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Original Article

AL amyloidosis with cardiac involvement: a case report with literature review

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Abstract

Objectives: To present a case of rapidly progressing cardiac immunoglobulin light chain (AL) amyloidosis, highlighting diagnostic challenges, management complexities, and the importance of early intervention. AL amyloidosis is a rare and severe disorder that causes organ damage, especially in the heart, leading to restrictive cardiomyopathy, heart failure, and arrhythmias. This case report highlights diagnostic difficulties and management issues, showcasing advanced imaging techniques and a multidisciplinary approach.

Methods: A 68-year-old man presented to Wigan Infirmary, Wrightington, Wigan, and Leigh (WWL) NHS Trust in July 2024 with dyspnea, nocturnal cough, and decreased exercise tolerance due to rapidly progressing cardiac AL amyloidosis. The diagnostic workup included chest X-ray, echocardiography, cardiac MRI, and a Technetium-99m-labeled 3, 3-diphosphono-1, 2-propanodicarboxylic acid (Tc-DPD) scan. Fat aspirate biopsy confirmed the diagnosis by showing Congo red positivity with characteristic apple-green birefringence under polarized light. Laboratory tests supported the diagnosis, revealing lambda free light chain levels over 2000 mg/L, elevated B-type natriuretic peptide (BNP) at 4174 pg/mL, and impaired kidney function. This case emphasizes the importance of early detection and treatment of cardiac amyloidosis, as well as the difficulties of managing this condition alongside concurrent infections.

Results: Despite early diagnosis and vigorous treatment, the patient's condition rapidly declined, leading to several hospitalizations for decompensated heart failure and infections. Treatment focused on reducing amyloid production and managing cardiac issues. For infection-related admissions, the treatment regimen included intravenous furosemide, dexamethasone, and piperacillin-tazobactam (Tazocin). However, over these admissions, the patient’s condition worsened due to recurring infections and the progressive decline in renal and hepatic function. Sadly, the patient died in early January 2025 during the final hospitalization due to severe refractory heart failure.

Conclusions: The case highlights the vital importance of early detection and a multidisciplinary approach to managing cardiac AL amyloidosis. It stresses the need for collaboration among various specialties, including cardiology, hematology, and infectious disease, to effectively handle the complexities of concurrent cardiac failure, arrhythmias, and infections. This coordinated care approach is essential for optimizing treatment planning and orders.

Keywords: Restrictive cardiomyopathy, AL amyloidosis, cardiac amyloidosis, heart failure, lambda free light chains, Tc-DPD scan, fat aspirate biopsy, multidisciplinary approach, infection, renal dysfunction

Introduction

Amyloidosis refers to a group of conditions characterized by the extracellular deposition of misfolded proteins that form insoluble fibrils, leading to organ dysfunction. Immunoglobulin light chain (AL) amyloidosis is notably significant due to its profound effects on multiple organs, particularly the heart [1]. It manifests in approximately 8-12 cases per million individuals annually, rendering it a relatively rare yet significant condition to identify and manage [2]. Cardiac involvement in AL amyloidosis carries a poor prognosis, with median survival ranging from 6 months to 2 years if left untreated [3]. The accumulation of amyloid fibrils in the heart results in restrictive cardiomyopathy, heart failure, and arrhythmias, significantly complicating the clinical picture [1]. Timely identification and diagnosis are essential for improving outcomes; however, this remains challenging due to nonspecific symptoms and the need for specialised testing [4]. The diagnostic process for cardiac amyloidosis encompasses a combination of clinical evaluation, laboratory tests, and advanced imaging techniques. Multimodality imaging, including echocardiography, cardiac magnetic resonance (CMR), and nuclear imaging, plays a pivotal role in identifying and characterising amyloid deposits in the heart. These imaging modalities facilitate diagnosis and offer valuable prognostic information, guiding treatment decisions and tracking disease progression [4]. Despite advancements in diagnostic techniques, the management of cardiac AL amyloidosis remains complex and challenging [1]. The disease's aggressive nature and the frequent occurrence of complications such as heart failure and infections require a multidisciplinary approach to care [1]. Current treatment approaches focus on reducing amyloid production, alleviating symptoms, and addressing complications to enhance patient outcomes [4, 5].

