SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Cardiology

Dexamethasone for the Treatment of Cardiac Al Amyloidosis: A Case Report and Literature Review

Mohamed Imad Rhoujjati[1*], Bourzeg Khaoula[1], Nehame Sana[1], Haffane Fadwa Mohammed El Jamili[1], Mustapha El Hattaoui[1]

[1]Department of Cardiology, Marrakech University Hospital of Mohammed VI, Morocco

DOI: https://doi.org/10.36347/sasjm.2024.v10i08.019 | **Received:** 15.07.2024 | **Accepted:** 24.08.2024 | **Published:** 27.08.2024

***Corresponding author:** Mohamed Imad Rhoujjati
Department of Cardiology, Marrakech University Hospital of Mohammed VI, Morocco

Abstract **Case Report**

Background: Systemic immunoglobulin light chain (AL) amyloidosis is a condition characterised by the conversion of light chains (LCs) from their soluble states into highly organised fibrillar aggregates that deposit in tissues, resulting in progressive organ damage and dysfunction. While previously considered incurable, treatment strategies are emerging for cardiac amyloidosis, underscoring the importance of early diagnosis. ***Case Summary***: We present the case of a 69-year-old male patient who was admitted with acute onset of dyspnea and diagnosed with heart failure. The diagnosis of cardiac amyloidosis was made on the basis of a discrepancy between the results of the electrocardiogram and the echocardiogram, a conclusion that was further substantiated by the use of scintigraphy and myelogram. Given the poor left ventricular fraction, the standard chemotherapy regimen was replaced with corticosteroid therapy, which led to a significant improvement within the first 48 hours, unfortunately reversible with rapid clinical deterioration followed by sudden death within a week. ***Conclusion:*** Our aim is to highlight that early administration of dexamethasone is associated with significant clinical improvement but a high mortality rate in patients with AL cardiac amyloidosis.

Keywords: Dexamethasone, Cardiac Al Amyloidosis, Light Chain, Diagnosis, heart failure.

INTRODUCTION

Systemic immunoglobulin light chain (AL) amyloidosis is a condition characterised by the conversion of light chains (LCs) from their soluble states into highly organised fibrillar aggregates that deposit in tissues, resulting in progressive organ damage and dysfunction.

Cardiac involvement is a common occurrence in AL amyloidosis and is associated with a poor prognosis. The chemotherapy regimen that combines cyclophosphamide, bortezomib, and dexamethasone is a widely used treatment for light-chain amyloidosis. However, the initial administration of dexamethasone during treatment is of particular importance. It should be noted that this may be linked to early cardiac deaths in severe cases [1-3].

CASE DESCRIPTION

A 69-year-old man with no modifiable cardiovascular risk factors presented to the emergency department with NYHA stage IV dyspnoea, lower limb edema, fatigue and weakness.

On clinical examination, he had signs of global cardiac heart failure, including bilateral basi-thoracic crepitations, lower limb oedema extending to the roots of the thighs, elevated jugular venous pressure (EJVP), hepatojugular reflux (HJR) and ascites, and bilateral erysipelas.

The electrocardiogram showed a regular sinus rhythm with a frequency of 88 beats per minute. Peripheral microvoltage was observed with poor R-wave progression in the anteroseptal leads.

Transthoracic echocardiography showed concentric left ventricular hypertrophy with severe systolic dysfunction, with a left ventricular ejection fraction of 25-30%. In addition, a hypertrophic interatrial septum was observed in the absence of systolic anterior motion or LVOTO. Moderate mitral regurgitation and moderate aortic regurgitation were also observed. Global longitudinal strain was reduced to -9.4% (Figs 1 & 2).

