ESC European Society of Cardiology
European Heart Journal - Case Reports (2021) **5**(8), 1–2
doi:10.1093/ehjcr/ytab321

Grade 3 myocardial uptake in ^{99m}technetium-pyrophosphate scintigraphy in light chain cardiac amyloidosis

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Received 10 June 2021; first decision 22 June 2021; accepted 22 July 2021; online publish-ahead-of-print 4 August 2021

A 73-year-old Japanese man was referred to our institution for progressive dyspnoea on exertion. Echocardiography showed biventricular hypertrophy [interventricular septum/left ventricular (LV) posterior wall thickness 15/14 mm (normal range 6–10 mm), right ventricular free wall thickness 8 mm (normal range 1–5 mm)] with LV ejection fraction 54%, thickening of valvular leaflets and interatrial septum, and LV global longitudinal strain showing apical sparing pattern (*Panel A*). Cardiac magnetic resonance showed diffuse subendocardial late gadolinium enhancement (*Panel B*). With high suspicion of cardiac amyloidosis (CA), ^{99m}technetium-pyrophosphate (^{99m}Tc-PYP) scintigraphy and serum/urine screening for light chain (AL) amyloidosis were performed for diagnosis and amyloid typing. ^{99m}Tc-PYP scintigraphy performed at 3 h after injection showed Grade 3 uptake (myocardial uptake greater than bone) with increased heart/contralateral ratio of 1.762 (*Panel C*), and single photon emission computed tomography confirmed biventricular myocardial uptake (*Panel D*). Concurrently, serum free light chain assay revealed low kappa: lambda ratio of 0.04 (kappa 14.4 mg/L: lambda 372.0 mg/L), and urine protein electrophoresis with immunofixation showed lambda type monoclonal protein. Endomyocardial biopsy confirmed amyloid deposits by positive direct first scarlet staining with apple-green birefringence under polarized light (*Panel E*), and immunohistochemical staining was positive for AL-lambda (*Panel F*), negative for transthyretin (TTR) (*Panel G*), and negative for AL-kappa. After haematology consultation, the patient was diagnosed as having AL–CA and is currently being treated with bortezomib, cyclophosphamide, and dexamethasone for 9 months since diagnosis.

Bone scintigraphy has gained importance for non-invasive diagnosis of TTR–CA, and TTR stabilizers and genetic silencers are novel disease-modifying therapeutic options for TTR amyloidosis. However, treatment of CA varies greatly depending on the amyloid type; thus, correct amyloid typing is essential. While it is generally recognized that Grade 2 or 3 ^{99m}Tc-PYP uptake (equal or greater myocardial uptake than bone) is a typical finding in TTR–CA and that mild uptake (usually up to Grade 1) can be observed in AL–CA, Grade 3 uptake was observed in our AL–CA case. Our case emphasizes the importance of screening for AL amyloidosis even in patients with typical ^{99m}Tc-PYP scintigraphy findings suggesting TTR–CA, and that diagnosis of TTR–CA should not be established without histological evaluation in cases with abnormal AL screening.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: Atsushi Okada reports grants and personal fees from Pfizer Inc. and personal fees from Alnylam Pharmaceuticals, outside the submitted work. All other authors declared no conflict of interest.

Funding: This work was supported by a Grant-in-Aid for Early-Career Scientists from the Japan Society for the Promotion of Science (20K17171).

