Case Report

Diagnosis of Cardiac Transthyretin Amyloidosis by Technetium-99m Pyrophosphate Heart Scan, Confirmed by Genetic Mutations: Case Report

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Amyloid deposition in the myocardium can cause clinically significant heart failure, which is very difficult to diagnose. The present case reported presented a patient with heart failure, with suspected cause of cardiac amyloidosis, but abdominal fat pad and endomyocardial with Congo red stain biopsies were negative. Due to high suspicion of cardiac amyloidosis, a technetium-99m pyrophosphate (Tc-99m PYP) heart scan was done, which was revealed as strongly suggestive for cardiac transthyretin amyloidosis. So, the patient was sent for genetic testing, and a TTR gene mutation [c.148G>A (p.Val50Met)] was found.

Keywords: Cardiac amyloidosis; Endomyocardial biopsy (EMB); Technetium-99m pyrophosphate (Tc-99m PYP) heart scan; Transthyretin amyloidosis (TTR)

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Amyloidosis is a rare condition involving the deposition of insoluble amyloid proteins in various tissues, finally leading to organ dysfunction. The myocardium is one of the common deposit sites, causing heart failure, which is difficult to diagnose. An endomyocardial biopsy (EMB) using Congo red stain is the gold standard for diagnosis[1-3]. Cardiac imaging such as a technetium-99m pyrophosphate (Tc-99m PYP) heart scan and cardiac magnetic resonance imaging (MRI) have high sensitivity and specificity for confirming a diagnosis of cardiac amyloidosis[2,4,5]. The Tc-99m PYP heart scan also has the advantage of being able to distinguish amyloid subtypes[4,6].

Case Report

A 78-year-old female presented at a private hospital with progressive dyspnea and orthopnea for two months. An echocardiogram showed biventricular hypertrophy, normal function with left ventricular ejection fraction 45.0% to 50.0%, marked interatrial septum (IAS) thickening, severe tricuspid regurgitation, and no pericardial effusion. She was sent for a coronary angiography, which showed no abnormality. After that, the patient was referred to the authors' hospital to rule out cardiac amyloidosis. Initial investigations showed marked cardiomegaly in a chest radiograph and first-degree atrioventricular block with left ventricular hypertrophy on 12 lead electrocardiography (EKG).

A cardiac MRI showed evidence of infiltrative cardiomyopathy with diffuse delayed subendocardial enhancement involving both atrial, IAS, and right ventricle areas suspicious of cardiac amyloidosis (Figure 1). An abdominal fat pad biopsy was negative, followed by negative Congo red stain for three pieces of endocardium and myocardium biopsies under echocardiographic guidance at right ventricle and interventricular septum. Serum protein electrophoresis showed a normal pattern with no proteinuria or proteinemia. Three months later she developed polyneuropathy, a sign that was highly suspicious for cardiac amyloidosis, and she was sent for a Tc-99m PYP heart scan to confirm the diagnosis.

In the Tc-99m PYP heart scan, chest planar and single photon emission computer tomography (SPECT) images were acquired one hour after an injection of Tc-99m PYP and delayed images at three hours. The patient was injected with Tc-99m PYP

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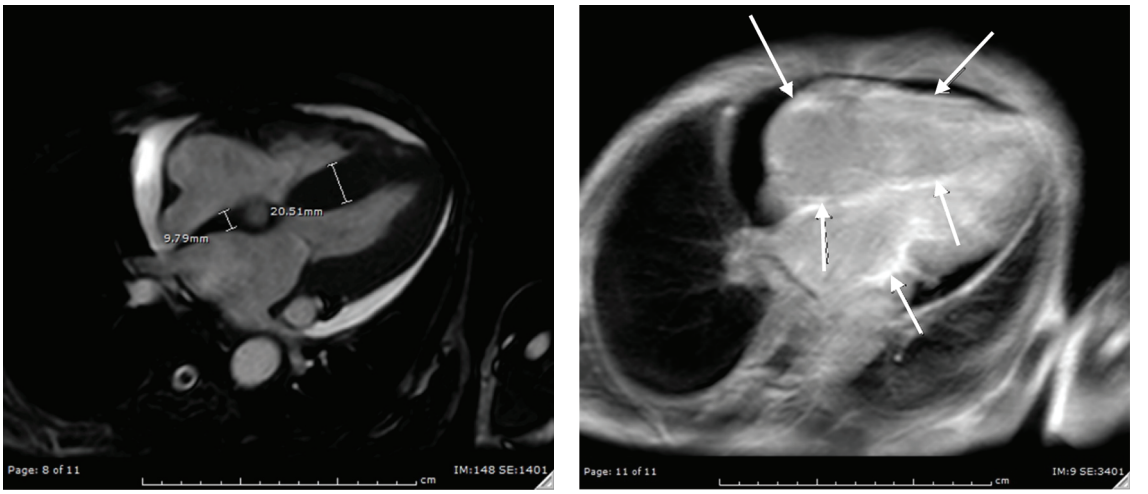