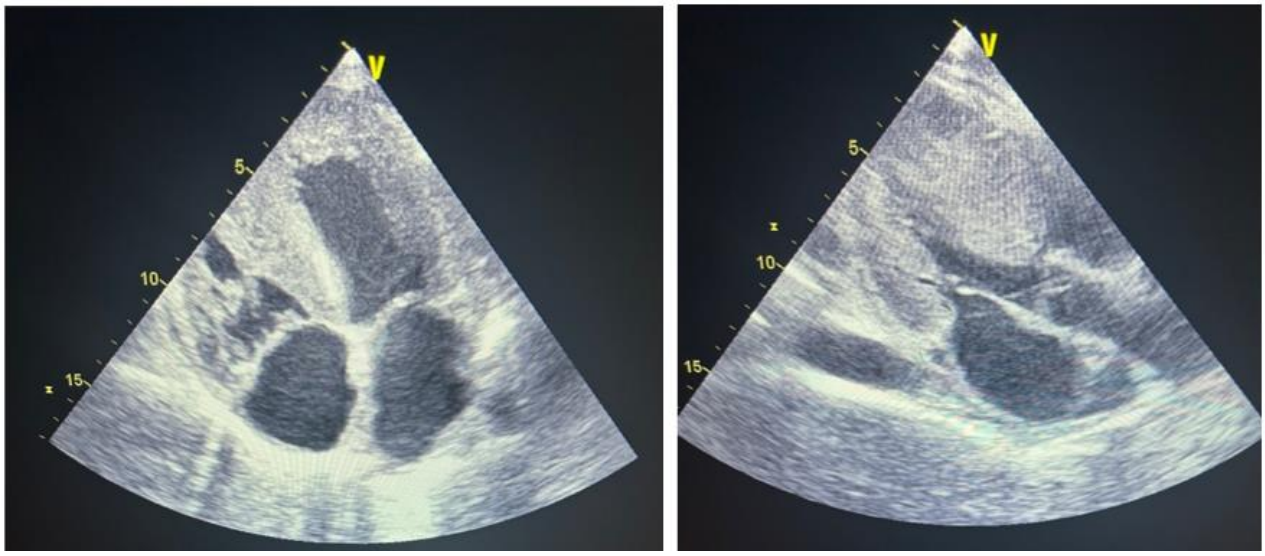

Figure 1: A four and PLAX views revealing hypertrophic ventricules with a thickning of both IVS and IAS

