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Case Report

Elusive Enemy and a Great Mimicker: Cardiac Sarcoidosis as a Cause of Advanced Heart Failure, a Case Report

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Abstract

Major advances have been made in the treatment of chronic heart failure in recent years, leading to further improvements in patient prognosis. In addition, advanced diagnostic tools, particularly cardiac imaging, allow more accurate characterization of the diseased myocardial tissue, enabling the use of specific treatments. The etiological diagnostic approach is therefore fundamental to optimize patient management but can sometimes be difficult because cardiac imaging findings can be misleading or non-specific. We report a case of rapidly progressive advanced heart failure with clinical and imaging features characteristic of cardiac sarcoidosis. Recognition of this uncommon presentation of heart failure will help clinicians avoid diagnostic delays which are detrimental to the patient's overall outcome. This report also discusses the specific challenges encountered during the care of a Jehovah's Witness patient requiring advanced heart failure therapies. There is limited data in this setting and the case illustrates specific challenges that are encountered when caring for patients who require advanced heart failure therapies but refuse allogenic blood or blood product transfusions based on religious beliefs.

Key Words: advanced heart failure; cardiac sarcoidosis; cardiomyopathies; case report; diagnosis; heart failure; jehovah's witness; palliative care

Abbreviations

ACS, CRT-D, CS, HF, HFrEF, HT, ICD, ICU, LGE, LOT-CRT, LV, LVEDD, LVEDVi, LVEF, MINOCA, MRI, PFO, S-ICD

ACS - Acute Coronary Syndrome

CRT-D - Defibrillator with cardiac resynchronization therapy

CS - Cardiac Sarcoidosis

HF - Heart Failure

HFrEF - Heart Failure with reduced Ejection Fraction

HT - Heart Transplantation

ICD - Implanted Cardioverter Defibrillator

ICU - Intensive Care Unit

LGE - Late Gadolinium Enhancement

LOT-CRT - Left bundle branch-Optimized Cardiac Resynchronization Therapy

LV - Left Ventricle

LVEDD - Left Ventricular End-Diastolic Diameter

LVEDVi - Left Ventricular End-Diastolic Volume Index

LVEF - Left Ventricular Ejection Fraction

MINOCA - Myocardial Infarction with Non-Obstructive Coronary Arteries

MRI - Magnetic Resonance Imaging

PFO - Patent Foramen Ovale

S-ICD - Sub-cutaneous Cardioverter Defibrillator

Introduction

The timely diagnosis of heart failure (HF) and the search for specific etiologies is now of paramount importance given the availability of specific therapies on top of guideline recommended therapies based on the four treatment pillars; i.e. beta-blockers, SGLT2-inhibitors, renin-angiotensin-

aldosterone system inhibitors, and mineralocorticoid receptor antagonists [1,2]. This is even more true and crucial in patients presenting either with advanced HF or those with rapidly progressive HF due to delays in starting prognostic medical therapy.

The first ever major international guideline to address cardiomyopathies other than hypertrophic cardiomyopathy recently published, highlights the need for a timely and precise diagnostic process to identify specific etiologies, allowing for the delivery of tailored disease-specific therapies [3]. Besides the genetic component of cardiomyopathy, infiltrative and inflammatory cardiomyopathies such as amyloidosis, sarcoidosis, eosinophilic cardiomyopathy, and hemochromatosis should not be overlooked.

Among these pathologies, sarcoidosis is an inflammatory disease of unknown cause that can present with non-specific cardiac manifestations such as heart failure, ventricular arrhythmias, or impaired atrioventricular conduction [4]. Clinicians must raise the suspicion of cardiac sarcoidosis (CS) to promptly initiate a specific diagnostic work-up and appropriate therapies aimed at suppressing deleterious myocardial inflammation.

We report a case of CS with progressive HF rapidly transitioning into advanced HF, highlighting specific challenges we encountered during the diagnostic process and management due to the patient religious beliefs.

