

From hypertrophic cardiomyopathy to transthyretin amyloidosis: an unusual case and challenging diagnosis

Paweł Petkow-Dimitrow^{1,2}, Renata Rajtar-Salwa¹, Katarzyna Holcman³, Magdalena Kostkiewicz³, Paweł Rubiś³

¹ 2nd Department of Cardiology and Cardiovascular Interventions, Institute of Cardiology, University Hospital, Kraków, Poland

² 2nd Department of Cardiology, Institute of Cardiology, Jagiellonian University Medical College, Kraków, Poland

³ Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University Medical College, John Paul II Hospital, Kraków, Poland

Transthyretin amyloidosis (ATTR) is a protein-misfolding disease, in which amyloid fibrils infiltrate the myocardium.¹ On echocardiography, ATTR may present as a phenocopy of hypertrophic cardiomyopathy (HCM). Several diagnostic tools may facilitate the diagnosis, such as echocardiography, scintigraphy, biomarkers, or genetic analysis.¹ We report a case that highlights the role of cardiac biomarkers, extracardiac symptoms, and genetic analysis in the differential diagnosis of cardiac amyloidosis.

A 47-year-old man with heart failure (New York Heart Association class II) and suspicion of HCM or amyloidosis was referred to our hospital for further diagnostic workup. Doppler echocardiography revealed asymmetric left ventricular (LV) septal hypertrophy (2.2 cm during diastole; **FIGURE 1A**) with preserved LV ejection fraction (61%), and LV outflow tract gradient of 22 mm Hg at rest and 36 mm Hg after provocation. The ratio of early to late diastolic transmitral flow velocity (E/A) was 1.6, indicating a non-restrictive filling pattern. The global longitudinal strain (GLS) was preserved in the apical segments, and there was no “apical sparing” pattern typical for ATTR. The mean GLS was –18.3%, but there was a marked abnormal gradient of deformation between the basic and apical segments (minimum value, –4%; maximum value, –32%; **FIGURE 1B**). For comparison, **FIGURE 1C** shows a totally abnormal GLS pattern of a patient with more advanced ATTR.²

The patient had normal high-sensitive troponin I (hs-TnI, 9.3 ng/ml) and N-terminal fragment of the prohormone brain natriuretic peptide (NT-proBNP, 98.5 pg/ml) levels (double-negative biomarkers), which might be explained by an early stage of the disease. A year later, the NT-proBNP

level was elevated (374 pg/ml; reference range, 125 pg/ml). Next, the patient experienced new-onset hand numbness (primarily in the left hand), indicating carpal tunnel syndrome with neural compression. This led us to change the tentative diagnosis from HCM to cardiac amyloidosis.^{1,2} We performed ^{99m}Tc-3, 3-diphosphono-1, 2-propanodicarboxylic acid scintigraphy, which showed radiotracer uptake in the heart, typical of ATTR.^{1,2}

Genetic analysis revealed the ATTR variant c.325G>A (p.Glu109Lys). This variant E109K in the *TTR* gene cannot be found in the ClinVar database; however, 2 other substitutions in the position of 109 in the *TTR* gene have been reported as pathogenic (E109Q) or of uncertain significance (E109D). This finding supports the diagnosis of ATTR.

The GLS polar plot map did not provide any conclusive findings. However, scintigraphy yielded strong evidence supporting the diagnosis of

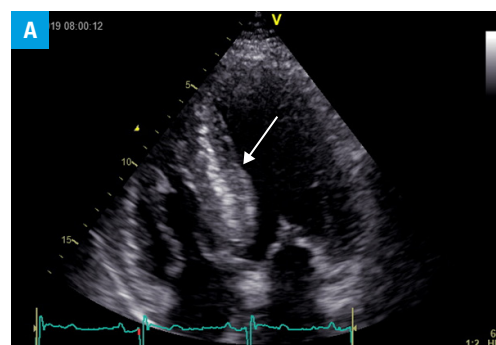


FIGURE 1 Echocardiography findings showing: **A** – asymmetric left ventricular septal hypertrophy characteristic of hypertrophic cardiomyopathy

Correspondence to:

Paweł Petkow-Dimitrow, MD, PhD,
2nd Department of Cardiology,
Institute of Cardiology, Jagiellonian
University Medical College,
ul. Jakubowskiego 2, 30-688 Kraków,
Poland, phone: +48 12 424 71 70,
email: dimitrow@mp.pl

Received: November 26, 2019.

