

Erythropoietin resistance reveals ICD lead endocarditis in a hemodialysis patient

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ABSTRACT

Erythropoietin (EPO) resistance in hemodialysis (HD) patients is typically attributed to factors like inflammation or malnutrition, but infectious causes are less commonly considered. We present a unique case where EPO resistance led to the discovery of *Streptococcus gordonii* infection causing cardiovascular implantable electronic device (CIED) lead endocarditis in an HD patient. A 66-year-old female on maintenance HD with an arteriovenous fistula who had heart failure and an implantable cardioverter-defibrillator (ICD) presented with fatigue, weight loss, and EPO resistance. She required monthly transfusions to maintain hemoglobin levels. Transesophageal echocardiography revealed vegetation on the ICD lead and blood cultures confirmed *S. gordonii* infection. After device removal and antibiotic treatment, the patient's condition improved, and she maintained hemoglobin levels with the usual EPO dosing. This case highlights the importance of considering infections in HD patients with refractory anemia and EPO resistance. CIED infections in HD patients may present atypically and can occur without catheters. *S. gordonii* can cause lead infections without traditional risk factors, emphasizing the need for a multidisciplinary approach to managing HD patients with CIEDs. To our knowledge, this is the first case of *S. gordonii* infection in an HD patient.

Resistencia a la EPO revela endocarditis del electrodo del ICD en paciente en hemodiálisis

RESUMEN

La resistencia a la eritropoyetina (EPO) en pacientes en hemodiálisis (HD) se atribuye típicamente a factores como la inflamación o la desnutrición, pero las causas infecciosas son menos consideradas. Presentamos un caso único en el que la resistencia a la EPO condujo al descubrimiento de una infección por *Streptococcus gordonii* que causó endocarditis del electrodo de un dispositivo electrónico implantable cardiovascular (DEIC) en una paciente en HD. Una mujer de 66 años en HD de mantenimiento con una fístula arteriovenosa que tenía insuficiencia cardíaca y un desfibrilador cardioversor implantable (DCI) presentó fatiga, pérdida de peso y resistencia a la EPO. Requirió transfusiones mensuales para mantener los niveles de hemoglobina. La ecocardiografía transesofágica reveló vegetaciones en el electrodo del DCI y los cultivos de sangre confirmaron la infección por *S. gordonii*. Tras la extracción del dispositivo y el tratamiento antibiótico, la situación de la paciente mejoró y mantuvo los niveles de hemoglobina con la dosificación habitual de EPO. Este caso destaca la importancia de considerar infecciones en pacientes en HD con anemia refractaria y resistencia a la EPO. Las infecciones de DEIC en pacientes en HD pueden presentarse de manera atípica y pueden ocurrir sin catéteres. *S. gordonii* puede causar infecciones del electrodo sin factores de riesgo tradicionales, enfatizando la necesidad de un enfoque multidisciplinario para manejar pacientes en HD con DEIC. Hasta donde sabemos, este es el primer caso de infección por *S. gordonii* en un paciente en HD.

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INTRODUCTION

Erythropoietin (EPO) resistance poses a significant challenge in hemodialysis (HD) patients, often linked to inflammation, malnutrition, and hyperparathyroidism¹. However, infectious etiologies are less frequently recognized but can have critical implications². This report presents a unique case where EPO resistance uncovered *Streptococcus gordonii* infection leading to cardiovascular implantable electronic device (CIED) lead endocarditis in an HD patient.

This is the first reported case of *S. gordonii* infection in an HD patient, highlighting the need for high suspicion of infections in patients with refractory anemia and CIEDs. We aim to present this case to discuss several vital teaching points on managing HD patients with CIED infections.

CASE REPORT

A 66-year-old female patient on thrice-weekly HD via a left arteriovenous fistula (AVF) for two years had a history of diabetes, coronary artery disease, heart failure, and ICD implantation four years ago. She presented with fatigue, weight loss, and EPO resistance over the past four months, requiring monthly transfusions to maintain hemoglobin levels. Despite maximal EPO dosing and proper iron indices, she needed at least two units of transfusions monthly to keep hemoglobin above 7 mg/dL. Five months ago, she underwent an endoscopy for dyspepsia. She was admitted for further evaluation.