Case Presentation

A 49-year-old woman, with a medical history of ankylosing spondylitis and positive HLA B27 status was transferred in our tertiary center from a private hospital because of severe arterial hypotension.

She had been hospitalized for 15 days for a first episode of acute HF presenting as a pulmonary oedema with bilateral pleural effusions. Clinically, the patient reported a dry cough for 6 months with progressive dyspnea on exertion. The ECG showed sinus rhythm with a nonspecific intraventricular conduction delay and a broad, fragmented QRS complex measuring 130ms (Fig. 1). Transthoracic echocardiography demonstrated a mildly dilated left ventricle (LV) (LVEDVi 76.9 mL/m^2, LVEDD 55 mm, 31,8 mm/m^2). Left ventricular ejection fraction (LVEF) was severely impaired (30%) with apical, anteroseptal and mid-anterior akinesia (Fig. 2). Coronary angiography revealed no significant coronary lesions. Cardiac MRI confirmed a dilated LV with an LVEF of 34% and a mild impairment of right ventricular ejection fraction at 44%. Native T1 mapping sequences indicated normal values (1052ms), and extracellular volume was estimated at 32%. Edema-sensitive sequences did not reveal any abnormality. Transmural late gadolinium enhancement was observed in anterior, antero-lateral, antero-septal and apical segments with subendocardial distribution at the basal level. Biological investigations included hs cardiac-troponin T plateauing at 175-182 ng/L, NT-proBNP at 2381 ng/L, normal liver tests, and normal calcium-phosphate balance. There was no vitamin deficiency (B1, B6, B9, B12) and thyroid function was normal. Mercury and lead toxicity tests, as well as HIV and hepatitis serologies, were negative. There was no evidence of autoimmunity, and serum protein electrophoresis revealed no monoclonal abnormality.