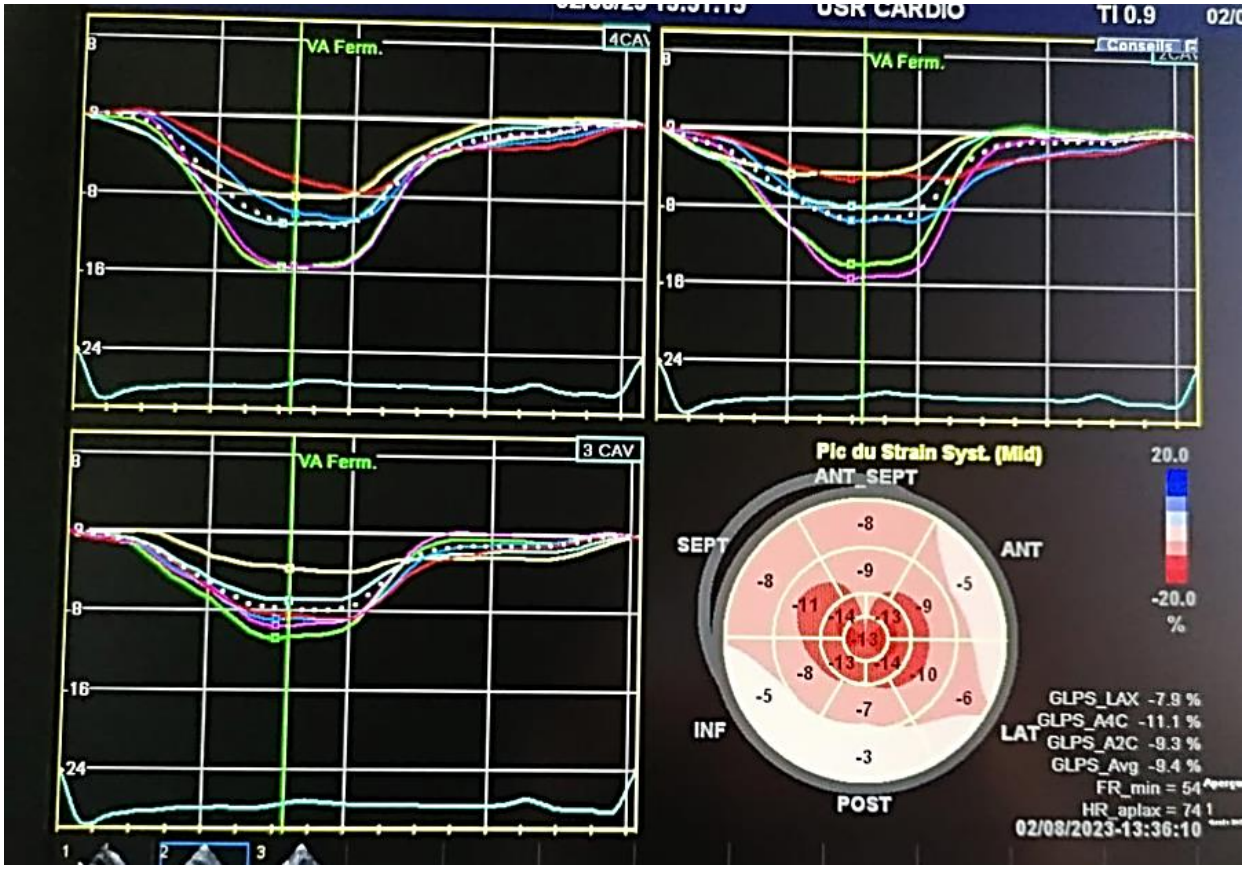

Figure 2: Alteration of the GLS

Once the patient's condition had been stabilised and the congestion had been relieved, an investigation was initiated to determine the underlying cause. The results demonstrated the absence of blood group deficiencies in the complete blood count (CBC), the absence of abnormalities in the calcium phosphate and renal laboratory tests, and the absence of amyloid deposits in the biopsy of the accessory salivary gland.

Serum protein electrophoresis revealed the presence of an inflammatory syndrome, characterised by a monoclonal gamma globulin peak with a quantified concentration of 10.7 g/L. Immunofixation demonstrated the presence of kappa free light chains at 92.85 mg/L and lambda free light chains at 122.44 mg/L, with a normal kappa free/lambda free ratio of 0.76 (Fig 3). Myelogram analysis revealed a rich marrow with 12% plasmacytosis.

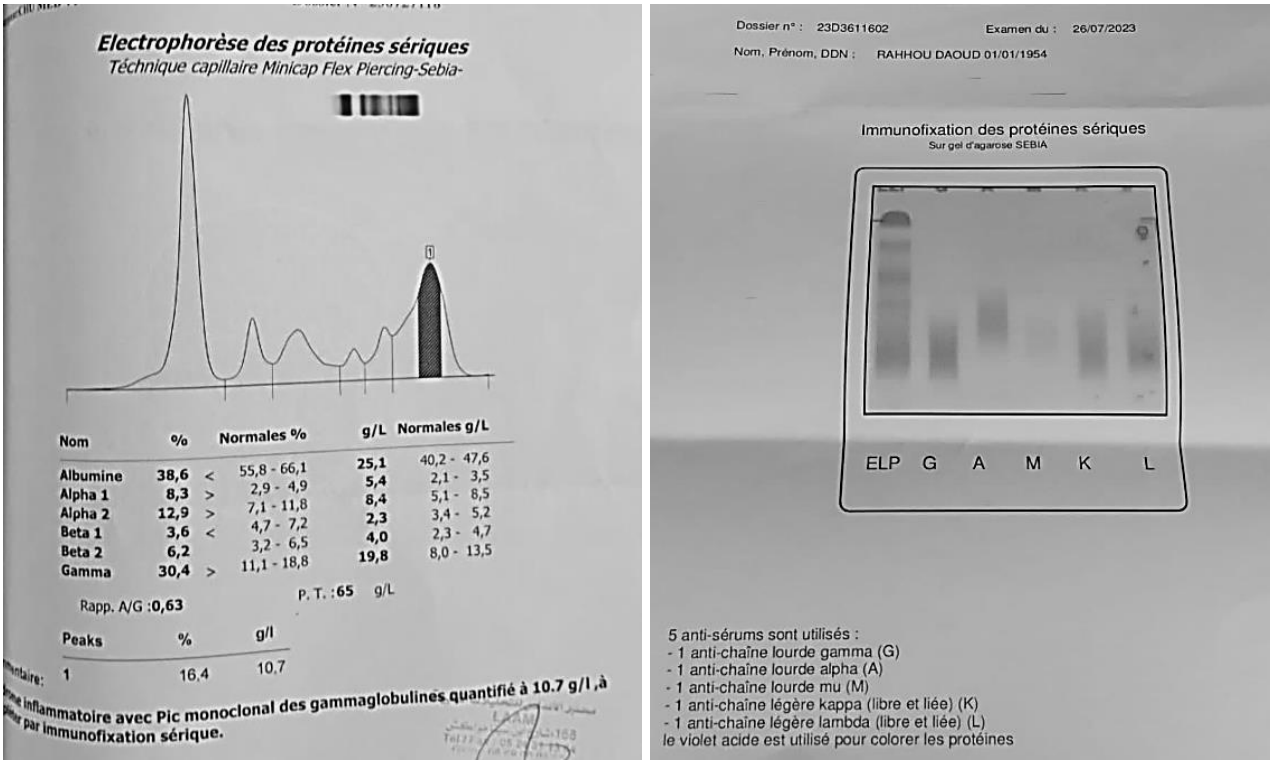

Figure 3: Serum protein electrophoresis showing a monoclonal peak/ Immunofixation revealing a normal kappa free/lambda free ratio