Literature Review

Recent epidemiological studies indicate that AL amyloidosis accounts for approximately 70% of all cardiac amyloidosis cases [5]. The Mayo stages system, which includes cardiac biomarkers such as troponin T and N-terminal pro B-type natriuretic peptide (NT-pro BNP), is considered the gold standard for risk stratification. Patients classified as stage 3A typically have a median survival of approximately 14 months without intervention. This staging approach is valuable in guiding treatment decisions and predicting patient outcomes [6]. Common echocardiographic findings consist of increased left ventricular wall thickness, sparkling myocardial texture, and a restrictive diastolic pattern [7]. Advanced echocardiographic techniques, such as speckle tracking, have revolutionised early detection, with longitudinal strain showing a distinctive apical sparing pattern, reported to have 93% sensitivity and 82% specificity. These sophisticated techniques enhance the ability to detect cardiac involvement at an earlier stage, improving the chances of timely intervention [8]. CMR has emerged as a fundamental component in diagnosis, offering unique advantages in tissue characterisation [9]. Late gadolinium enhancement exhibits characteristic diffuse subendocardial enhancement, with sensitivity exceeding 95% [10].T1 mapping and extracellular volume quantification improved diagnostic precision, offering comprehensive insights into the rate of amyloid infiltration. These imaging biomarkers serve both diagnostic and prognostic functions, correlating with disease severity and patient outcomes [11]. Bone scintigraphy, especially using Technetium-99m-labeled 3, 3-diphosphono-1, 2-propanodicarboxylic acid (99mTc-DPD), is vital for differentiation in this context [12]. The Perugini grading system guides interpretation, with AL amyloidosis generally exhibiting grade 0-1 uptake. Meta-analyses indicate a sensitivity of 86.5% and a specificity of 83.6% for the identification of cardiac amyloidosis. This non-invasive imaging modality is especially beneficial for differentiating between AL and transthyretin (ATTR) amyloidosis, guiding appropriate management [13]. Treatment strategies for cardiac AL amyloidosis aim to reduce amyloid production by suppressing the abnormal immunoglobulin light chains in the bone marrow [5, 6]. This is accomplished through chemotherapy regimens, often including bortezomib, cyclophosphamide, and dexamethasone, along with stem cell transplantation [5, 6]. Newer agents like daratumumab are increasingly utilized to improve treatment effectiveness [5]. Autologous stem cell transplantation (ASCT) can provide long-term remission for suitable patients [5, 6]. Concurrent management of cardiac complications, such as heart failure and arrhythmias, is essential for enhancing patient outcomes and quality of life [4, 7]. Palliative care plays a key role in symptom management and overall well-being for patients with advanced disease

[4, 7]. A multidisciplinary team involving cardiologists, hematologists, and imaging specialists helps optimize patient care and maximize results in cardiac AL amyloidosis.

Detailed Case Presentation

A 68-year-old male initially presented in July 2024 with worsening shortness of breath, nighttime cough, and decreasing ability to exercise. Previously active, he regularly cycled 100 km weekly but experienced a significant reduction in exercise capacity along with a 3-4 pound weight loss. The initial diagnostic workup included a chest X-ray, which showed borderline cardiomegaly and a mild right-sided pleural effusion. A follow-up CT scan of the chest in September 2024, Figure 1, confirmed moderate right-sided and small left-sided pleural effusions, leading to further cardiac evaluation.

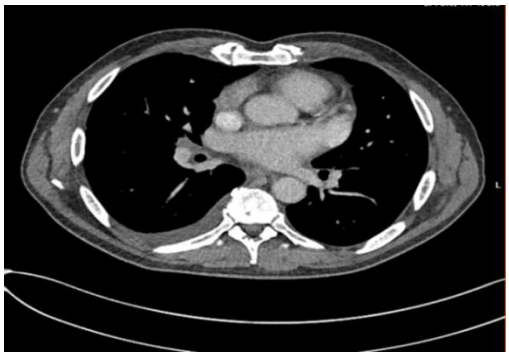

Figure 1. CT of Thorax and Abdomen with Contrast 07/09/2024

(Some thoracic lymph nodes, mild pleural thickening on both sides, a moderate-sized pleural effusion on the right, and a trace of pleural fluid at the left lung base.)