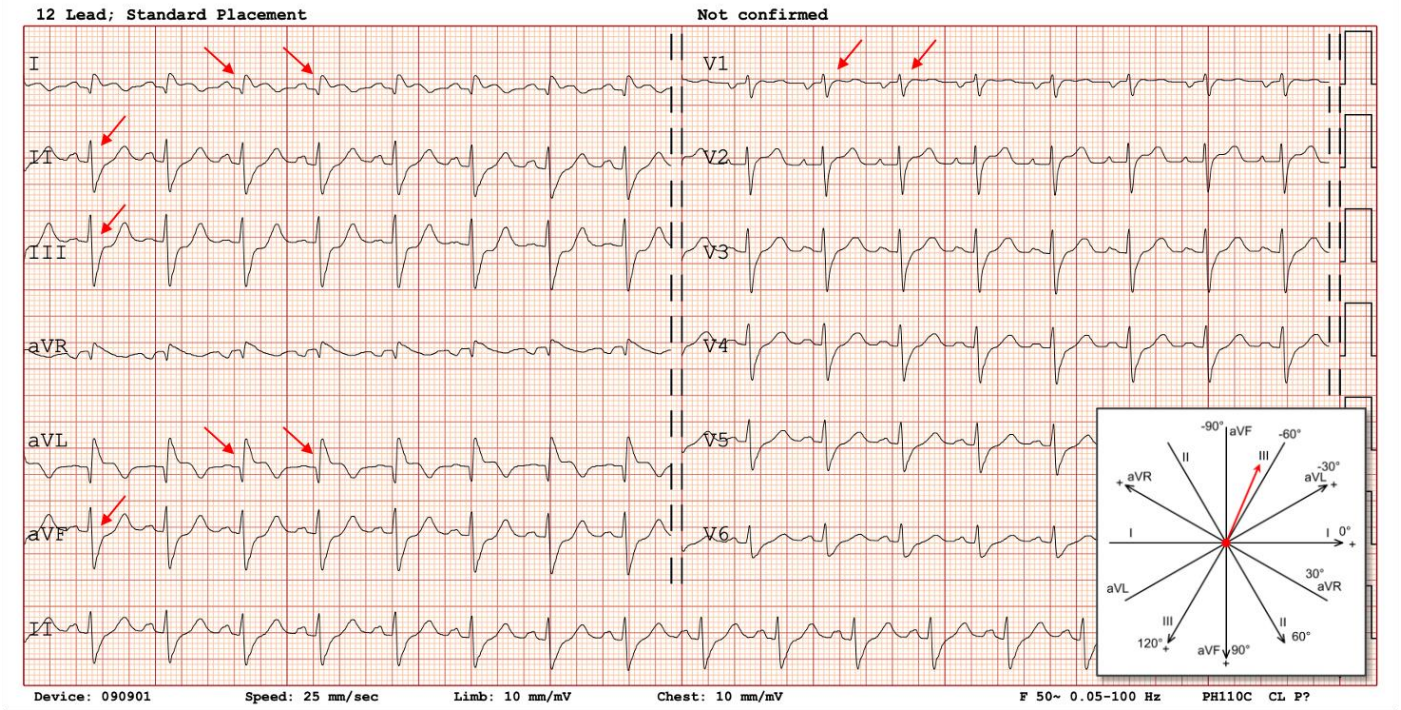

Figure 1: Baseline ECG showing sinus rhythm with a nonspecific intraventricular conduction delay and a broad, fragmented QRS complex measuring 130ms (red arrows showing atypical right bundle branch block with no R' in V1 lead and probable left anterior fascicular block with left axis deviation (-66°, see QRS axis in the bottom right corner), qR in I and aVL, rS in inferior leads).

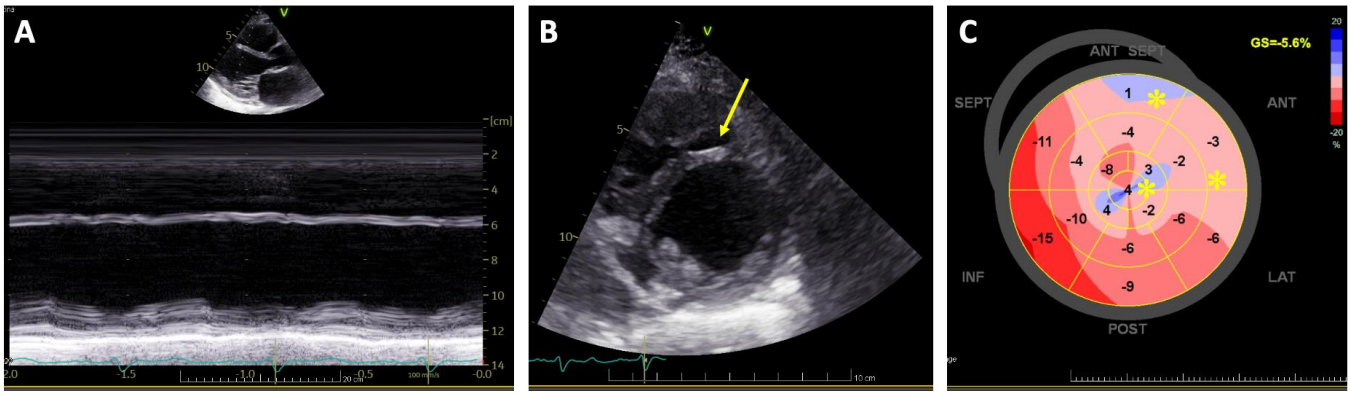

Figure 2: Echocardiography findings: A/Mildly dilated LV with akinesia and thinning of the antero-septal segments; B/ Focal thinning and scar of the antero-septal medial segments (yellow arrow) with preserved thickness of the adjacent myocardium; C/Longitudinal strain pattern showing global severe impairment especially in the antero-septal, anterior and apical segments (yellow asterisks).