Bone scintigraphy (SPECT-CT MDP Tc 99m) showed intracardiac radiotracer uptake in favor of cardiac amyloidosis (Fig 4).

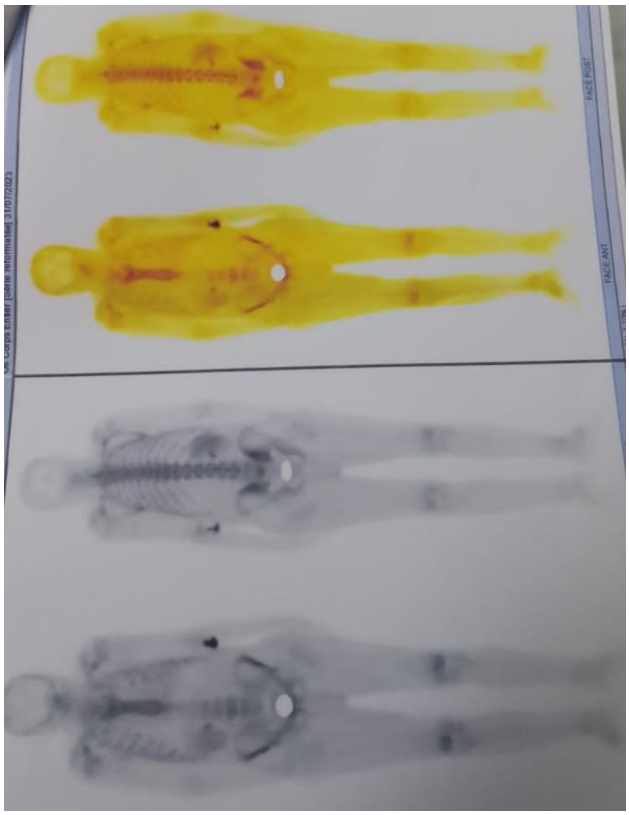

Figure 4: Bone scintigraphy (SPECT-CT MDP Tc 99m) with intracardiac radiotracer uptake

Following consultation with the haematologists, the diagnosis of AL cardiac amyloidosis was confirmed. Given the poor left ventricular fraction, the standard chemotherapy regimen was replaced with corticosteroid therapy. Dexamethasone 40 mg/day for five days was initiated, with close echocardiographic monitoring. The patient's symptoms significantly improved within the first 48 hours. Additionally, the left ventricular ejection fraction increased from 25-30% to 45-50%.

Due to the significant clinical improvement and increase in LVEF, the remainder of the chemotherapy protocol was scheduled to commence. However, the patient passed away one one week later.

DISCUSSION

AL amyloidosis is the most common form of systemic amyloidosis. It is caused by the production of free light chain (FLC) by clonal plasma cells in bone marrow [4].

Patients with cardiac AL amyloidosis have a particularly poor prognosis compared to those with other types of AL amyloidosis.

Cardiac amyloid infiltration is the primary cause of death, accounting for over 61% of fatalities and the main determinant of survival in patients with AL amyloidosis [5].

Proteotoxicity induced by LCs, LC aggregates, or preceding intermediaries can lead to cardiac cell dysfunction and death [6].

Up-front chemotherapy combining cyclophosphamide, bortezomib and dexamethasone (CyBorD) has improved survival rates.

Dexamethasone treatment results in complete haematologic remission in 65% of patients and significantly prolongs their survival, with a 2-year overall survival rate of 94.4% at stage III [7].

However, serious cardiac events, including sudden death, syncope, arrhythmia, and heart failure, often occur during the first cycle of treatment, occasionally leading to death [8].

Studies have shown that delaying dexamethasone during the first chemotherapy cycle reduces the number of early deaths without affecting survival [9, 10].

It is suspected that dexamethasone, even at high doses, may lead to cardiac events due to increased fluid retention and arrhythmia. This has been previously observed in patients [9].

