Usefulness of ^{99}mTc -HDP scintigraphy in the diagnosis of suspected cardiac amyloidosis revealed by heart failure: A case report of an amyloidogenic transthyretin mutation

Geraldine Celine Bera, Lavinia Vija, Pierre Jean Fouret, Nathanaëlle Yeni

ABSTRACT

Abstract is not required for Clinical Images

International Journal of Case Reports and Images (IJCRI)

International Journal of Case Reports and Images (IJCRI) is an international, peer reviewed, monthly, open access, online journal, publishing high-quality, articles in all areas of basic medical sciences and clinical specialties.

Aim of IJCRI is to encourage the publication of new information by providing a platform for reporting of unique, unusual and rare cases which enhance understanding of disease process, its diagnosis, management and clinico-pathologic correlations.

IJCRI publishes Review Articles, Case Series, Case Reports, Case in Images, Clinical Images and Letters to Editor.

Website: www.ijcasereportsandimages.com

CLINICAL IMAGES

PEER REVIEWED | OPEN ACCESS

Usefulness of ^{99m}Tc -HDP scintigraphy in the diagnosis of suspected cardiac amyloidosis revealed by heart failure: A case report of an amyloidogenic transthyretin mutation

Geraldine Celine Bera, Lavinia Vija, Pierre Jean Fouret, Nathanaëlle Yeni

CASE REPORT

A 54-years-old Guadeloupean patient known to have hypertrophic cardiomyopathy with severe left ventricular systolic dysfunction was hospitalized for cardiogenic shock. Ventricular arrhythmia lead to an implantable cardioverter-defibrillator (ICD). While most investigations proved to be unsuccessful, cardiological assessment showed: a micro-voltage on electrocardiogram (ECG); an increased level of N-terminal form of B-type natriuretic peptide (nT-pro-BNP) to 12000 ng/L; a restrictive infiltrative cardiomyopathy with concentric and homogeneous left ventricular hypertrophy and a

severe biventricular dysfunction on echocardiography (Figure 1). A cardiac single photon emission computed tomography (SPECT), performed three hours after the intravenous injection of 600 MBq of ^{99m}Tc -technetium oxidronate (^{99m}Tc -HDP) revealed abnormal myocardial uptake (Figure 2A–B) that was prominent on apical and anteroapical walls and moderate on antero-medial-septal wall (Figure 2C). In this context, the scintigraphy was highly suggestive of cardiac amyloidosis. This diagnostic was confirmed thereafter by myocardial biopsy that showed extracellular amyloid deposits (Figure 3). Antibody anti-transthyretin revealed by immunohistochemical analysis of amyloidosis was in favor of a transthyretin form. Genetic sampling showed homozygous missense mutation valine to isoleucine substitution at position 122 (V122I) of TTR gene.

Geraldine Celine Bera¹, Lavinia Vija², Pierre Jean Fouret³, Nathanaëlle Yeni⁴

Affiliations: ¹MD, University Medical Assistante, Department of Nuclear Medicine, AP-HP Hospital La Pitié-Salpêtrière, 47-83 Bd de l'hôpital 75651 Paris Cedex 13 France and Departement of Biophysic UPMC Paris VI, 91 Bd de l'hôpital 75651 Paris Cedex 13, France; ²MD, Ph.D, Practitioner Attached, Department of Nuclear Medicine and Biophysic, AP-HP Hospital Le Kremlin-Bicêtre 78 rue du Général Leclerc 94275 Le Kremlin-Bicêtre Paris Cedex, France; ³MD, Professor at Department of Pathology and UPMC Paris VI, AP-HP Hospital La Pitié-Salpêtrière, 47-83 Bd de l'hôpital 75651 Paris Cedex 13, France; ⁴MD, Contractual Hospital Practitioner, Department of Nuclear Medicine, AP-HP Hospital La Pitié-Salpêtrière, 47-83 Bd de l'hôpital 75651 Paris Cedex 13 France and Departement of Biophysic UPMC Paris VI, 91 Bd de l'hôpital 75651 Paris Cedex 13, France.