Physical examination revealed a weak thrill on the AVF and low-grade fever (37.5-37.9 °C) unrelated to HD sessions. She had severe periodontal disease with recent teeth loss. Her ICD pocket site was non-tender. Iron, B12, folate, and copper deficiencies were ruled out. Laboratory results showed an elevated C-reactive

protein of 80 mg/dL (normal 0-5 mg/dL) and a recent hemoglobin level of 8 g/dL post-transfusion.

Transthoracic echocardiography (TTE) showed an ejection fraction of 45% with no valve vegetations but an ICD lead in the right atrium. Transesophageal echocardiography (TEE) revealed vegetation on the ICD lead (fig. 1). Simultaneously, blood cultures grew *S. gordonii*, confirming CIED infection.

The patient had no central lines that could be associated with bacteremia. Our two potential culprits were her severe periodontal disease and the endoscopy she had undergone. She was treated with sulbactam-ampicillin, and the ICD was removed. Appropriate dental treatment was provided. Following device removal and two weeks of IV antibiotics, she was completely healed.

Her ICD control revealed no ventricular tachycardia (VT) episodes in four years. Given the lack of VT demonstration and her ejection fraction over 35%, we decided not to re-implement the ICD.

Six months post-treatment, she regained weight and maintained hemoglobin levels of 10.5-11.5 g/dL with usual EPO dosing. She had no worsening heart failure symptoms.

DISCUSSION

Here we present a case of ICD lead endocarditis of a hemodialysis patient causing EPO resistance completely healing with device removal and antibiotics. Exploration for EPO resistance, the main reason the patient was referred to us in the first place, revealed the infection.

EPO resistance is defined as the failure to elevate hemoglobin levels with standard or maximal doses of EPO, given that iron indices are standard and other micronutrients such as B12, folate, and others are not deficient. 5-10% of all hemodialysis patients are likely affected by this condition. Inadequate dialysis, chronic inflammation, hyperparathyroidism, drugs, malignancies, several other factors, and rarely not easily recognizable infections are blamed for EPO resistance. However, in 1/3 of the cases, an apparent reason cannot be established¹⁻³. Our case again proves that EPO resistance may be caused by a subacute/chronic infection such as CIED lead endocarditis.

We were unable to trace the etiology of *S. gordonii* in our patient. We hypothesize that her severe periodontal disease, combined with her endoscopic procedure, caused a transient bacteremia and resulted in endocarditis. Current guidelines do not recommend routine antibiotic prophylaxis before endoscopy for patients with CIEDs⁴. However, HD patients can be more vulnerable than the normal population; antibiotic prophylaxis before specific procedures should be an area of further interest for this patient group.

Cardiovascular implantable electronic devices include permanent pacemakers (PM), ICD, and cardiac resynchronization ther-

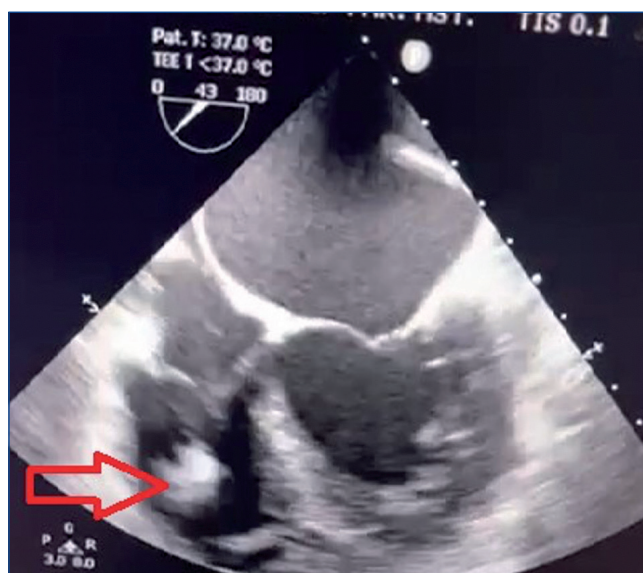


Figure 1. Transesophageal echocardiography showing vegetation attached to ICD lead (arrow).

