

## Trifascicular block as primary presentation of the cardiac amyloidosis; A rare case report

Mohsen Yaghubi<sup>(1)</sup>, Hossein Dinpanah<sup>(2)</sup>, Fahimeh Ghanei-Motlagh<sup>(3)</sup>,  
Samaneh Kakhki<sup>(4)</sup>, Reza Ghasemi<sup>(5)</sup>

### Case Report

#### Abstract

**BACKGROUND:** Amyloidosis is a severe systemic disorder produces by the accumulation of inappropriately amyloid deposition in tissues. Cardiac involvement, as a main type of amyloidosis, has a major impact on prognosis. We describe a biopsy-proven cardiac amyloidosis in an old man with unexpected presentation.

**CASE REPORT:** A 70-year-old man, with a complaint of severe weakness, lightheadedness, and lower limb paresthesia, was admitted to the emergency department. Electrocardiography revealed right bundle branch block and Trifascicular block. Echocardiography study showed a moderately increased thickness of left ventricular wall with concentric pattern as well. Laboratory investigations including serum and urine electrophoresis, and serum free light chain examination as immunofixation assay revealed that  $\kappa$  chains predominated over  $\lambda$  chains in a ratio of 3:2. Our patient with final diagnosis of amyloid light-chain (AL) amyloidosis underwent chemotherapy with melphalan combined with high-dose dexamethasone, CPHPC and monoclonal antibodies for 2 weeks.

**CONCLUSION:** It shows that rapid diagnosis of AL amyloidosis can enhance the prognosis. Applying an optimal strategy for the treatment leads to effective therapy, too.

**Keywords:** Amyloidosis, Bundle Branch Block, Echocardiography

*Date of submission:* 27 Aug. 2017, *Date of acceptance:* 30 Dec. 2017

#### Introduction

Cardiac amyloidosis is determined as dramatically extracellular infiltration of amyloid in the heart.<sup>1</sup>

The predominant organ affected by depositions of amyloids is the heart; however, in some types of this disease, isolated heart involvement can occur. Anatomical distributions of amyloid deposition in the heart include atria, ventricles, and perivascular space as well as valves and conduction system.<sup>2</sup>

Amyloidosis in senile patients affects some organs such as liver, gastrointestinal tract, bone marrow, upper gastrointestinal tract, and endocrine glands; but, the dramatically clinical appearance of cardiac amyloidosis in this patients are very rare.<sup>3</sup>

Hereby, we present an old man with cardiac amyloidosis presented only with Trifascicular block, with early diagnosis and successful management.

#### Case Report

A 70-year-old man patient weighing 55 kg was admitted to emergency department with a complaint of severe weakness, lightheadedness, and lower limb paresthesia. Before this admission, he also presented worsening of symptoms in the last two weeks. He had no family history of cardiovascular disease, sudden cardiac death, or syncope.

On admission, hemodynamic parameters were in acceptable condition. He had blood pressure of 79/99 mmHg, heart rate of 57 beats/minute, and respiratory rate of 20 breath/minute, and he was also afebrile. Oxygen saturation, at rest, with finger pulse oximeter in index finger was 95%.

Primary physical examination was also done and we found the S4 sound in the apex, in cardiac auscultation. He was in class 2 of the New York Heart Association (NYHA) Functional Classification. Laboratory findings showed a mild hypochromic

1- MSc Student, Student Research Committee AND Department of Cardiac Surgery, Mashhad University of Medical Sciences, Mashhad, Iran  
2- Assistant Professor, Department of Emergency, Dey 9<sup>th</sup> Hospital, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran  
3- Department of Obstetrics and Gynecology, Dey 9<sup>th</sup> Hospital, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran  
4- Assistant Professor, Department of Pharmacology, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran  
5- Assistant Professor, Department of Cardiology, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran  
Correspondence to: Reza Ghasemi, Email: rezaghasemi152@yahoo.com