Corresponding Author: Geraldine Celine Bera, Department of Nuclear Medicine, AP-HP Hospital Pitié-Salpêtrière, 47-83 Bd de l' Hôpital Paris Cedex 13 75651, France; Tel: +33.1.42.17.62.81, Fax: +33.1.42.17.62.92; Email: berageraldine@gmail.com

Received: 04 April 2015

Accepted: 25 May 2015

Published: 01 September 2015

Figure 1: Short-axis echocardiography showing homogenous left ventricular hypertrophy.

Figure 2: (A) Whole body, (B) Left-anterior oblique chest view of ^{99m}Tc -HDP scintigraphy highlighted an abnormal myocardial uptake, and (C) Cardiac scintigraphy allows both accurate localization and graduation of the intensity of radio-tracer retention: high uptake on apical and antero-apical walls (black arrow) and moderate on antero-medial-septal wall (white arrow).

Figure 3: (a-f) Staining with Congo Red on histological sections of myocardial biopsy magnifications ((a-d) x20 and (e-f) x40); natural-light (a, c, e) and polarized-light (b, d, f) microscopy showing birefringent deposits as orange and green (white arrows) cells next to deposits are cardiomyocytes (black arrows).

DISCUSSION

Amyloidosis is characterized by extracellular tissue deposition in vital organs of misfolded proteins [1, 2]. Among systemic amyloidosis, immunoglobulin light-chain amyloid (AL-form) and transthyretin amyloid (ATTR-form) are known to infiltrate the heart leading to congestive heart failure, atrial fibrillation and conduction abnormalities [2, 3]. The TTR-form of cardiac amyloidosis, an underdiagnosed cause of heart failure, is slowly progressive and clinically well tolerated while AL-form often lead to rapidly progressive cardiac dysfunction. An early recognition and accurate classification of both entities, potentially fatal, is necessary because treatment depends on amyloidosis type. The ATTR-form may be either familial (variant TTR) caused by a mutation, or sporadic (aged-related) due to misaggregation of a wild-type transthyretin [2]. TTR is a transport protein primarily expressed by the liver and circulates

as homotetramer; under genetic mutation or aging, tetramers dissociate to monomers leading to amyloid fibrils [2]. Aggregate autopsy data show presence of wild-type TTR in 25–30% of hearts, leading to cardiac dysfunction in a smaller but significant elderly population [2, 4]. As for variant TTR more than 80 mutations have been described [1]. V122I TTR variant is one of the most widespread with a population prevalence of 4% in Afro-Caribbeans [2, 4]. Its diagnosis has to be confirmed by the immunohistochemical demonstration of amyloidogenic TTR-form on a biopsy specimen and by the presence of an ATTR mutation on protein/DNA analysis [2–4]. However myocardial biopsy is not often performed in practice because it is invasive, results are late with the possibility of false-negatives. Non-invasive diagnostic approaches such as ECG and echocardiography have low specificity and sensitivity, respectively [2]. Cardiac magnetic resonance (CMR) is hampered by limited availability and inability to image patients with pacemaker or ICD. This modality is able to identify amyloid infiltration by late gadolinium enhancement imaging (with a sensitivity and specificity of 90%), keeping in mind the potential risk of nephrogenic systemic fibrosis in these patients with frequent chronic kidney disease [2]. To note, radionuclide imaging shows a potential interest for identification cardiac amyloid deposits. With SPECT, a myocardial uptake of ^{99m}Tc -diphosphono-propanodicarboxylic acid (^{99m}Tc -DPD) is able to differentiate mutation carriers from the AL-form [1], likely due to higher concentrations of calcium-containing products in TTR amyloid [5]. Quantification of amyloid burden by scintigraphy could predict cardiac events and thus have an impact on determining therapeutic strategies. ^{99m}Tc -DPD cardiac retention can be scored as follow:

Grade 0 for no visible myocardial uptake in both the delayed planar or cardiac SPECT;

Grade 1 for cardiac uptake on SPECT only or cardiac uptake of less intensity than the accompanying normal bone distribution;