Finally, the diagnosis of myocardial infarction with non-obstructive coronary arteries (MINOCA) was considered to explain the findings. Transesophageal echocardiography identified a patent foramen ovale (PFO) with a left-to-right shunt without inversion during the Valsalva maneuver. She was initially implanted for primary prevention with a subcutaneous implantable cardioverter defibrillator (S-ICD). This device was likely selected due to the patient's young age and the absence of a strong indication for cardiac resynchronization therapy (CRT).

After her transfer to our tertiary center (Figure. 3), management initially focused on stabilizing the patient by increasing diuretic treatment and titrating guideline-directed medical therapies of HF with reduced ejection fraction (HFrEF). The patient completed a three-week inpatient cardiac rehabilitation program without further clinical deterioration. After initial improvement in symptoms, she was discharged to outpatient care with close follow-up organized to continue drug up titration. A few days after discharge from rehabilitation, the patient experienced inappropriate S-ICD shocks due to oversensing of P and T waves. Despite attempts to adjust the sensitivity settings using the three different vectors available with the S-ICD, no adequate setting could be determined. Consequently, therapies were temporarily deactivated. Shortly after, she was readmitted for worsening HF as she presented almost continuously at home in NYHA class IV and experienced severe hypotension that required dose reductions of most of her medications. This was her third hospitalization for acute HF in 3 months.

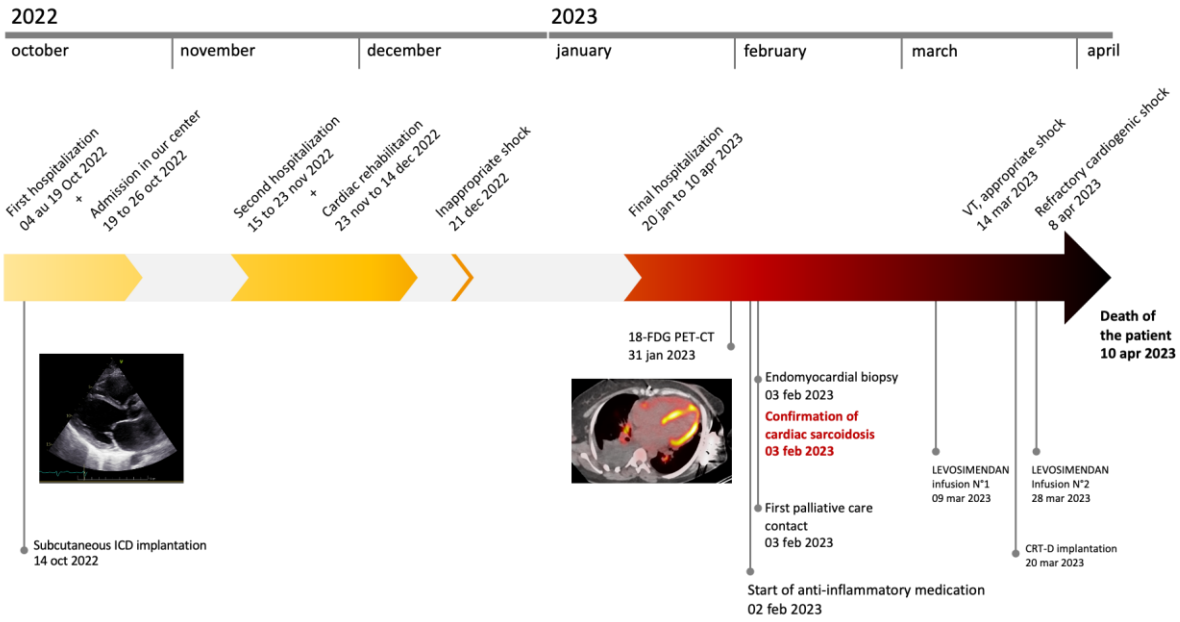

Figure 3: Timeline of major case events from the first admission for heart failure in October 2022 to the last long hospitalization conducting to patient's death.