The diagnostic workup continued with electrocardiography showing low voltage and pseudo-infarct patterns typical of cardiac amyloidosis. Echocardiography performed in September demonstrated severe left ventricular hypertrophy with septal and posterior wall measurements of 14 mm and 16 mm, respectively, maintaining a preserved ejection fraction of 50% and reduced global longitudinal strain in strain imaging Figure 2. ECG Figure 3 showed low voltage and pseudo-infarct patterns. A comprehensive cardiac magnetic resonance study conducted in October identified a restrictive cardiomyopathy pattern with abnormal native T1 values and notable late gadolinium enhancement. The scan revealed a reduced ejection fraction of 44% and a significantly increased extracellular volume fraction in the spleen, measuring 0.80. A DPD scan yielded Perugini grade 1 cardiac uptake, further supporting the diagnosis.

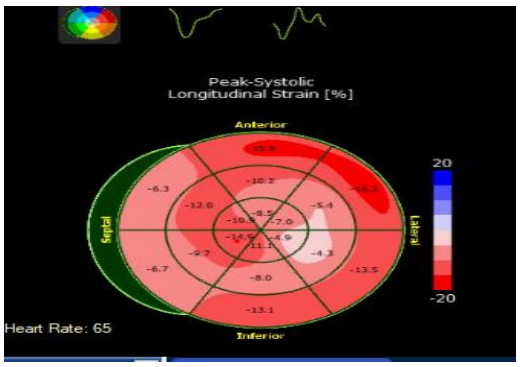

Figure 2. Trans thoracic echo 11/09/2024

(Reduced GLS indices, especially in the mid and basal segments)

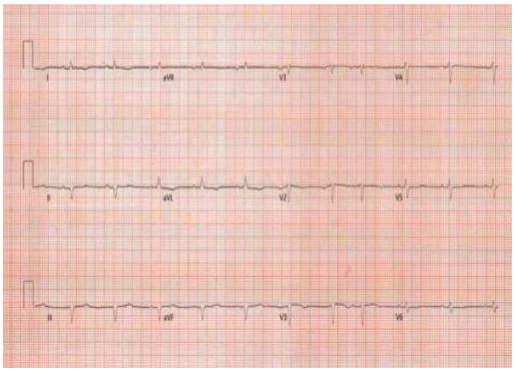

Figure 3. ECG 26/11/2024

(Low voltage and pseudo-infarct pattern)

Laboratory investigations confirmed the diagnosis, with lambda free light chain levels exceeding 2000 mg/L, significantly elevated BNP at 174 mg/L, and impaired renal function indicated by a creatinine of 122 and GFR of 47. The definitive diagnosis was verified through an abdominal fat aspiration biopsy, which showed Congo red positivity with the characteristic apple-green birefringence under polarized light. The patient's condition rapidly worsened, leading to the first hospital admission on December 17, 2024. He presented with decompensated cardiac failure, hypoxia requiring supplemental oxygen, and acute kidney injury with GFR decreasing to 29. Chest X-ray Figure 4 revealed bilateral pleural effusions, basal atelectasis, and consolidation, possibly due to infection or probable heart failure. Clinical examination showed hypotension (BP 100/70 dropping to 87/68), fever (38.5°C), and significant bilateral pitting edema. Initial treatment included IV furosemide, dexamethasone 20mg daily, and IV Tazocin for concomitant pneumonia.