The study by Benzard *et al*., indicates that administering dexamethasone earlier in the CyBorDComb and DCyBorSeq regimens, either alone or in combination, resulted in significantly more early deaths compared to later administration in the first cycle using the CyBorDSeq regimen. The study also provides preliminary evidence that delaying the administration of dexamethasone during the first cycle of treatment for light chain amyloidosis with severe cardiac involvement reduces early deaths.

Strategies that limit abrupt exposure to corticoids during the first cycles, such as reducing the dose to below 20 mg per week or sequentially introducing the drugs, or reducing the corticoid dose, may achieve the objective of preserving heart function during the onset of treatment while maintaining cytotoxicity against the clonal plasma cells [11].

The patient's case aligns with the findings of several studies in the literature, which indicate that early administration of dexamethasone is associated with a high mortality rate among patients with AL cardiac amyloidosis.

CONCLUSION

Further research is required to elucidate the impact of dexamethasone in the treatment of AL cardiac amyloidosis.

It is imperative to identify the optimal sequence and standardise the therapeutic protocol in order to enhance the management of these patients.

REFERENCES

1. Merlini, G., Dispenzieri, A., Sanchorawala, V., Schönland, S. O., Palladini, G., Hawkins, P. N., & Gertz, M. A. (2018). Systemic immunoglobulin light chain amyloidosis. *Nature reviews Disease primers*, *4*(1), 38.
2. Dietrich, S., Schönland, S. O., Benner, A., Bochtler, T., Kristen, A. V., Beimler, J., ... & Hegenbart, U. (2010). Treatment with intravenous melphalan and dexamethasone is not able to overcome the poor prognosis of patients with newly diagnosed systemic light chain amyloidosis and severe cardiac involvement. *Blood, The Journal of the American Society of Hematology*, *116*(4), 522-528.
3. Falk, R. H., Alexander, K. M., Liao, R., & Dorbala, S. (2016). AL (light-chain) cardiac amyloidosis: a review of diagnosis and therapy. *Journal of the American College of Cardiology*, *68*(12), 1323-1341.
4. Grogan, M., & Dispenzieri, A. (2015). Natural history and therapy of AL cardiac amyloidosis. *Heart Failure Reviews*, *20*, 155-162.
5. Merlini, G. (2017). AL amyloidosis: from molecular mechanisms to targeted therapies. *Hematology 2014, the American Society of Hematology Education Program Book*, *2017*(1), 1-12.

6. Palladini, G., Milani, P., & Merlini, G. (2020). Management of AL amyloidosis in 2020. Hematology (Am Soc Hematol Educ Program), 2020(1), 363-371.
7. Venner, C. P., Lane, T., Foard, D., Rannigan, L., Gibbs, S. D., Pinney, J. H., ... & Wechalekar, A. D. (2012). Cyclophosphamide, bortezomib, and dexamethasone therapy in AL amyloidosis is associated with high clonal response rates and prolonged progression-free survival. *Blood, The Journal of the American Society of Hematology*, *119*(19), 4387-4390.
8. Chamarthi, B., Dubrey, S. W., Cha, K., Skinner, M., & Falk, R. H. (1997). Features and prognosis of exertional syncope in light-chain associated AL cardiac amyloidosis. *American Journal of Cardiology*, *80*(9), 1242-1245.
9. Jaccard, A., Comenzo, R. L., Hari, P., Hawkins, P. N., Roussel, M., Morel, P., ... & Venner, C. P. (2014). Efficacy of bortezomib, cyclophosphamide and dexamethasone in treatment-naive patients with high-risk cardiac AL amyloidosis (Mayo Clinic stage III). *haematologica*, *99*(9), 1479-1485.
10. Bézard, M., Oghina, S., Vitiello, D., Kharoubi, M., Kordeli, E., Galat, A., ... & Damy, T. (2021). Dexamethasone is associated with early deaths in light chain amyloidosis patients with severe cardiac involvement. *PLoS One*, *16*(9), e0257189.
11. Le Bras, F., Molinier-Frenkel, V., Guellich, A., Dupuis, J., Belhadj, K., Guendouz, S., ... & Damy, T. (2017). Sequential cyclophosphamide-bortezomib-dexamethasone unmasks the harmful cardiac effect of dexamethasone in primary light-chain cardiac amyloidosis. *European Journal of Cancer*, *76*, 183-187.