Due to her clinical and biological deterioration on medication and progression to advanced HF, further etiological work-up was performed. The rapidly progressive nature of her disease was suspicious for an inflammatory cardiomyopathy and the 18F-FDG PET/CT revealed intense abnormal LV myocardial uptake of septal, lateral and apical segments, matching the positive LGE pattern observed on cardiac MRI. There was also evidence of abnormal 18F-FDG uptake in the right ventricle, mediastinal lymph nodes, and the lungs. The angiotensin-converting enzyme assay was normal. Right ventricular septal endomyocardial biopsies revealed non-necrotizing giant-cell granulomas. According to the Heart Rhythm Society histological diagnostic criteria for CS, we finally considered the diagnosis of cardiac, lymph nodes and pulmonary sarcoidosis. IV methylprednisolone was started and later switched to oral prednisone 1mg/kg daily combined one month later with methotrexate.

Unfortunately, the patient's cardiac condition further deteriorated, requiring admission in the intensive care unit (ICU) for inotropic support (levosimendan). The patient exhibited a wide non-LBBB QRS and sustained ventricular tachycardia was observed multiple times. As the S-ICD had to be deactivated due to a high risk of inappropriate shocks, it was decided to upgrade the patient to a transvenous system and a cardiac resynchronization therapy. Given the severity of HF, we aimed for more physiological QRS and performed left bundle branch-optimized cardiac resynchronization therapy (LOT-CRT). We implanted a total of 4 leads: an ICD lead at the RV apex, a LBBAP lead capturing the conduction system, a coronary sinus lead and an atrial lead (Figure. 4). After the implantation, the QRS duration decreased from 130ms to 100ms (Figure. 4). Since the patient was too fragile for general anesthesia, it was decided not to remove the S-ICD and to leave it switched off.

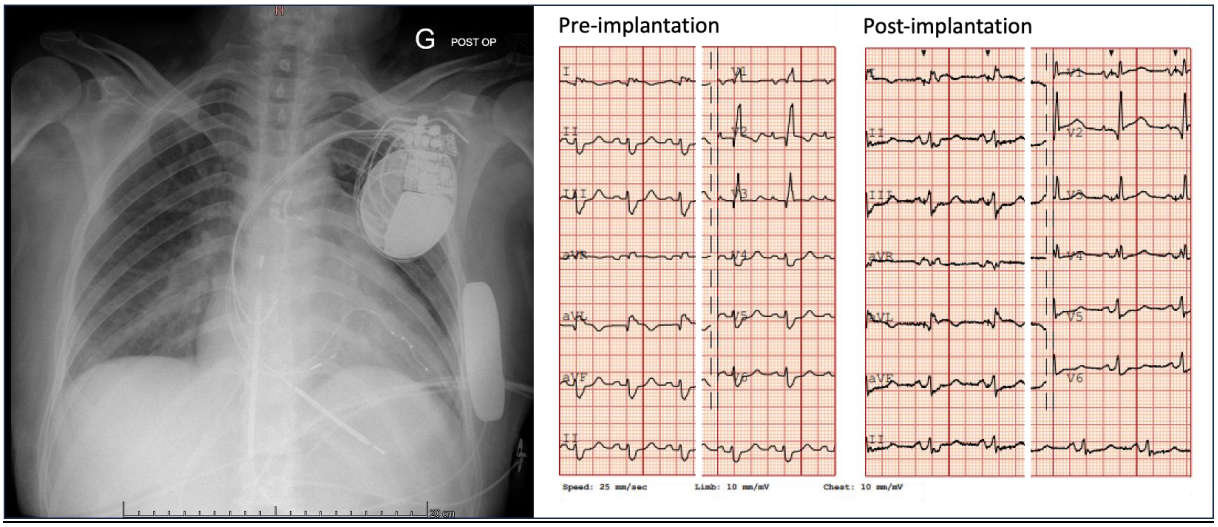

Figure 4: Post-operative chest X-ray showing both S-ICD and the LOT-CRT-D system (ICD lead at the RV apex, LBBAP lead capturing the conduction system, a coronary sinus lead and an atrial lead). On the right side of the figure, we show pre and post-implantation ECG showing narrowing of QRS from 130 to 100ms with LOT-CRT.