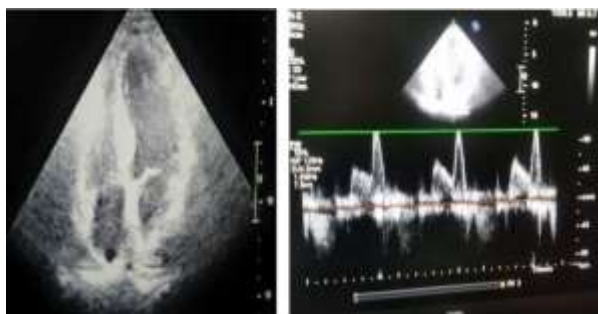
microcytic anemia [hemoglobin = 10.9 g/dl, hematocrit = 30.3%, mean corpuscular volume (MCV) = 73.09 fl, and mean corpuscular hemoglobin (MCH) = 21.67 pg]. He had degrees of hypothyroidism with thyroid stimulating hormone (TSH) of 20 mU/l and serum thyroxine (T4) of 2.4 µg/dl.

Electrocardiography (ECG) showed right bundle branch block (RBBB) with right axis deviation and complete atrioventricular block that diagnosed as a Trifascicular block (Figure 1).



**Figure 1.** 12-leads electrocardiogram (ECG) of the patient after admission  
There is right axis deviation, left bundle branch block, and complete atrioventricular block revealed as Trifascicular block. Secondary ST-T change is also present.

The patient referred to echocardiography unit and transthoracic echocardiography showed a moderate increase in thickness of left ventricular (LV) wall as a concentric pattern and LV diastolic dysfunction (grade 2). The ejection fraction of LV (LVEF) was 55%. Echocardiography revealed normal right ventricle size and function as well [tricuspid annular plane systolic excursion (TAPSE) = 1.9 cm] (Figure 2). Cardiac biomarkers revealed that troponin I was negative with elevated N-terminal prohormone of brain natriuretic peptide (NT-ProBNP) equal to 288 pg/ml.



**Figure 2.** Apical four-chamber view echocardiography  
Left ventricular (LV) thickening free wall is seen. No evidences of both dilated atria and interatrial septum are seen. Any evidences of thickening of mitral and tricuspid valve cusps are not seen as well.

Regard to severe weakness and paresthesia, he referred to neurology department for electrodiagnostic study. The electrodiagnostic evaluation revealed absent sensory nerve action potential (SNAP) with low amplitude compound muscle action potentials (CMAPs) of upper and lower limbs. These findings were compatible with chronic sensory-motor polyneuropathy with axonal features, and evidence of ongoing axonal loss.

According to the sustained anemic situation and severe weakness, the patient underwent bone marrow aspiration. Microscopic evaluation of bone marrow aspiration revealed elevated cellularity with myeloid hyperplasia to erythroid hypoplasia ratio of 3:1, and complete maturation. Plasma cells were 22% of all nucleated cells. This finding was compatible with plasma cell myeloma.

Laboratory investigations including serum and urine electrophoresis and serum free light chain examination as immunofixation assay were also done. The results showed that kappa ( $\kappa$ ) chains predominated over lambda ( $\lambda$ ) chains in a ratio of 3:2. The hepatic test showed elevated alkaline phosphatase value equal to 215 U/l.

Ultimately, by considering all clinical aspects and paraclinical investigations mentioned above, final diagnosis for the patient was amyloid light-chain (AL) cardiac amyloidosis.

Immediately, the targeted therapy was established. Regarding clinical and paraclinical parameters, the patient received melphalan combined with high-dose dexamethasone. Concurrently, immunotherapeutic strategy with CPHPC and monoclonal antibodies were also prescribed. The patient closely monitored for 2 weeks and during this treatment period, he showed hematologic and organ response to the therapy. After this period, kappa to lambda ratio in urine immunofixation electrophoresis was normal, and serum level had a negative result. Heart response included no change in normal left ventricular ejection fraction (55 %), enhance the NYHA class of 2 to 1 without using any medications such as diuretic, and no wall thickness enhancement. NT-ProBNP was in normal range (100 pg/ml). The hepatic test revealed that alkaline phosphatase value had a dramatic decrease in 101 U/l (more than 50%).

