 4). No malignant tumours were observed. The pleural effusion had a high triglyceride level of 559 mg/dL and a low total cholesterol level of 54 mg/dL, indicating chylothorax.[2]

MULTIDISCIPLINARY EXPERT CONSULTATION (optional):

The differential diagnoses included transudative pleural effusion, exudative pleural effusion, haemothorax, pyrothorax, and chylothorax. However, the effusion was milky white without any foul odour, and a bacterial culture was negative; thus, the patient was diagnosed with chylothorax. The causes of chylothorax may be traumatic or non-traumatic; however, the patient had no history of trauma and had not travelled overseas. Furthermore, she had no history of tuberculosis, and cavitary lesions were absent on CT. Systemic findings were not suggestive of sarcoidosis or amyloidosis. CECT revealed no malignant disease, even near the thoracic duct. Echocardiography revealed no evidence of heart failure.

FINAL DIAGNOSIS:*

Therefore, chylothorax was considered to have been caused by the SVC syndrome.

TREATMENT:*

SVC recanalization by removal of the dislodged RV lead was considered; however, it was deemed too high-risk because the patient was very old and the RV lead implanted eight years ago could have adhered strongly to the innominate vein. Furthermore, thrombolysis was considered potentially ineffective because the patient had received anticoagulation therapy thrice a week during dialysis. Thus, we decided to perform a catheter intervention. A guide sheath was placed in the right atrium (RA). SVC venography was performed from the RA, but the SVC was not contrasted. SVC venography was also performed from the right internal shunt, and an SVC occlusion was noted. Subsequently, the RA was contrasted from the inferior vena cava via the developed azygos and hemiazygos veins (Figure. 5A). SVC venography from the left forearm vein revealed innominate vein occlusion and a contrasted highly collateral venous circulation in the abdominal wall; however, the SVC and RA were not contrasted (Figure. 5B). The RA pressure (RAP) was low despite the tendency for fluid retention (a/v/m: 1/-4/-2 mmHg). A guidewire was passed through the SVC obstruction, and an angiographic catheter was inserted into the SVC. The SVC pressure was clearly different from the RAP and was extremely high (a/v/m: 30/26/28 mmHg). The localised upper body oedema, lower BNP level despite fluid retention, and chylothorax could be explained by an impaired venous return caused by the SVC occlusion. After confirming the vessel diameter

with intravascular ultrasound, a balloon venoplasty was performed carefully (Figure. 6A). At this moment, the heart rhythm shifted from sinus bradycardia to an atrial paced rhythm, possibly due to a sinus node injury arising from the balloon venoplasty. However, sinus rhythm was recovered a few minutes later. The SVC pressure (a/v/m: 17/15/16 mmHg) and RAP (a/v/m: 12/2/8 mmHg) dramatically decreased and increased, respectively, and each value was approximated. Though both pressures were still high, we considered the venous return to have improved successfully. When venography was performed from the SVC, the blood flowed into the RA directly (Figure. 6B). SVC venography from the left forearm vein revealed that the blood flowing from the left subclavian vein returned to the SVC via the left internal jugular vein retrogradely into the intracranial vein and then through the right internal jugular vein in an antegrade manner (Figure. 6C).

OUTCOME AND FOLLOW-UP:*

After catheter intervention, chylothorax, cyanosis, and upper body oedema improved immediately (Figure. 7). Dialysis was performed stably without catecholamine administration; however, the BNP level markedly increased from 139 pg/mL to 1506 pg/mL due to the increased venous return, resulting in left-sided heart failure. Thus, DW was lowered from 38.0 kg to 33.8 kg. The BNP level decreased to 356.6 pg/mL, and heart failure symptoms improved. She was discharged from our hospital on the 32nd day after undergoing rehabilitation.

DISCUSSION:*

The SVC syndrome is most commonly caused by malignancy.[2] Alternatively, it is also caused by benign aetiologies, such as PM leads, central venous ports, and vascular access catheters.[3-8] Some reports of chylothorax caused by the occlusion of the thrombotic subclavian vein, jugular vein, or innominate vein have also been reported.[9,10] The SVC syndrome is considered a 'late' complication of PM implantation; however, in the present case, it was considered to have had an 'acute' onset because the symptoms occurred suddenly after resolution of bacteraemia, although a highly developed collateral circulation was noted. Therefore, SVC obstruction might be caused by thrombosis or by biofilm formation in the PM lead during ESBL E.coli bacteraemia.[11]