Advanced HF therapies including left ventricular assist device and heart transplantation (HT) were discussed on several occasions but not considered because the patient, belonging to the JEHOVA Witness community, refused heterologous and autologous blood transfusions. We also sought the support of our local clinical ethical committee during complex discussions with the patient and her family. Ultimately, she developed refractory cardiogenic shock and died in the ICU after approximately four months of inpatient care and eight months following her initial HF episode. Throughout this prolonged hospitalization, both the patient and her family were supported by our palliative care team.

Discussion

More than 3 months had elapsed since the patient's first episode of HF and the diagnosis of cardiac sarcoidosis. There were numerous poor prognostic factors at the time of initial presentation, including the extent of LGE on MRI, severe impairment of LVEF and high NT-proBNP levels[1,4]. Although there is some uncertainty about the prognostic benefit of immunosuppressive therapy[4], it can be assumed that the regression of the extensive inflammation observed with 18F-FDG PET/CT in this case could have led to a more favorable outcome for the patient, since HF reflects widespread LV infiltration and systolic dysfunction. Inflammatory cardiomyopathies and infiltrative cardiomyopathies such as cardiac sarcoidosis and amyloidosis must be detected as early as possible because progression of myocardial lesions worsens the prognosis of patients even if specific treatment is given [5].

This case highlights the diagnostic challenge that CS represents for the clinician [6]. The most common ECG manifestations that should suggest a diagnosis of cardiac sarcoidosis are atrio-ventricular block, fragmented broad QRS, frequent premature ventricular beats, VT and abnormal cardiac repolarization4. Echocardiographic findings are reduced LVEF, local akinesia or dyskinesia, LV wall thickening or thinning and reduced global LV longitudinal strain4. In our case, beyond low ejection fraction, transthoracic echocardiography showed several regional wall motion abnormalities that are known to occur in 35 to 50% patients with CS. Furthermore, akinesia and thinning of the basal septum in the absence of coronary obstruction are highly suggestive of cardiac sarcoidosis and must be highlighted [7].

In this observation, the initial diagnosis of MINOCA raised with the MRI results must be criticized. Indeed, the term MINOCA should never be a final diagnosis. This term corresponds to a clinical presentation suggestive of acute coronary syndrome (ACS) with elevated troponin level without angiographic coronary lesion and should prompt the clinician to consider various etiologies that can explain the clinical presentation and cardiac injury [8]. In this case, the patient's presentation was not suggestive of ACS and there was no dynamic troponin movement at the time of the patient's initial presentation. Furthermore, the presence of PFO raised the suspicion of embolic myocardial infarction and misled the clinicians in charge of the patient. Finally, the existence of a clinically severe HF with impaired LVEF of undetermined origin without improvement with guideline-directed therapies might have been an indication for an endomyocardial biopsy earlier in this patient [9].

Having a proper diagnosis, apart from management of patient's HFrEF, is also critical when considering the implantation of cardiac electronic devices. Indeed, despite the considerable advantages of the S-ICD with less infection and lead fracture, it can neither stimulate nor perform cardiac resynchronization therapy and would not have been implanted if the diagnosis of sarcoidosis was known due to the risk of high degree AV block or potential need of a cardiac resynchronization therapy. Furthermore, even with the high pass filter, the rate of inappropriate therapy remains high up to 3.1% at 1 year and it is suspected that the broad, fragmented and relative low voltage QRS explains the P and T wave oversensing [10]. This case shows as well that conduction system pacing (in this case LBBAP) plus coronary sinus lead could maximize electrical resynchronization aiming for the more physiological QRS complex especially in non LBBB patients where CRT response is generally less favorable. The last consideration is the advantage of the DF1 defibrillator standard instead of the more recent DF 4 standard.

In this patient, we abandoned the IS-1 part of the ICD lead and connected the LBBAP lead in the IS-1 port to perform LOT CRT [11]. This complex configuration would not have been possible with a DF4 pulse generator.

