LETTER TO THE EDITOR

Bone scintigraphy for early detection of transthyretin cardiac amyloidosis

Asad Ikram

Cardiac amyloidosis (CA) is an underdiagnosed condition which was considered rare. Recent autopsy data shows that 25% of elderly heart tissues contain amyloid on biopsy.[1] CA occurs when certain proteins misfold to beta-pleated confirmation and aggregate in the interstitium of the cardiac tissue. The accurate diagnosis of CA traditionally requires a gold standard endomyocardial biopsy (EMBx) with 1% risk of perforation if performed by skilled operators.[2] The use of Congo red staining methods to diagnose CA and further subtyping with immunofixation, serum free light chains, and mass spectrometry help differentiate light chain amyloidosis (AL) from transthyretin amyloidosis (ATTR): the two most common types of CA.

Combining several clinical and laboratory parameters lead to a diagnosis. Determination by race, risk factors, genetic predisposition, biomarkers, electrocardiography, echocardiography with strain, cardiac magnetic resonance imaging are routinely performed.[3] Technetium Pyrophosphate (TcPYP99) imaging of heart is very sensitive and specific for the diagnosis of ATTR.[4] It is essential to diagnose early and direct treatment accordingly, as the disease is uniformly fatal.[5]

Since the early 1980s, bone scintigraphy (TcPYP scan) has been used as a tool to diagnose CA. In the United States, only FDA approved nuclear tracer is TcPYP99. Technetium 3, 3-diphosphono-1, 2-propanodicarboxylic acid (TcDPD99) imaging is widely used worldwide and proved to have a high sensitivity and specificity for ATTR-CA with a high negative predictive value (NPV) of 100% for ruling out AL-CA and positive predictive value (PPV) of 88% for ATTR-CA. Studies showed that preferential binding of TcDPD99 is comparable to those of TcPYP99. A large pooled data on TcPYP99 from large amyloid centers in the United States show 90% sensitivity, 90% specificity, 80% NPV and PPV of 95%. It also allows diagnosis before electrocardiographic and echocardiographic manifestations are apparent.

In very early disease TcPYP99 scan may not show the uptake as clearly due to little amyloid in the heart and only experienced radiologist can detect at this stage. Quantification of disease severity and myocardial uptake of TcPYP99 at the time of diagnosis is predictive of mortality.(Vranian, Sperry et al. 2016). In the countries where the invasive techniques are unavailable, the disease is being ignored for a long time. Even in developed countries CA is not always diagnosed by the invasive biopsy and treatment is started by using the clinical judgment and non-invasive methods. New treatments are showing promising results and non-invasive diagnosis will improve survival if treatment is started early.

Department of Cardiovascular Medicine, Cleveland Clinic, OH, USA.
Correspondence: Email: asad.ikram@email.com

References

1. Tanskanen M, Peuralinna T, Polvikoski T, Notkola IL, Sulkava R, Hardy J, et al. Senile systemic amyloidosis affects 25% of the very aged and associates with genetic variation in alpha2-macroglobulin and tau: a population-based autopsy study. Ann Med. 2008; 40:232-9.
2. Veinot JP. Diagnostic endomyocardial biopsy - still useful after all these years. Can J Cardiol. 2009; 25:e55-6.
3. Maurer MS. Noninvasive Identification of ATTRwt Cardiac Amyloid: The Re-emergence of Nuclear Cardiology. Am J Med. 2015; 128:1275-80.
4. Bokhari S, Castaño A, Pozniakoff T, Deslisle S, Latif F, Maurer MS. et al. (99m)Tc-Pyrophosphate scintigraphy for differentiating light-chain cardiac amyloidosis from the transthyretin-related familial and senile cardiac amyloidoses. Circ Cardiovasc Imaging. 2013; 6:195-201.
5. Glaudemans AW, van Rheenen RW, van den Berg MP, Noordzij W, Koole M, Blokzijl H, et al. Bone scintigraphy with (99m)technetium-hydroxymethylene diphosphonate allows early diagnosis of cardiac involvement in patients with transthyretin-derived systemic amyloidosis. Amyloid. 2014; 21:35-44.