Grade 2 for moderate cardiac uptake with some attenuation of bone signal

Grade 3 for strong cardiac uptake with little or no bone uptake [6]. The possibility of a prognostic assessment by quantification allows to follow-up the course of the disease while new specific therapies for TTR amyloidosis are emerging (such as TTR stabilizers and small RNA silencing molecules). ^{18}F -florbetapir positron emission tomography (^{18}F -Florbetapir PET) approved for beta amyloid plaque in the brain, was investigated in cardiac amyloidosis and showed high myocardial radiotracer uptake and late retention of ^{18}F -Florbetapir in amyloid subjects suggesting a correlation with amyloid protein. However, its value in the diagnosis of cardiac amyloidosis remains to be confirmed [7]. Another interesting SPECT tracer is ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) for imaging of myocardial innervation. The localization of MIBG relates to the presence of sympathetic nerves. Myocardial defects in MIBG activity seems to correlate

with impaired cardiac sympathetic nerve endings due to amyloid deposits and can be identified very early in cardiac amyloidosis. Furthermore, the clinical severity of disease correlates with a decrease in MIBG uptake [1].

CONCLUSION

In conclusion ^{99m}Tc -HDP or ^{99m}Tc -DPD scintigraphy appears to be a major examination to establish the aetiology of cardiac amyloidosis with a high specificity, especially as age-related ATTR could become the most common form of this disease in the future. This could facilitate the ATTR specific care (genetic counselling, preventing measures and interference with medications). Furthermore with a simple and non-invasive method, whole-body tracer retention and specifically myocardial tracer retention correlated with disease severity could be used for prognostic assessment.

How to cite this article

Bera GC, Vija L, Fouret PJ, Yeni N. Usefulness of ^{99m}Tc -HDP scintigraphy in the diagnosis of suspected cardiac amyloidosis revealed by heart failure: A case report of an amyloidogenic transthyretin mutation. Int J Case Rep Images 2015;6(9):596–599.

doi:10.5348/ijcri-201525-CL-10080

Author Contributions

Geraldine Celine Bera – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

Lavinia Vija – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published

Pierre Jean Fouret – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Nathanaëlle Yeni – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© 2015 Geraldine Celine Bera et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

REFERENCES

1. Glaudemans AW, Slart RH, Zeebregts CJ, et al. Nuclear imaging in cardiac amyloidosis. Eur J Nucl Med Mol Imaging 2009 Apr;36(4):702–14.
2. Ruberg FL, Berk JL. Transthyretin (TTR) cardiac amyloidosis. Circulation 2012 Sep 4;126(10):1286–300.
3. Puille M, Altland K, Linke RP, et al. ^{99m}Tc -DPD scintigraphy in transthyretin-related familial amyloidotic polyneuropathy. Eur J Nucl Med Mol Imaging 2002 Mar;29(3):376–9.
4. Bokhari S, Shahzad R, Castaño A, Maurer MS. Nuclear imaging modalities for cardiac amyloidosis. J Nucl Cardiol 2014 Feb;21(1):175–84.
5. Bokhari S, Castaño A, Pozniakoff T, Deslisle S, Latif F, Maurer MS. (99m)Tc-pyrophosphate scintigraphy for differentiating light-chain cardiac amyloidosis from the transthyretin-related familial and senile cardiac amyloidoses. Circ Cardiovasc Imaging 2013 Mar 1;6(2):195–201.
6. Perugini E, Guidalotti PL, Salvi F, et al. Noninvasive etiologic diagnosis of cardiac amyloidosis using ^{99m}Tc -3,3-diphosphono-1,2-propanodicarboxylic acid scintigraphy. J Am Coll Cardiol 2005 Sep 20;46(6):1076–84.
7. Dorbala S, Vangala D, Semer J, et al. Imaging cardiac amyloidosis: a pilot study using ^{18}F -florbetapir positron emission tomography. Eur J Nucl Med Mol Imaging 2014 Sep;41(9):1652–62.

Access full text article on
other devices

Access PDF of article on
other devices

Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals

Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission

We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?

In less than 10 words - we give you what no one does.

Vision of being the best

We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services

We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review

All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review

All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version

Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status

From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks

You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.

Four weeks

After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.

Most Favored Author program

Join this program and publish any number of articles free of charge for one to five years.

Favored Author program

One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program

Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence

We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...

We request you to have a look at our website to know more about us and our services.

We welcome you to interact with us, share with us, join us and of course publish with us.

Edorium Journals: On Web

Browse Journals

CONNECT WITH US