In addition to the diagnostic and therapeutic aspects already discussed, the context of the patient's religious beliefs had to be considered at every step of the diagnostic process and management options, especially regarding invasive tests or treatments (e.g., invasive hemodynamic monitoring). The patient was steadfast in her decision not to receive any blood products, whether autologous or allogenic, due to her beliefs as a Jehovah's Witness. For instance, the choice to proceed with an endomyocardial biopsy was thoroughly discussed, weighing the benefits against risks of complications such as cardiac tamponade and the potential need for blood transfusion. These discussions, although necessary, were time-consuming and might have slowed down the diagnostic process. Supportive therapies, such as hemodialysis or ultrafiltration, though indicated as her condition deteriorated, were not possible due to the exposure to blood products. Lawson et al. in their review on perioperative care for Jehovah's Witnesses, emphasize that successful care relies on a holistic approach that integrates pre-optimization, referral to specialized surgical teams, and perioperative blood-conservation techniques [12].

This patient would have been an ideal candidate for "super-urgent" HT, but this was not possible in part due to her beliefs and because she did not meet the criteria for inclusion in the Swiss transplant list as one of the major criteria included acceptance of autologous blood transfusions. There are few published clinical data are available for this circumstance. However, it appears feasible to perform HT in these patients with similar results to patients not belonging to this community [13,14]. Appropriate selection of recipients is a crucial stage in transplantation. The HT team of Cedar-Sinai Heart Institute in Los Angeles proposes the following specific additional criteria for Jehovah Witness candidates: no prior cardiac surgery, normal hemoglobin and platelet count, ability to remain off all antiplatelet agents and anticoagulation while on HT waiting list and no need for multi-organ transplantation [13]. Specific pre-operative preventive measures are proposed such as iron supplementation and erythropoietin for bone marrow stimulation. Planning for autologous blood transfusion before an elective or semi-elective complex cardiac surgery is associated with a reduction in the need for allogenic blood transfusions during and after major surgeries [15,16]. This strategy is sometimes accepted by patients despite their religious beliefs. In our case the patient declined this proposal. Other intra-operative and post-operative measures are also important in limiting blood loss: adequate management of gauze, rigorous hemostasis, cell-saver management if discussed prior to the surgery, use of tranexamic acid and desmopressin [13,17]. Of note, in this case it was deemed that mechanical assist device as a bridge to transplantation was not an option due to concomitant right HF that would require a more complex surgery with the implantation of biventricular assistance which would be associated with a higher risk of requiring perioperative blood transfusion.

Lastly, the support of our local clinical ethics committee was crucial during complex discussions throughout the care of this patient in critical condition as well as during interactions with her family and Jehovah's Witness representatives. The ethics committee provided not only information on legal aspects of caring for Jehovah's Witnesses but also relayed the position of the hospital's medical and administrative governance. They also ensured that the management of the patient adhered to Beauchamp and Childress' four principles of bioethics: autonomy, beneficence, non-maleficence, and justice [18]. The palliative care team was also heavily involved not only in helping to define the patients' advance directives but also provided support for the staff at every level during the patient's 4-month hospital stay. This case highlights the value of a multidisciplinary care in advanced HF management, and this included early access to palliative care teams [19,20].

Conclusion

This case highlights the diagnostic and therapeutic challenges faced by clinicians when managing rapidly progressive severe heart failure. Cardiac sarcoidosis should be considered in severe cases like the one described, especially since presentations with impaired LVEF have a poor prognosis without specific management and advanced HF therapies. Unfortunately, due to the patient's religious beliefs, these therapies could not be implemented, posing significant ethical dilemmas. We believe that only a multidisciplinary team can navigate these complex situations effectively, ensuring that patient care adheres to ethical principles while addressing medical needs.

Acknowledgments

None

Conflict of interest

All authors have no conflicts of interest to declare.