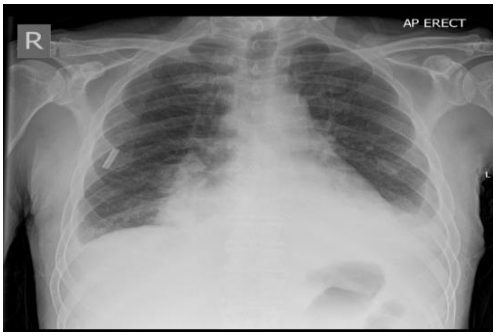

Figure 4. Chest X-Ray 16/12/2024

(Bilateral pleural effusions, basal atelectasis, and consolidation, which may be secondary to infection or possibly heart failure.)

Between December 2024 and January 2025, the patient had multiple hospital admissions, illustrating the difficulty of managing cardiac amyloidosis alongside infections. After a short period of improvement and discharge for virtual ward monitoring, he was readmitted on December 26th with severe breathing symptoms. CXR Figure 5 showed worsening consolidation in the right mid and lower zones and a stable left retrocardiac consolidation along with bibasal effusions, indicating a mix of infection and heart failure. Inflammatory markers were heightened (CRP 98 mg/L, WBC 23.0 × 1000/µl), and there was a gradual decline in kidney and liver function. This underscores a common challenge for cardiac amyloidosis patients, where balancing heart failure treatment with worsening renal function is crucial.

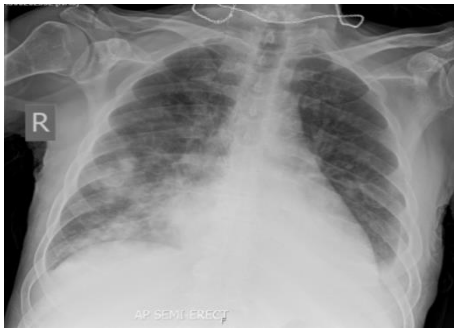

Figure 5. Chest X-Ray 26/12/2024

(Progressive consolidation in the right mid and lower zones and stable left retrocardiac consolidation on bibasal effusions may indicate a combination of infection and heart failure.)

Treatment evolved throughout these admissions, beginning with IV furosemide infusion and dexamethasone, later transitioning to oral medications with monitoring through a virtual ward system. Eventually, treatment involved a split diuretic regimen and targeted antibiotic therapy with meropenem for the resistant infection. This progression aligns with the known poor prognosis of cardiac AL amyloidosis, particularly in patients with Mayo stage 3A disease. The patient's final admission on January 3, 2025, introduced new complications, including Mobitz type 2 atrial fibrillation and a resistant Klebsiella infection He experienced episodes of erratic breathing and blood pressure instability, requiring careful medication adjustments. The patient received concurrent management from the cardiology and haematology departments. A bone marrow biopsy revealed over 10% plasma cells, indicating the presence of myeloma with amyloidosis. Confirmation remains outstanding for the cell markers. In light of these findings, chemotherapy consisting of DVCD(Darzalex, Velcade, Cyclophosphamide, and Dexamethasone) was prescribed. This case spanned over 6 months, exemplifying the rapid progression in cardiac AL amyloidosis and highlighting the complex interplay between cardiac dysfunction, infection susceptibility, and multi-organ involvement. Unfortunately, the patient died during this last admission due to severe heart failure symptoms.

Discussion

This case offers valuable insight into both the diagnostic approach and management challenges of cardiac AL amyloidosis. Our diagnostic approach demonstrates the modern, systematic multimodality imaging strategy recommended by current expert consensus [14]. The multimodality imaging used in our case—particularly the combination of echocardiography, cardiac MRI, and nuclear imaging—proved essential for both diagnosis and monitoring disease progression. This comprehensive approach aligns with current best practices, enabling us to assess the extent of cardiac involvement and disease progression [4]. The cardiac MRI results in our patient, particularly the high native T1 values and distinctive late gadolinium enhancement patterns, align with Maceira et al.'s findings showing over 95% sensitivity [15]. The grade 1 DPD uptake seen in nuclear imaging was especially important in our diagnosis, matching Gillmore et al.'s research on different uptake patterns between AL and ATTR amyloidosis [16]. This moderate uptake pattern, typical of AL amyloidosis, provided crucial diagnostic clues that influenced subsequent management decisions. The combination of multiple imaging modalities proved especially valuable: Echocardiography showed structural changes and diastolic dysfunction. - CMR provided detailed tissue characterization confirming amyloid infiltration. - Nuclear imaging helped differentiate amyloid subtypes and assess disease extent. Despite early detection, the patient experienced rapid disease progression, highlighting both the aggressive nature of cardiac AL amyloidosis and the ongoing management challenges. [14]. The swift decline from initial diagnosis to multiple hospitalizations within six weeks reflects the poor prognosis associated with cardiac AL amyloidosis, especially in Mayo stage III disease. This pattern of progression aligns with Wechalekar et al.'s European collaborative study of 346 patients, which showed similar rapid deterioration with a median survival of 3.5 months without treatment [17]. The recurring infections and