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Figure 1. Cardiac magnetic resonance imaging; (A) Four-chamber view bright blood image showing marked interatrial septum thickening and (B) an inversion recovery turbo field echo image of the left ventricle showing infiltrative cardiomyopathy with diffuse delayed subendocardial enhancement involving both atrial and right ventricle areas (arrow).

20.3 millicurie and planar images of the chest were obtained one hour later. Those revealed myocardial uptake significantly greater than the rib uptake with a heart and contralateral lung (H/CL) ratio of 2.2, which the normal is less than 1.5. Delayed and SPECT images also showed abnormal increased radiotracer accumulation at the myocardium equal to the rib uptake. Myocardial uptake equal to or greater than rib uptake or with an H/CL ratio of more than 1.5 uptake was strongly suggestive of transthyretin (TTR) amyloidosis (ATTR) (Figure 2).

After that, the patient was sent for genetic testing and a TTR gene mutation (c.148G>A (p.Val50Met)) was found.

Discussion

The main cause of cardiac amyloidosis is the abnormal synthesis of monoclonal immunoglobulin light chains (AL) from an abnormal proliferation of plasma cells or ATTR. Left ventricular failure in this disease can worsen if the only treatment is with traditional regimens, thus a prompt and accurate diagnosis is important[7]. The EMB has traditionally been the gold standard for diagnosis, however, in recent years, advances in radiographic imaging have allowed accurate non-invasive diagnosis without the need for an EMB[8]. These radiographic modalities, notably the Tc-99m PYP heart scan and cardiac MRI, have high sensitivity and specificity. The Tc-99m PYP heart scan is particularly useful as it can distinguish AL from the other ATTR subtypes. Early and accurate diagnosis is important as TTR has a poor prognosis. The primary treatment is transplantation[2,3].

Since the Tc-99m PYP heart scan was introduced, many patients have been saved due to its ability to confirm a diagnosis of TTR. The interpretations of the Tc-99m PYP heart scan study are based on two methods. Firstly, the quantitative method by quantitative assessment of myocardial Tc-99m PYP uptake to compare the uptakes of the H/CL ratio on a 1-hour planar image. The second method is the semi-quantitative method by visual interpretation, using delayed planar and SPECT images at 3-hour, comparing the intensity of Tc-99m PYP uptake between the heart and ribs. If the H/CL ratios was 1.5 or greater, and the score was 2.0 or greater, the sensitivities are 97.0% and 58.0%, respectively, with 100% specificity of both for classifying ATTR positive[4]. Both H/CL at 1.5 or greater uptake or score of 2.0 or greater are strongly suggestive of the TTR subtype of amyloidosis[8,9]. Recent studies suggested that planar and SPECT images at 1-hour has comparable diagnostic performance to a 3-hour protocol and suggests that SPECT images should be performed[10].

However, the gold standard diagnosis (EMB) in the present case was limited from inadequate number of tissue sample and electron microscopy (EM) was not done. Earlier studies have suggested a minimum of four specimens is necessary[11] and that EM could provide a diagnosis as EM will reveal the presence of rigid, non-branching fibrils of 7.0 to 10.0 nm in