References

1. Authors/Task Force Members, McDonagh TA, Metra M, et al. (2021) ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2022 24(1):4-131.
2. Authors/Task Force Members, McDonagh TA, Metra M, et al. (2023) Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2024; 26(1):5-17.
3. Arbelo E, Protonotarios A, Gimeno JR, et al. (2023) ESC Guidelines for the management of cardiomyopathies. *Eur Heart J*. 2023; 44(37):3503-3626.
4. Lehtonen J, Uusitalo V, Pöyhönen P, Mäyränpää MI, Kupari M. (2023). Cardiac sarcoidosis: phenotypes, diagnosis, treatment, and prognosis. *Eur Heart J*. 44(17):1495-1510.
5. Garcia-Pavia P, Rapezzi C, Adler Y, et al. (2021). Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur J Heart Fail*., 23(4):512-526.
6. Ueberham L, Hagendorff A, Klingel K, et al. (2023). Pathophysiological Gaps, Diagnostic Challenges, and Uncertainties in Cardiac Sarcoidosis. *J Am Heart Assoc*.;12(6): e027971.
7. Okafor J, Khattar R, Sharma R, Kouranos V. (2023). The Role of Echocardiography in the Contemporary Diagnosis and Prognosis of Cardiac Sarcoidosis: A Comprehensive Review. *Life Basel Switz*. 13(8):1653.
8. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J Acute Cardiovasc Care*. 2024;13(1):55-161. doi:10.1093/ehjacc/zuad107
9. Seferović PM, Tsutsui H, McNamara DM, et al. Heart Failure Association of the ESC, Heart Failure Society of America and Japanese Heart Failure Society Position statement on endomyocardial biopsy. Eur J Heart Fail. 2021;23(6):854-871.
10. Gold MR, Lambiase PD, El-Chami MF, et al. (2021). Primary Results from the Understanding Outcomes With the S-ICD in Primary Prevention Patients with Low Ejection Fraction (UNTOUCHED) Trial. *Circulation*. 143(1):7-17.
11. Sticherling C, Ellenbogen KA, Burri H. (2024). Stepping back for good reasons: a reappraisal of the DF-1 connector for

defibrillator leads. Eur Eur Pacing Arrhythm Card Electrophysiol *J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol*. 26(3): euae057.

12. Lawson T, Ralph C. (2015). Perioperative Jehovah's Witnesses: a review. *Br J Anaesth*. 115(5):676-687.
13. Sander S, Singer-Englar T, Nishihara K, et al. (2021). Heart transplant in Jehovah's Witness patients: A case-control study. *J Heart Lung Transplant Off Publ Int Soc Heart Transplant*. 40(7):575-579.
14. Elmistekawy E, Mesana TG, Ruel M. (2012). Should Jehovah's Witness patients be listed for heart transplantation? *Interact Cardiovasc Thorac Surg*. 15(4):716-719.
15. Ashworth A, Klein AA. (2010). Cell salvage as part of a blood conservation strategy in anaesthesia. *Br J Anaesth*, 105(4):401-416.
16. Casati V, D'Angelo A, Barbato L, et al. (2007). Perioperative management of four anaemic female Jehovah's Witnesses undergoing urgent complex cardiac surgery. *Br J Anaesth*. 99(3):349-352.
17. Tsukioka Y, Jeevanandam V. (2024). Successful Heart Transplantation Without Blood Transfusion in a Jehovah's Witness Patient with Congenitally Corrected Transposition of the Great Arteries: A Case Report. *Cureus*. Published online March 26.
18. Beauchamp TL, Childress JF. (2001). Principles of Biomedical Ethics. 5th ed. *Oxford University Press*.
19. Jaarsma T, Beattie JM, Ryder M, et al. (2009). Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 11(5):433-443.
20. Tomasoni D, Vishram-Nielsen JKK, Pagnesi M, et al. (2022). Advanced heart failure: guideline-directed medical therapy, diuretics, inotropes, and palliative care. ESC Heart Fail. 9(3):1507-1523.

DOI:10.31579/2690-8808/199