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Imaging in the Diagnosis of Transthyretin Cardiac Amyloidosis (ATTR)

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INTRODUCTION

Amyloidosis is determined by extracellular deposition of amyloid fibrils in organs and tissues, resulting in the destruction of the structure and function impairment. The disease can be localized or systemic and is categorized by the type of precursor protein. Any organ can be affected, including heart, kidney, lung, peripheral nervous system, liver, eyes, skin, and blood vessels. The deposition is associated with the conversion of the precursor proteins from their soluble functional states into highly organized fibrillar aggregates showing a cross-beta-sheet secondary structure termed "amyloid". (1) There are many types of amyloidosis worldwide (more than 27 proteins have been described as amyloidogenic precursor) but three main subtypes account for most cases of heart involvement: light chain amyloidosis (AL), wild-type transthyretin amyloidosis (wtATTR), formerly called *Senile* because it appears in people aged over 60, and hereditary transthyretin amyloidosis (mATTR). In Cardiac Amyloidosis (CA) there is a fibrillar protein deposition into the myocardium wall that determines arrhythmias (atrial fibrillation, affection of the conduction system) and heart failure (HF). Signs of right heart failure, including peripheral edema, hepatomegaly and ascites are common, while pulmonary edema is rare (2, 3).

The current reference standard for diagnosis of CA is Endomyocardial Biopsy (EMB), but there is an increasing interest in using noninvasive cardiac imaging techniques to diagnose CA. Electrocardiogram (ECG) display a low QRS voltage (amplitude of ≤ 0.5mV in limb leads or

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≤ 1.0 mV in precordial leads), especially in disproportion to a hypertrophic left ventricle (LV) seen on echocardiogram that shows a LV wall thickening and an evidence of restrictive ventricular filling. Cardiac Magnetic Resonance (CMR) can evaluate distinct facets of CA (myocardial structure, function, and tissue characteristics) and ventricular late gadolinium enhancement (LGE) provides a strong indication for the diagnosis. Some studies demonstrated that (99m) Tc-3,3-diphosphono-1,2propanodicarboxylic acid (99mTc-DPD) and (99m) Tc-pyrophosphate (99mTc-PYP) have only ATTR uptake and thus can differentiate this from AL (4). For these reasons, nuclear scintigraphy may ultimately obviate the need of biopsy to diagnose ATTR-CA (5).

Here we describe an 88-year-old man with history of hypertension, permanent atrial fibrillation, pace maker implantation, carpal tunnel syndrome occurred eight years before, admitted to our hospital with worsening shortness of breath (SOB), orthopnea, ascites, bilateral pleural effusions and lower limbs edema. Laboratory investigations showed an increase of NT-proBNP (3324ng/dl) and hs-Troponin T 80 ng/dl. Complete Blood Count (CBC), creatinine, ALT, TSH, urine protein electrophoresis and serum protein electrophoresis results were not significant. He was treated with high dose of intravenous furosemide, beta blockers, ACE-Inhibitors and oral anticoagulant. Conventional 2-D echocardiography showed an increased wall

