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PEER-REVIEW REPORT

Name of journal: *World Journal of Cardiology*

Manuscript NO: 79843

Title: Early and aggressive presentation of wild-type transthyretin amyloid cardiomyopathy: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02446694
Position: Editorial Board
Academic degree: FACC, FACP, FAHA, FESC, MD, PhD
Professional title: Director
Reviewer's Country/Territory: Japan
Author's Country/Territory: United States

Manuscript submission date: 2022-09-08

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-15 15:36

Reviewer performed review: 2022-09-21 20:11

Review time: 6 Days and 4 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

We believe that this is a rare case of ATTR amyloidosis diagnosed at a young age with severe HFrEF that deserves to be reported. #1 Was there anything in the extracardiac findings such as carpal tunnel syndrome? #2 The authors should add about physical examination, such as physique, vital signs, etc. #3 The authors should comment on ECG findings. #4 The authors should add the following information about echocardiographic findings and figures; Left ventricular inflow waveform (E/A, DcT, etc.), GLS (presence of apical sparing). Also, since the readers do not know if there is left ventricular wall motion reduction, it would be easier to understand if the authors could show the diastole and systole figures side by side. Also, is there a mild pericardial effusion? #5 The authors showed a macroscopic figure of the cardiac transplant, but the readers are not sure of the size of heart, thus, the authors should have a picture with the scale included. After all, the authors should show figures of the histology, especially the immunostaining of ATTR. #6 This case has undergone cardiac transplantation, but it is not a fundamental treatment for amyloidosis, and the possibility of amyloid deposition again cannot be ruled out. The authors should discuss whether there are any such reports, and whether or not there is any preventive effect of oral medication to prevent the deposition of amyloid again.

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Reviewer's code: 03257640
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: Sweden
Author's Country/Territory: United States

Manuscript submission date: 2022-09-08
Reviewer chosen by: AI Technique
Reviewer accepted review: 2022-09-30 06:36
Reviewer performed review: 2022-10-09 15:38
Review time: 9 Days and 9 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors describe an interesting case of ATTRwt amyloidosis with severe heart failure in a relatively young male patient. This is important since ATTR amyloidosis is still overlooked and underdiagnosed all over the world, and since the disease also can affect younger patients. The manuscript is generally well written and the diagnostic work-up seems appropriate and is quite well described. However, some revisions are needed before the manuscript is ready for publication. 1. Title: Although 58 years of age is relatively young for a patient with severe ATTRwt cardiomyopathy, I wouldn't consider him a young patient. Therefore, please consider revising the title somewhat. 2. Absctract: Please see above. 3. Introduction: The introduction is very short and is lacking references. Please update and add some key references to give the reader some more background information. 4. History of past illness: Please add information about any history of arrhytmias, which is also common in these patients. 5. Personal and family history: There is no information on the race of the patient. This would be of interest since ATTRwt amyloidosis seems to be more common in Caucasian males, whereas ATTRv amyloidosis (ATTRV122I) is more common in Afro-Americans. Please add this information if available and if permitted. 6. Further diagnostic work-up: Please add information on cardiac rhythm also here. Was the Tc PYP scan graded according to the Perugini scale? If not, please state what grading that was used. Finally, regarding the genetic testing, which genes were screened and what were the two "genes of inknown significance"? An unremarkable screening of the TTR gene should be the bottom-line here. 7. Final diagnosis: I agree that ATTRwt amylodiosis was the most likely etiology since ATTR was found in the endomyocardial biopsy if both AL and

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ATTRv amyloidosis has been ruled out. However, a negative genetic testing needs to be clearly stated in the previous section in order for this to apply. 8. Discussion: Although it's not known yet it would be nice if the authors could speculate a bit about why some patients are affected earlier from ATTRwt amyloidosis. In our experience, long-distance athletes and heavy-workers seem to be at risk for an early disease development. Also, the non-biopsy diagnosis of ATTR cardiomyopathy (first described by Gillmore et al) is now widely accepted and deserves to be mentioned. Finally, tafamidis is the only drug approved for ATTR cardiomyopathy so far, although trials with patisiran, vutrisiran, inotersen and eplontersen are underway. Please update accordingly.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Cardiology*

Manuscript NO: 79843

Title: Early and aggressive presentation of wild-type transthyretin amyloid cardiomyopathy: A case report

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Reviewer's code: 02446694
Position: Editorial Board
Academic degree: FACC, FACP, FAHA, FESC, MD, PhD

Professional title: Director

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2022-09-08

Reviewer chosen by: Li-Li Wang

Reviewer accepted review: 2022-11-08 04:55

Reviewer performed review: 2022-11-08 15:29

Review time: 10 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Please correct the following points #1 It is necessary to describe how many times the histological image is enlarged. #2 I apologize for not pointing this out at the first check, but I think "transthoracic echocardiography" is more common than "transthoracic echo.