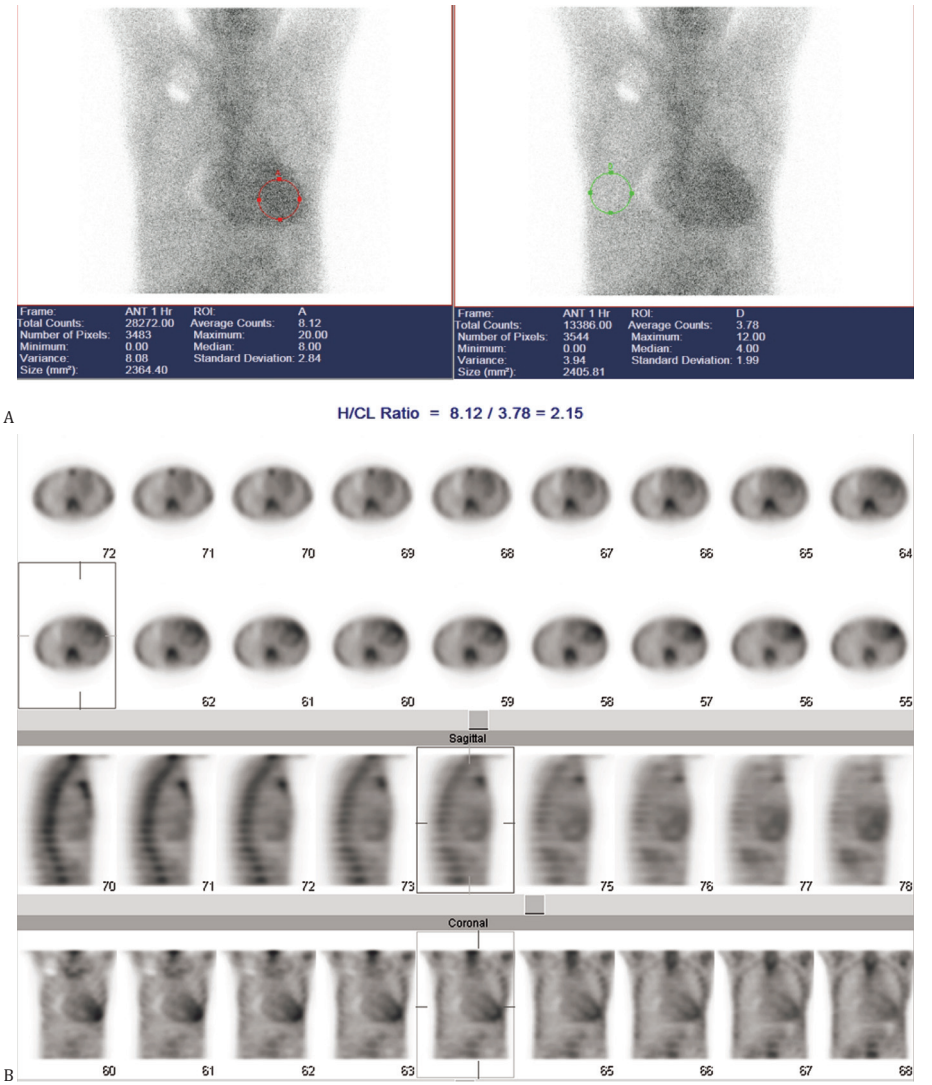

Figure 2. Technetium-99m pyrophosphate heart scan; (A) At 1 hour after injection a technetium-99m pyrophosphate showing regions of interest drawn over the myocardium and mirrored over the contralateral lung for calculated mean counts for quantification assessment of heart to contralateral ratios. (B) A single photon emission computed tomography image 3 hour after a technetium-99m pyrophosphate injection showing left ventricle uptake equal to rib uptake.

diameter[1]. Therefore, the present case study reminds that adequate samples of EM are important tools to make a definite diagnosis of amyloidosis, and a non-invasive Tc-99m PYP heart scan can support the diagnosis.

Conclusion

A non-invasive Tc-99m PYP heart scan was able to a confirm the diagnosis of ATTR in a highly suspected case of cardiac amyloidosis due to the high sensitivity and specificity of this test. In advanced clinical work up, could be useful to reduce the need for invasive procedures, such as endocardium or myocardium biopsies. Further studies would be helpful to confirm these non-invasive investigations.

What is already known on this topic?

A Tc-99m PYP heart scan has high sensitivity and specificity to confirm the diagnosis of ATTR cardiac amyloidosis, which is a non-invasive technique. The endomyocardial tissue samples, an invasive technique, is a gold standard of diagnosis.

What this study adds?

A Tc-99m PYP heart scan, a non-invasive technique, can diagnose the ATTR cardiac amyloidosis

with high sensitivity and specificity. In the case of highly suspicious of ATTR, the Tc-99m PYP heart scan can be one of the non-invasive diagnostic techniques for investigation action.

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Conflicts of interest

The authors declare no conflict of interest in this manuscript.

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