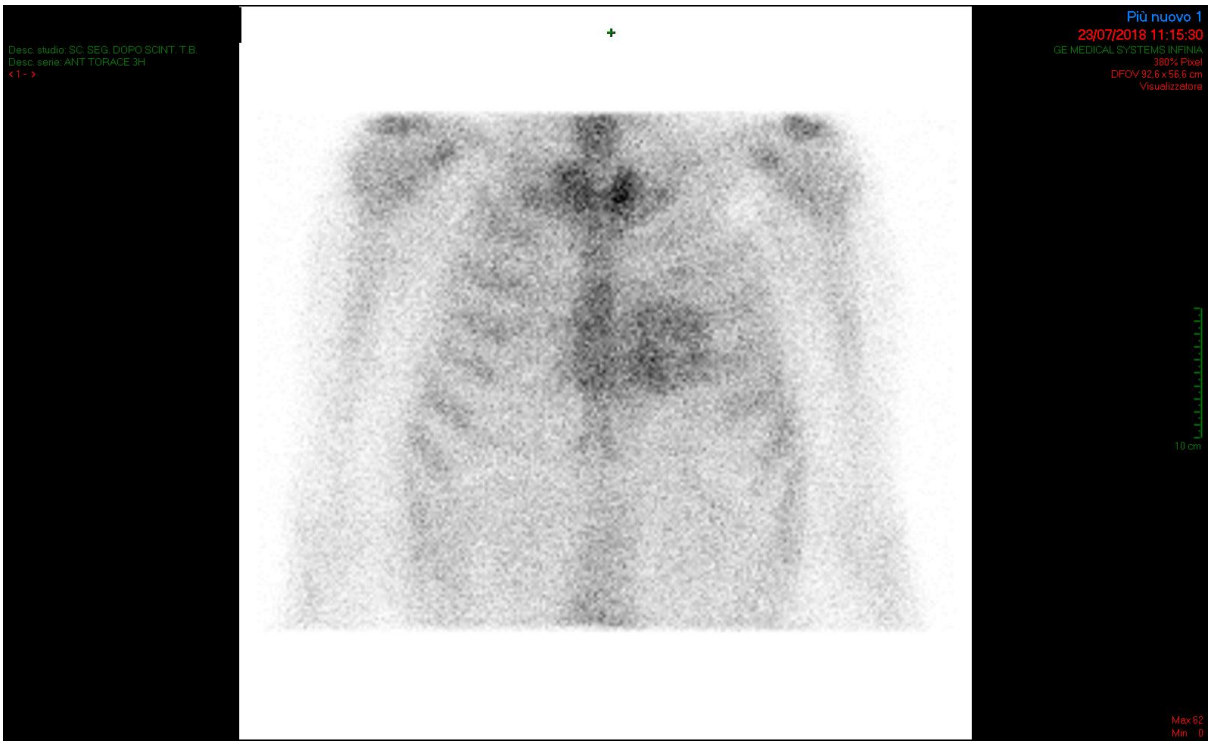

Figure 1. Strong myocardial 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) uptake at 10 minutes from the administration of the tracer