heart failure observed in this case reinforce recent literature describing the complex relationship between cardiac dysfunction and immune system compromise [2]. The management difficulties faced, particularly regarding fluid balance and antibiotic choice, mirror similar issues reported in current research [3]. The development of resistant Klebsiella infection and conduction abnormalities in the heart corresponds with Merlini et al.'s findings on under-reported but significant complications affecting treatment options and survival [18]. The onset of atrial fibrillation adds to the growing evidence of electrical changes in cardiac amyloidosis. Sidana et al.'s study shows that atrial fibrillation and non-sustained ventricular tachycardia seen during 24-hour Holter monitoring are linked to poorer short-term survival outcomes. This underscores the importance of early detection, thorough cardiovascular monitoring, and proactive management strategies in patients with cardiac amyloidosis [19]. Moreover, our experience with virtual ward monitoring demonstrated its potential and limitations in this patient group. While it helped identify early deterioration, it did not prevent readmissions, a challenge also noted in recent studies [6]. The need for regular medication adjustments and managing resistant infections highlights the complexity of outpatient care and the necessity for rapid intervention capabilities [7]. In hindsight, an earlier bone marrow biopsy could have helped confirm the presence of myeloma at an earlier stage, allowing prompt initiation of targeted therapies aimed at reducing amyloid production. However, the disease's rapid and aggressive course makes it uncertain whether an earlier diagnosis of amyloidosis and sooner treatment would have significantly changed this patient's outcome. This case emphasizes the importance of a coordinated multidisciplinary approach involving cardiology, hematology, and infectious disease specialists. It provides a detailed account of a rare presentation of amyloidosis, offering valuable insights into its clinical features and diagnostic hurdles [4]. Nonetheless, as a single case report, the findings may not be applicable to all patients with amyloidosis.

Conclusion

This case underscores the importance of combining modern imaging techniques to accurately diagnose and stage cardiac amyloidosis. It also illustrates the rapid progression and management challenges, emphasizing the need for imaging protocols and new techniques for earlier detection, along with standardized management practices to enhance patient outcomes. Overall, the findings from this case study reinforce the significance of a comprehensive, multidisciplinary approach to cardiac amyloidosis care that integrates advanced imaging with clinical monitoring and aggressive management of complications. Incorporating emerging diagnostic tools with refined treatment protocols will be key to improving prognosis for this difficult patient group.

Ethical Consideration

Ethical standards have been upheld in accordance with Wwl NHS Trust regulations. Informed consent for the publication of this case report was obtained from the patient while he was alive and is documented in the HIS system. All patient data has been anonymized to ensure privacy is protected.

Acknowledgments

We would like to thank the patient for his cooperation and consent to share this case, which he provided while he was alive. We also express our gratitude to the medical staff at Wigan Infirmary for their exceptional care and support throughout the patient's treatment.

Author's Contribution

Professor Sanjay Arya: Formulated the treatment strategy, provided supervision, and offered guidance. The patient was under the supervision of Professor Arya.

Dr. Venus Shahabi Rabori: Gathered data and images, authored the initial version of the case report, and secured the patient's consent.

Dr. Sara Azim: Reviewed the case report and prepared the final edition.

Conflicts of Interest

The authors declare no conflict of interests.

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