Revision accepted: January 3, 2020.

Published online: January 14, 2020.

Pol Arch Intern Med. 2020;

130 (2): 153-154

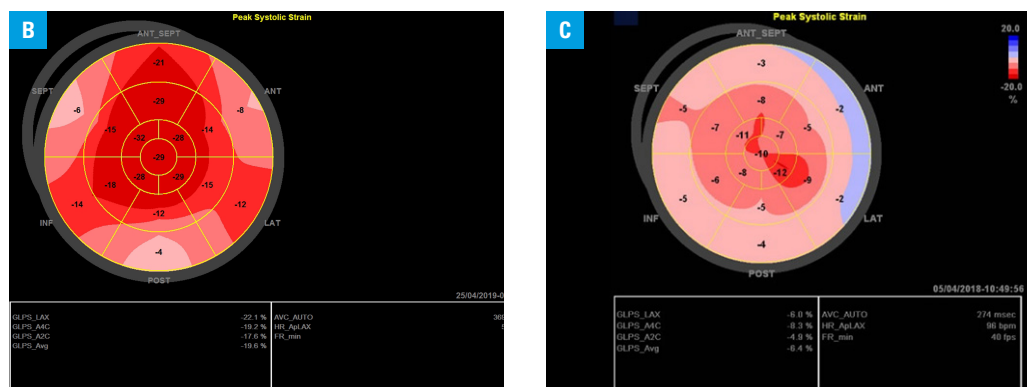
doi:10.20452/pamw.15140

Copyright by Medycyna Praktyczna,

Kraków 2020

FIGURE 1

Echocardiography findings showing: **B** – a near-normal global longitudinal strain pattern without typical features of transthyretin amyloidosis, seen in our patient; **C** – an abnormal global longitudinal strain pattern typically seen in patients with advanced ATTR



ATTP confirmed by genotyping. The patient presented with normal hs-TnI and NT-proBNP levels despite several echocardiographic features typical of HCM with mild obstruction. Therefore, we postulate that the normal levels of hs-TnI and NT-proBNP may help distinguish HCM from ATTR (at an early stage of the disease).

Our hypothesis could be useful in interpreting the study by Zhang et al.³ The authors did not provide data on the minimal value of NT-proBNP in the HCM subgroup with negative troponin results, but observed very high median and lower quartile NT-proBNP values (median [IQR], 1166.7 [775.5–1818.5] pg/ml). Probably, there were no troponin/NT-proBNP-negative patients. In the Methods section, the authors did not mention that the HCM phenocopies were excluded. They did not use any specific tests or examinations for a differential diagnosis of ATTR. It might be speculated, in our opinion, that some patients with HCM and normal NT-proBNP levels had undiagnosed ATTR.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

OPEN ACCESS This is an Open Access article distributed under the terms of the Creative Commons AttributionNonCommercialShareAlike 4.0 International License (CC BY-NC-SA 4.0), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material, provided the original work is properly cited, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at pamw@mp.pl.

HOW TO CITE Petkow-Dimitrow P, Rajtar-Salwa R, Holcman K, et al. From hypertrophic cardiomyopathy to transthyretin amyloidosis: an unusual case and challenging diagnosis. *Pol Arch Intern Med.* 2020; 130: 153-154. doi:10.20452/pamw.15140

REFERENCES

- 1 Agha AM, Parwani P, Guha A, et al. Role of cardiovascular imaging for the diagnosis and prognosis of cardiac amyloidosis. *Open Heart.* 2018; 5: e000881. [↗](#)
- 2 Rajtar-Salwa R, Gębka A, Petkow-Dimitrow P. Non-invasive cardiac imaging methods in transthyretin amyloidosis. *Kardiol Pol.* 2019; 77: 234. [↗](#)
- 3 Zhang C, Liu R, Yuan J, et al. Significance and determinants of cardiac troponin I in patients with obstructive hypertrophic cardiomyopathy. *Am J Cardiol.* 2015; 116: 1744-1755. [↗](#)