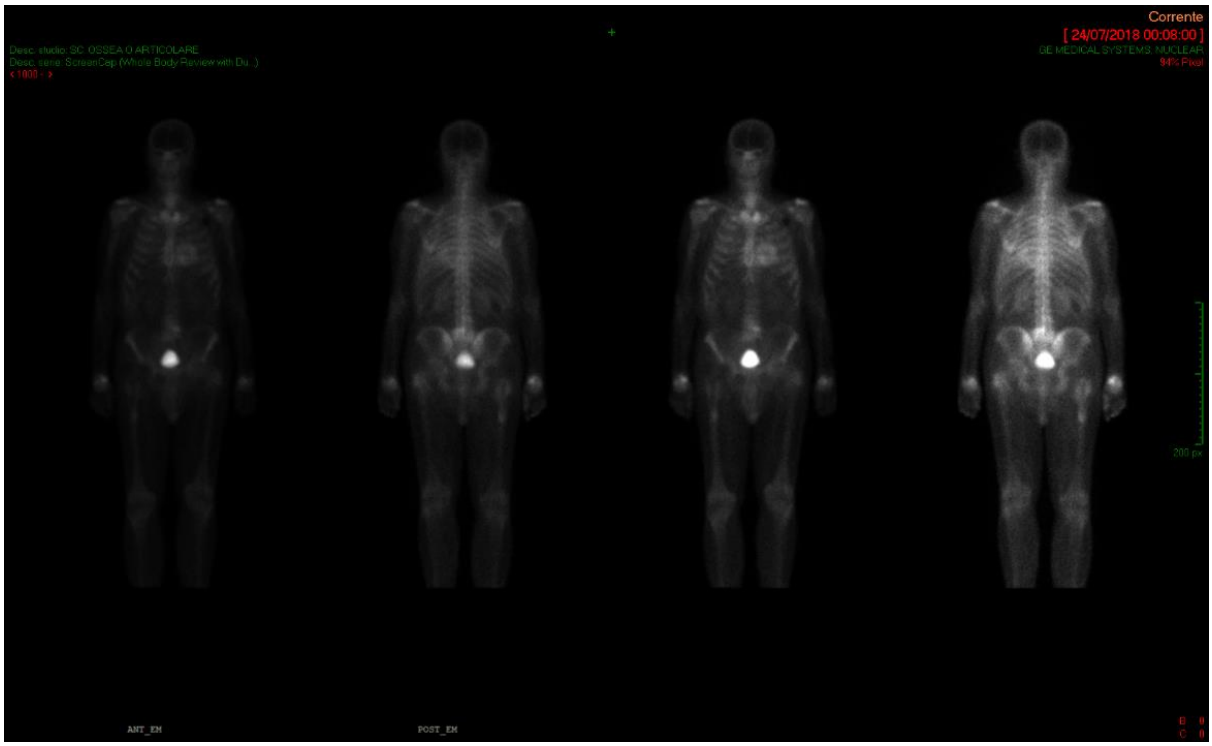

Figure 2. Total Body acquisition after 180 minutes from the administration of the tracer (99mTc-DPD)

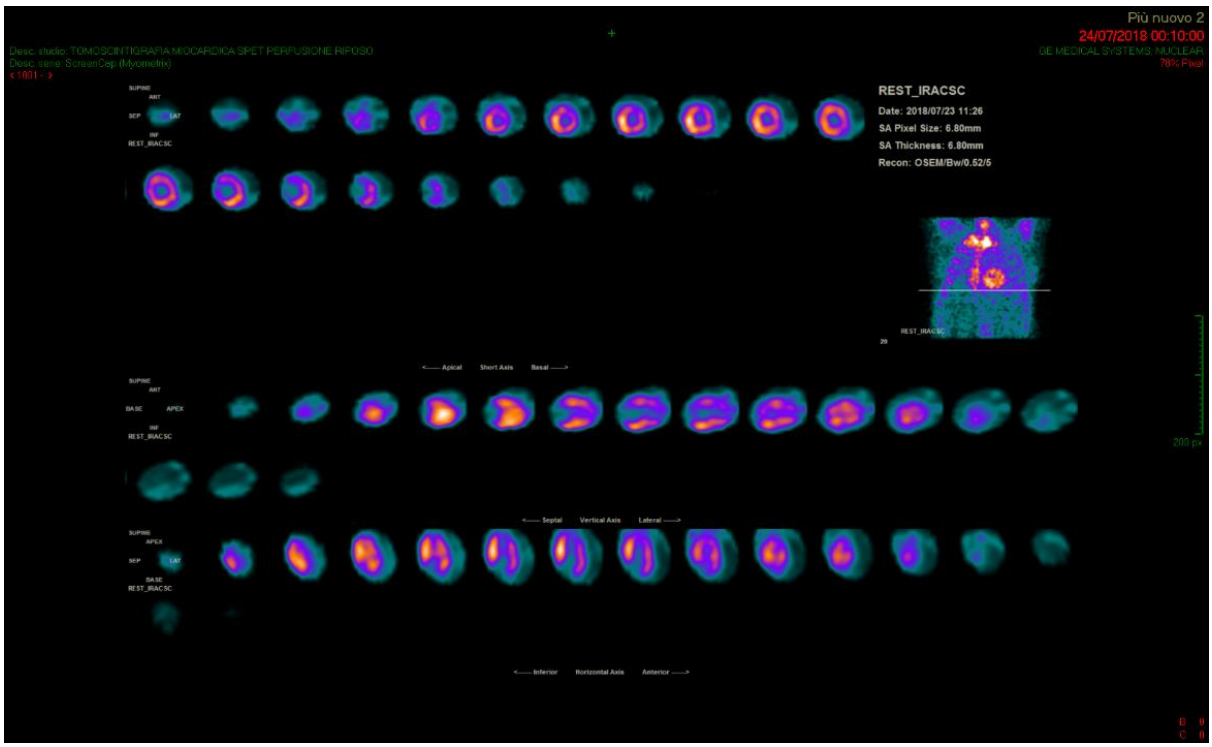

Figure 3. SPECT acquisition of the thorax after about 220 minutes from the administration of the tracer (99mTc-**DPD)**

thickness and a “granular” appearance of the LV myocardium. Patient underwent to scintigraphy with 99mTc - 3,3 - diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) that demonstrated an intense positive cardiac uptake diagnostic for wtATTR (Figures 1, 2, 3).

In old patients with recent onset HF, amyloidosis should be considered as a cause of the disease. Echocardiography, nuclear scintigraphy combined with assessment for monoclonal proteins are eliminating the need for tissue confirmation in ATTR cardiac amyloid.

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Conflict of Interest Disclosure: None declared.

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