Case report

Fatal refractory cardiac arrest as presentation of systemic amyloidosis

Peter Chung a,*, Sarah Wheeler b, Andrew Fong b, Kyle Hurth b, Bassam Yaghmour a

a Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, Keck School of Medicine at the University of Southern California, Los Angeles, CA, USA
b Department of Pathology, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA

1. Introduction

Amyloidosis is a rare but well-described disease that is characterised by extracellular tissue deposition of misfolded precursor protein involving fibril formation. Both systemic and localized amyloidosis have been reported with different types such as AL, AA, and ATTR. Although initial diagnosis may be challenging, a thorough clinical evaluation coupled with laboratory and radiographic studies as well as histological tissue confirmation is diagnostic. The usual age of onset has been reported to be in the fifth and sixth decade of life. Symptoms manifest through various organ systems including autonomic neuropathy associated with postural hypotension, syncope, arrhythmias, fatigue, cachexia, pleural effusion, dyspnea, nephrotic syndrome, macroglia, and telangiectasia. Treatment options vary depending on the type of fibrin precursor as well as hereditary versus non-hereditary or localized versus systemic manifestation. Some examples include organ transplantation, chemotherapy, stem cell transplantation, biologic agents, and antibodies that inhibit fibrin formation. We report two unusual cases of systemic amyloidosis with the first presentation as acute, refractory, and persistent cardiopulmonary arrests when patients had no prior diagnosis or symptoms.

2. Case presentation

Patient #1: Patient is a 54 year-old male with past medical history significant for polycystic kidney disease who presented with gastro-esophageal reflux disease. He had been trialed on medical therapy without relief in symptoms which consisted of heart burn, globus sensation, and difficulty swallowing both solids and liquids. His symptoms first began at age 25 and continually worsened. Otherwise, review of systems was negative. His surgical history was only significant for coronary artery disease or pulmonary embolism. He did not show evidence of anatomical shunt, myocardial ischemia, coronary artery disease or pulmonary embolism.

Intraoperatively, the trocar was inserted in the abdomen in usual fashion and insufflation was started. No abnormalities were noted on direct visual inspection with laparoscope. The patient then became acutely bradycardic and went into PEA cardiac arrest. The abdomen was de-sufflated and ACLS was initiated immediately. Bilateral chest tubes were placed with no extravasation of air and no apparent tension pneumothorax. ROSC was achieved after a total of seven rounds of CPR, and hemodynamic stabilization was achieved only after cannulation with VA ECMO support. Etiology of cardiac arrest was not clear. Evaluations including echocardiogram, cardiac catheterization, and CT chest did not show evidence of anatomical shunt, myocardial ischemia, coronary artery disease or pulmonary embolism.

* Corresponding author.
E-mail address: peter.chung@med.usc.edu (P. Chung).

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Hospitalization was further complicated by multi-organ failure, but the patient recovered, was decannulated off ECMO, and extubated successfully. However, he experienced an acute hypoxic respiratory failure leading to two additional episodes of PEA cardiac arrests. This time, etiology was a pulmonary embolism from a right lower extremity deep venous thrombus. He was intubated for cardiogenic, obstructive shock and was given thrombolytics followed by systemic anticoagulation. His shock eventually resolved and was extubated again with stabilization in his overall clinical condition. He then experienced an episode of atrial fibrillation with rapid ventricular response followed by acute hypotension leading to a fourth episode of cardiac arrest. No sustained ROSC was achieved this time, and another VA ECMO was unlikely to change the outcome. Despite all resuscitative efforts, he remained pulseless with asystole and expired. Autopsy was performed which revealed diffuse, systemic amyloidosis with predominantly serum AA protein involving the pulmonary, cardiovascular, gastrointestinal, and endocrine system (Fig. 1).

Patient #2: Patient is an 82 year-old male with a past medical history of hemochromatosis, hypertension, diabetes and lung cancer who presented for cardiology evaluation after new diagnosis of heart failure with preserved ejection fraction. He had developed progressive dyspnea, decreased exercise capacity, and anasarca requiring outside hospitalization with improvement after diuresis. He had noted one episode of syncope the week prior to presentation. Otherwise, review of systems was negative. He had a history of ventricular tachycardia 17 years ago with a normal coronary angiogram at that time. He underwent partial lobectomy without chemotherapy or radiation for his lung cancer 9 years prior. Other surgical history included bilateral hip arthroplasties with multiple revisions on the right side. Family history was non-contributory, and social history was negative for alcohol, tobacco, and drug use. Medications included metoprolol, furosemide, aspirin, atorvastatin, metformin, and allopurinol.

On initial evaluation, patient had normal vital signs. His physical exam was notable for elevated JVD, left parasternal lift, abdominal fluid wave, and bilateral lower extremity edema to ankles. Laboratory values consisted of elevated pro-BNP levels. EKG showed normal sinus rhythm, low voltage in limb leads and left axis deviation. CXR and VQ scan were unremarkable. Ambulatory cardiac rhythm monitoring showed brady-cardiac episodes. Due to concern for an infiltrative cardiomyopathy in the setting of hemochromatosis, he was admitted for right and left heart catheterization, right ventricle biopsy, dual chamber pacemaker, and CardioMEMs placement which he underwent without immediate complications.