An acute disdialysis syndrome caused by the SVC syndrome, as in the present case, is a very rare presentation. Acute SVC occlusion results in localised oedema in the upper body despite the existence of a collateral circulation. Due to PM-associated innominate vein obstruction, venous return from the left upper body flows into the SVC through the collateral circulation in the abdominal wall and the jugular venous reflux (JVR). However, in the present case, due

to the acute occlusion of the SVC, the development of the collateral circulation may not have occurred in a timely manner; accordingly, the venous pressure in the right upper half of the body may have increased rapidly, making left JVR impossible. Consequently, the pressure around the left subclavian vein could have increased, impairing the lymphatic return and causing a rapid increase in the chylous pleural effusion.[10] If the SVC occlusion had a chronic course, a considerable increase in the SVC pressure would not have occurred; acute obstruction of the SVC may have contributed to chylous pleural effusion Acute SVC occlusion resulted in a significant decrease in the cardiac preload. Moreover, dialysis caused a further reduction in the preload, resulting in an excessive blood pressure drop. The PM leads had no vegetation on echocardiography, and we did not remove and observe the leads directly; therefore, the exact cause of the sudden onset of the SVC syndrome remains unknown. Treatments for symptomatic catheter-related SVC syndrome include anticoagulation therapy, percutaneous angioplasty, intravenous stent placement, and surgical removal of the PM lead. Some reports have described venous stent placement performed without recurrence for up to 4 years.[14] However, balloon venoplasty and stent placement may damage the PM leads; thus, it is desirable to remove the PM before treatment and reimplant it thereafter. The risk of complications following lead removal in older adults has been reported to be relatively low[15]; however, it is essential to consider cases individually. In the present case, the RV lead was dislodged previously, and the atrial lead was bent strongly during venoplasty (Figure. 6). The RA lead may have been dislodged and disconnected. In the worst possible case, this could lead to a cardiac arrest because of the simultaneous sinus node injury and RA pacing failure. Therefore, a PM should be placed temporarily before venoplasty.

Prompt revascularization due to the disdialysis syndrome was needed because of a worsening respiratory condition, and we decided to perform SVC revascularization without removing the lead. This treatment was safe and highly effective considering the patient's age. Compared with the previously reported more invasive approach of PM removal, subsequent stenting, and PM reimplantation, treatment with percutaneous old balloon angioplasty (POBA) alone was less invasive and more successful in achieving a good prognosis during the follow-up period. In cases wherein Gram negative bacteria are detected, PM removal is not necessary if the antibiotic therapy is successful; however, when bacteraemia recurs, complete device and lead removal are recommended.[16]

This report details a single case; nonetheless, our observations indicate that POBA alone may not only be less invasive, but may also lead to a reduction in the medical costs. Acute SVC occlusion after PM implantation has been rarely reported, and its long-term outcomes are currently unknown. The SVC syndrome may recur within a relatively short time after

treatment, and stent placement should be considered in such cases. Thus, it is necessary to follow up cases for future relapses. A year has passed since our patient was discharged from the hospital. The limitation of this report is that it details both a single case and one year is too short to determine the outcomes. Further cases and long-term follow-up data are needed to evaluate outcomes with POBA alone for PM-associated SVC syndrome.

CONCLUSION:*

We have reported a case of the disdialysis syndrome secondary to an acute-onset SVC syndrome with chylothorax caused by a suspected PM lead infection. Venoplasty for SVC occlusion significantly improved the patient's condition without postoperative complications. Future follow-up examinations are essential for management of relapses. The SVC syndrome should be included in the differential diagnoses of patients with the disdialysis syndrome undergoing PM implantation or central venous catheterisation following bacteraemia.

References

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Figure 1: Imaging examinations on admission. A: chest radiograph; B: chest computed tomography image. Both images show a massive right pleural effusion.

Figure 2: Chest tube drainage persistently shows a milky white pleural effusion.

Figure 3: Physical findings. A: facial oedema and cyanosis, B: oedema in both upper limbs, and C: no lower limb oedema.

Figure 4: Contrast-enhanced computed tomography of the SVC. A: coronal section of the upper body, B–D: transverse sections of the upper body; the dashed red line represents the SVC. D: the most stenotic site. E: 3D volume-rendered image of the collateral circulation (inside the yellow-dashed rectangle). SVC: superior vena cava.

Figure 5: DSV before venoplasty. A: DSV for the SVC, B: DSV from the left forearm. Red arrow indicates the SVC occlusion site. * represents the azygos vein. ** represents the right ventricle. Yellow arrow indicates an occluded innominate vein. Red dashed line represents a non-contrasted left internal jugular vein. SVC: superior vena cava. DSV: digital subtraction venography.

Figure 6: DSV before and after venoplasty. A: balloon venoplasty for the SVC, B: DSV from the SVC after venoplasty, C: DSV from the left forearm after venoplasty. The red dashed arrow indicates the dislodged right ventricular lead. The red arrow shows the bent RA lead caused by balloon expansion; the blood moved directly into the RA. The blue arrow shows the direction of the blood flow. Some blood flowed into the collateral circulation in the abdominal wall. The yellow arrow shows the jugular venous reflux　SVC: superior vena cava. RA: right atrium, DSV: digital subtraction venography.

Figure 7: Physical findings. A: facial oedema and cyanosis improved after venoplasty; B: oedema in both the upper limbs disappeared after venoplasty; and C: chylothorax improved, and the pleural effusion turned a transparent yellow.