apy (CRT). CIEDs are employed for heart failure with low ejection fraction, arrhythmia, and other indications⁵. Patients on hemodialysis (HD) frequently have cardiac problems that may require CIEDs. Recent studies suggest that 6-10% of all HD patients have CIED implanted⁶. Furthermore, when a CIED infection is present, those patients face a worse prognosis with increased mortality, more frequent urgent device removals, and an increased duration of hospitalization⁷. The most critical factor in precipitating CIED infection in this cohort of patients seems to be tunneled catheters⁸. The best way to tackle this issue is to refrain from HD catheters. The placement of the AVF contralateral to CIED is highly suggested. This was not the case for our patient, resulting in poor AVF function. We were fortunate that we did not have to re-implement the CIED. Another measure for patients who already have CIEDs that need renal replacement therapy can be switching to or starting with peritoneal dialysis (PD). For patients without a chance of a viable AVF or PD, CIEDs with epicardial leads or leadless pacemakers can be the solution⁹.

Echocardiography guidelines recommend initially evaluating patients with suspicious infectious complications associated with central lines and CIEDs with a combination of transthoracic and transesophageal echocardiography but not the initial alone¹⁰. Positron emission tomography should be pursued whenever needed since echocardiography cannot readily differentiate thrombus, infected material, and intracardiac masses in some cases⁵. In our case, blood cultures rendered PET unnecessary since *Streptococcus gordonii* was repeatedly reported for CIED-related or unrelated endocarditis^{11,12}.

The most frequently responsible organisms for CIED infections are gram-positive species like *S. aureus* and *S. epidermidis*, often associated with tunneled catheter infections¹³. *S. gordonii* is an opportunistic pathogen generally found in the oral cavity which causes infection in those with poor dental hygiene, periodontal disease, and foreign bodies such as CIED or artificial valves. This selective infectious pattern is better explained by the bacteria's ability to form biofilms on medical devices¹⁴.

The novelty of this case lies in the fact that *S. gordonii* caused a lead infection in an HD patient without a catheter, suggesting that *S. gordonii* can cause CIED infections even without traditional risk factors such as central venous catheters. To our

knowledge, *S. gordonii* has not been reported in hemodialysis patients but was reported in several episodes of PD peritonitis. Some of those PD patients also had poor dental status as the culprit^{15,16}.

American Heart Association guidelines on CIED treatment are unambiguous. Any CIED that is associated with lead or heart valve infections must be removed as immediately as possible. Failure to use this approach may increase mortality and hospital stays several fold. On the ground that the device is removed, proper antibiotics should be employed for at least 10-14 days⁴.

However, a cohort of patients like those with PM dependency will need re-implantation of the CIED. Fortunately, that was not the situation for our case; we thought the ICD was unnecessary since her EF was over 35% and she had not developed a VT attack in four years, so we decided not to re-implant the ICD. Furthermore, her AVF was created after ICD implantation but, unfortunately, to the ipsilateral side. Device removal also solved this AVF site selection problem. However, if we were obliged to re-implant the CIED, we should have chosen the patient's right side for the ICD pocket⁹.

CONCLUSION

EPO resistance can be the presenting sign of subacute CIED endocarditis. Rare pathogens should not be missed. Managing HD patients with CIEDs requires a multidisciplinary approach and a high index of suspicion to avoid disastrous results.

Conflict of interest

Written consent has been obtained from the patient. The authors declare no conflict of interest.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Grammarly professional and Chat-GPT 4 in order to detect grammar mistakes and provide a better English for the readers. After using this tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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