After completion of treatment, the patient was discharged and advised to follow his situation and disease by referring to heart clinic every 2 weeks until 6 months, and referring electrophysiologist to consult the indications of an implantable cardiac defibrillator.

## Discussion

Cardiac amyloidosis might possibly be related to the inclusion of different organs. The presence of different type features of the clinical and paraclinical evidence shall almost enhance the hesitancy for this disorder. These findings prompt a stepwise indicative process to confirm cardiac amyloidosis.<sup>3</sup> Early diagnosis is a key requisite for successful treatment of AL amyloidosis allowing insulation of the organ damage, and safety treatment to avoid toxicity.<sup>4</sup> The target of common therapies is to put down the pathological plasma cells, and to remove misfolded free light chains. The treatment with this approach can lead to a relapse of amyloid deposits with yield organ enhancement and long-term survival.<sup>5</sup>

Clinical detections in patients with cardiac amyloidosis may had an extensive range of features involving many organs. In AL amyloidosis, there is a massive amount of possible extracardiac findings such as macroglossia, periorbital purpura, and petechial lesions of eyelids due to vascular fragility, neuropathic conditions, and severe fatigue. Hepatic and renal involvements are usual in AL amyloidosis;<sup>6</sup> but nephropathy is a very scarce presentation. Nervous system involvement results in a progressive sensorimotor neuropathy.<sup>3</sup> In our patient, clinical features on admission were only cardiac conductive disturbances that presented with complete atrioventricular block. Another investigation revealed other manifestations such as neuropathy that presented with severe weakness. This manifestation first seemed to be completely independent, and a massive challenge for the diagnosis.

The most prevalent echocardiographic presentation in cardiac amyloidosis is involvement of the LV wall, merely in the absence of hypertension.<sup>7,8</sup> In our patient, we found moderate concentric LV wall thickening of about 2 cm, without any hypertensive manifestation. This is often referred to incorrectly as “hypertrophy” because the pathological process is infiltration, not myocyte hypertrophy.<sup>7</sup>

The composition of increased LV mass in the absence of high ECG voltages may be due to infiltrative diseases, of which amyloidosis is the most ordinary. In our patient, the ECG was not accompanied by low-voltage and pseudo-infarct pattern; this can be sound in 75% of AL cardiac amyloidosis cases.<sup>7</sup> Moreover, our patient had a conductive abnormality with complete AV block. Conduction abnormality in AL cardiac amyloidosis is an often unusual presentation and this event may

be dependent on the risk of sudden death.<sup>9</sup> So, these patients should be closely monitored.

Blood tests represent a crucial part of the assessment in suspected amyloidosis. Nowadays, a serum immunoglobulin free light chain (FLC) assay with quantitative analysis of kappa to lambda ratio has become the most useful laboratory method for establishing the diagnosis, prognostic, and follow-up of AL amyloidosis.<sup>10</sup> In this case, we observed a kappa to lambda ratio of 3:1, which revealed definite diagnostic laboratory test of AL amyloidosis.

Cardiac biomarkers represents by negative troponin I with elevated NT-proBNP in patients with amyloid heart disease.<sup>11</sup> In our patient, NT-proBNP levels were increased asymmetrically to the intensity of symptoms of congestive heart failure (CHF) (NYHA class 2). This may be related to the fact that increase the NT-proBNP levels is not only a result of heart failure, but also reflects hormone production by myocytes that are compressed by extracellular amyloid deposits.<sup>3</sup>