In the evening post-procedure, the patient became unresponsive, pulseless, with paced rhythm on telemetry. He underwent ACLS resuscitation and ROSC was achieved within 2 minutes. ABG was without hypoxemia or major metabolic alterations. He was transferred to the ICU where he again became unresponsive with PEA arrest and circulatory collapse. He underwent ACLS with ROSC achieved in less than 2 min. He was intubated for airway protection. Bedside ultrasound showed severe biventricular hypokinesis with EF of <30% and hyperkinetic apex consistent with cardiogenic shock/stunned myocardium but no peri-cardial effusion or pneumothorax. CXR showed bilateral pulmonary edema and bibasilar consolidation. Pacemaker interrogation was unremarkable. Mechanical circulatory support was planned in the setting of escalating inotropic requirements, but he experienced another PEA followed by ROSC with ACLS. Angiogram and diagnostic studies did not show evidence of focal amyloidosis, aortic stenosis, or hemorrhage. Mechanical circulatory support device Impella was placed, but he experienced two additional episodes of PEA arrests. Subsequent CT head, chest, abdomen, and pelvis were without obvious pathology. A few hours later, he had a fifth PEA arrest and the clinical picture was consistent with multi-organ failure from cardiogenic shock despite maximal vasopressor and mechanical support. Given poor prognosis, family opted for comfort care and the patient expired. Cardiac biopsy showed amyloid with monoclonal IgG deposition and SPEP had a monoclonal band consistent with AL amyloidosis. Autopsy was also notable for diffuse systemic amyloidosis.

3. Discussion

Gastrointestinal involvement of systemic amyloidosis, in particular, has been reported to result in poorer outcome [4,8]. In the absence of any symptoms, Patient #1 interestingly exhibited only severe reflux symptoms for which he was undergoing an elective LINX surgical procedure after failing medical therapy. Although pulmonary embolism was a cause for one of the cardiac arrests in Patient #1, the initial and the recurrent arrests that led to the death of this patient with no significant underlying medical condition may have been secondary to an undiagnosed systemic amyloidosis with reflux as the sole clinical presentation. We speculate that his polycystic kidney disease may have impaired the clearance of amyloid proteins causing systemic accumulation. However, there is no strong association between amyloidosis and polycystic kidney disease beyond several rare case reports where chronically infected cysts or other infection caused amyloidosis secondarily [5,7]. As for the patient’s pulmonary embolism and his right lower extremity deep venous thrombosis, previous cases and studies have reported increased incidence of deep venous thrombosis in amyloidosis patients when compared to general population [1]. The incidence rate is comparable to those in multiple myeloma patients due to dysregulation in thrombin-antithrombin pathway [3]. While immobility and others factors may have predisposed Patient #1 to thrombus formation, we suspect that the underlying amyloidosis increased this risk furthermore [2,6].

In Patient #2, the concern for infiltrative cardiomyopathy from hemochromatosis may have deterred physicians’ suspicion for cardiac amyloidosis. However, the patient was asymptomatic besides the exertional dysnea from his cardiomyopathy. There were also no positive diagnostic studies for amyloidosis. Amyloidosis is often unrecognized unless certain symptoms are present that lead to further evaluation. While long-term outcome of localized disease is excellent, systemic manifestation outcome has been reported to be poor [3,8]. Both of our patients did not exhibit any of the typical symptoms of autonomic neuropathy, chest pain, palpitations, postural hypotension, macro-glossia, telangiectasia, diarrhea, malabsorption, or proteinuria. All diagnostic studies including EKG, echocardiogram, laboratory results, urinalysis, and radiographs were not specifically suggestive of amyloidosis, and the differential diagnosis list for our patients did not particularly include amyloidosis. However, both patients were diagnosed with biopsy-proven systemic amyloidosis after presenting with sudden, refractory, and recurrent cardiac arrests that led to death. Cardiac arrests were similar in both cases – acute and persistent with PEA rhythms.

Our two cases highlight the importance of considering amyloidosis as a potential diagnosis even in asymptomatic patients as the outcome with this disease could be fatal. We suggest having a higher index of suspicion for systemic amyloidosis when patients present with sudden and recurrent PEA arrests with unclear etiologies or with etiology that does not fully explain the severity degree of patient’s cardiac arrest. Based on these two cases, prognosis is poor, and there may not be many treatment options. However, clinicians should be aware of these rare and lethal presentations of systemic amyloidosis.

Declaration of competing interest

The authors have no conflicts of interest or financial ties to disclose with respect to publication of this article.

CRediT authorship contribution statement

Peter Chung: Conceptualization, Writing - original draft, Writing - review & editing. Sarah Wheeler: Writing - original draft. Andrew

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Heart

A B C

Lung

D E F

Kidney

G H I

Other

J K L

M (caption on next page)
Fig. 1. Pathology from Patient #1 Autopsy.
Heart: H&E of myocyte hypertrophy and thickened cardiac vessels with pink amorphous material (A). Congo Red with perivascular apple-green birefringent amyloid deposition in cardiac vessels (B). Protein P immunohistochemistry with patchy staining of amorphous material within vessel walls (C). Lung: H&E showing a vessel with thickened walls containing pink amorphous material (D). Congo Red with perivascular apple-green birefringent amyloid deposition (E). Amyloid A immunohistochemistry showing strong perivascular staining (F). Kidney. H&E showing a large deposit of pink amorphous material (G) and a vessel with thickened walls containing pink amorphous material (H). Congo Red with perivascular apple-green birefringent amyloid deposition (I). Stomach (J), Large Bowel (K), Bladder (L), and Prostate (M). H&E showing vessels with thickened walls containing pink amorphous material. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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