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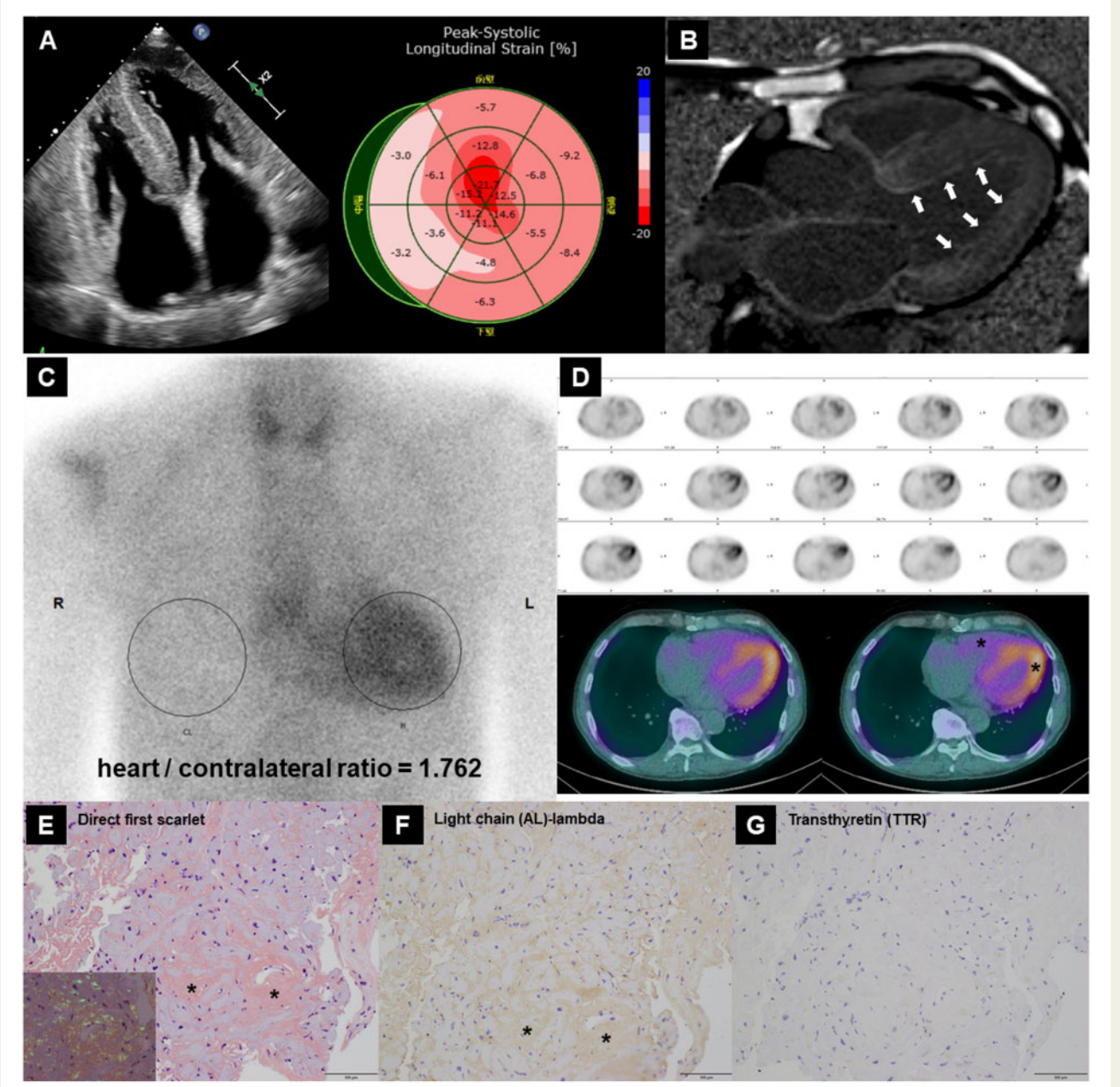
Handling Editor: Christophe Vandenbriele


A
Peak-Systolic
Longitudinal Strain [%]
20
-20
-5.7
-12.8
-3.0
-9.2
-6.1
-6.8
-21.7
-15.1
-12.5
-11.2
-14.6
-11.1
-3.6
-5.5
-3.2
-8.4
-4.8
-6.3
B
C
R
L
heart / contralateral ratio = 1.762
D
E
Direct first scarlet
F
Light chain (AL)-lambda
G
Transthyretin (TTR)