Chemotherapy is withstood poorly in many patients with AL amyloidosis,<sup>7</sup> but our patient had a good outcome with protocol therapy and eventually, he discharged with an acceptable situation after 2 weeks of admission. This may be due to considering the indication criteria for other treatment such as high dose melphalan and autologous stem cell transplant (HDM/SCT), and shift the protocol to melphalan combined with a high dose of dexamethasone. This restricted criterion includes age lower than 65 years old, involvement of two or more organs, NT-proBNP and troponin I levels lower than 35 ng/l and 0.1 ug/l, respectively, LV ejection fraction more than 45%, creatinine clearance more than 50 ml/minute, and systolic blood pressure of 90 mmHg.<sup>12</sup> In our case, all of the mentioned parameters were not seen. So, optimal target therapy in this patient was done.

Despite significant developments in chemotherapy for AL amyloidosis, the prognosis of patients with advanced cardiac involvement remains poor. So, early diagnosis of AL amyloidosis is critical, and this approach leads to effective therapy.

## Acknowledgments

We would like to thank the patient participated in this study. We would also like to thank the cardiology, pathology, and pharmacology departments of Mashhad University of Medical Sciences, Mashhad, Iran.

**Conflict of Interests**

Authors have no conflict of interests.

**References**

1. Bunker D, Gorevic P. AA amyloidosis: Mount Sinai experience, 1997-2012. *Mount Sinai Journal of Medicine: A Journal of Translational and Personalized Medicine* 2012; 79(6): 749-56.
2. Dubrey SW, Hawkins PN, Falk RH. Amyloid diseases of the heart: Assessment, diagnosis, and referral. *Heart* 2011; 97(1): 75-84.
3. Falk RH. Diagnosis and management of the cardiac amyloidoses. *Circulation* 2005; 112(13): 2047-60.
4. Fikrle M, Palecek T, Kuchynka P, Nemecek E, Bauerova L, Straub J, et al. Cardiac amyloidosis: A comprehensive review. *Cor et Vasa* 2013; 55(1): e60-e75.
5. Koyama J, Falk RH. Prognostic significance of strain Doppler imaging in light-chain amyloidosis. *JACC Cardiovasc Imaging* 2010; 3(4): 333-42.
6. Palladini G, Lavatelli F, Russo P, Perlini S, Perfetti V, Bosoni T, et al. Circulating amyloidogenic free light chains and serum N-terminal natriuretic peptide type B decrease simultaneously in association with improvement of survival in AL. *Blood* 2006; 107(10): 3854-8.
7. Merlini G, Seldin DC, Gertz MA. Amyloidosis: Pathogenesis and new therapeutic options. *J Clin Oncol* 2011; 29(14): 1924-33.
8. Mohty D, Damy T, Cosnay P, Echahidi N, Casset-Senon D, Viot P, et al. Cardiac amyloidosis: Updates in diagnosis and management. *Arch Cardiovasc Dis* 2013; 106(10): 528-40.
9. Nordlinger M, Magnani B, Skinner M, Falk RH. Is elevated plasma B-natriuretic peptide in amyloidosis simply a function of the presence of heart failure? *Am J Cardiol* 2005; 96(7): 982-4.
10. Palladini G, Merlini G. Current treatment of AL amyloidosis. *Haematologica* 2009; 94(8): 1044-8.
11. Reyners AK, Hazenberg BP, Reitsma WD, Smit AJ. Heart rate variability as a predictor of mortality in patients with AA and AL amyloidosis. *Eur Heart J* 2002; 23(2): 157-61.
12. Selvanayagam JB, Hawkins PN, Paul B, Myerson SG, Neubauer S. Evaluation and management of the cardiac amyloidosis. *J Am Coll Cardiol* 2007; 50(22): 2101-10.

**How to cite this article:** Yaghubi M, Dinpanah H, Ghanei-Motlagh F, Kakhki S, Ghasemi R. **Trifascicular block as primary presentation of the cardiac amyloidosis; A rare case report.** *ARYA Atheroscler* 2018; 14(2): 101-104.