Peer Review File

Article Information: https://dx.doi.org/10.21037/tp-23-255

Reviewer A

Comment 1: The search terms for the systematic review described in the Methods are not consistent with what is given in the Abstract. In any case, 14 articles seem to be very few for such broad terms. There is also no explanation why from the 36 eligible studies, only 14 were included in their literature appraisal.

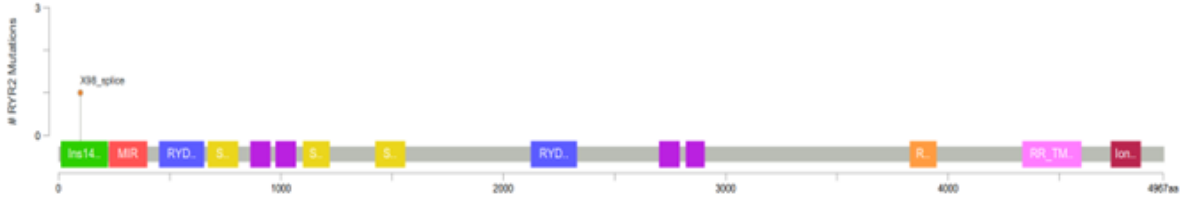
Reply 1: Correction was done. The search terms are RYR2 gene mutation", and "catecholaminergic polymorphic ventricular tachycardia (CPVT)". 36 eligible studies were included initially, however only 14 studies were included in literature appraisal in view of the remaining 22 studies were not described the specific variant or coding effect in RYR2 gene mutation.

Changes in the text (all changes in red): We have modified our text as advised (see Page 1 line 19-21)

Comment 2: Can you indicate if the novel nucleotide mutation results in amino acid change, insertion, frameshift? Also, can you show the nucleotide change(s) in a figure in parallel to the wild type of sequence.

Reply 2: The sequence change falls in intron 4 of the RYR2 gene. It does not directly change the encoded amino acid sequence of RYR gene protein. It affects nucleotide within the consensus splice site.

Changes in the text: Additional figure 3 for changes in nucleotide sequence (see Page 6 line 146/Page 20 line 435-438)



Comment 3: Table 1: it will be easier to follow if you list the mutations in ascending order of amino acid change. Also, in Figure 2: some mutations are given as nucleotide variant and others as amino acid change. You can include two columns, one for nucleotide, the other for amino acid variation.

Reply 3: Figure 1 corrected in ascending order. In figure 2, I included both amino acid variant/ coding effects in view of only small number of coding variant included from my literature review search.

Changes in the text: Table 1 adjusted according to ascending order (see Page 16-19 line 407). There are no changes made for figure 2 and the reason as per reply above.

Comment 4: The English language, spelling, and grammar, needs improvement.

Changes in the text: Spelling and grammar changed accordingly.

Reviewer B

Comment 1:

very interesting and well written article. in the introduction I would add that CPVT can also give cardiac rhythm disturbances and be associated with overlap syndromes with non-compact myocardium citing this recent article: Petrungaro M, Scarà A, Borrelli A, Sciarra L. CPVT and Complete Atrio-Ventricular Block: The Flipside of the Same Coin. J Cardiovasc Dev Dis. 2023 Feb 23;10(3):97. doi: 10.3390/jcdd10030097. PMID: 36975861; PMCID: PMC10054025.

Reply 1:

We have cited the article as per suggestion.

Changes in the text: (all changes in red):

-We have modified our text as advised (see Page 3 line 63-65)

-References no 3 (Page 11 Line 245-247)

Comment 2:

I wonder if there are any prognostic differences based on the phenotype of the genetic mutation and if there is a picture of the cardiac tumors.

While this may be common in children, in adults, cardiac tumors are subject to surgery, and the reason why this case was treated conservatively should be stated.

This article is interesting because of the rare combination of cardiac tumor and CPVT.

Reply 2:

-To date, there is no articles suggest the prognostic differences based on the phenotype of genetic mutation.

Changes in the text: (all changes in red):

-We have modified our text as advised (see Page 5 line 113-114)/ (Page 20-21line 440-442)

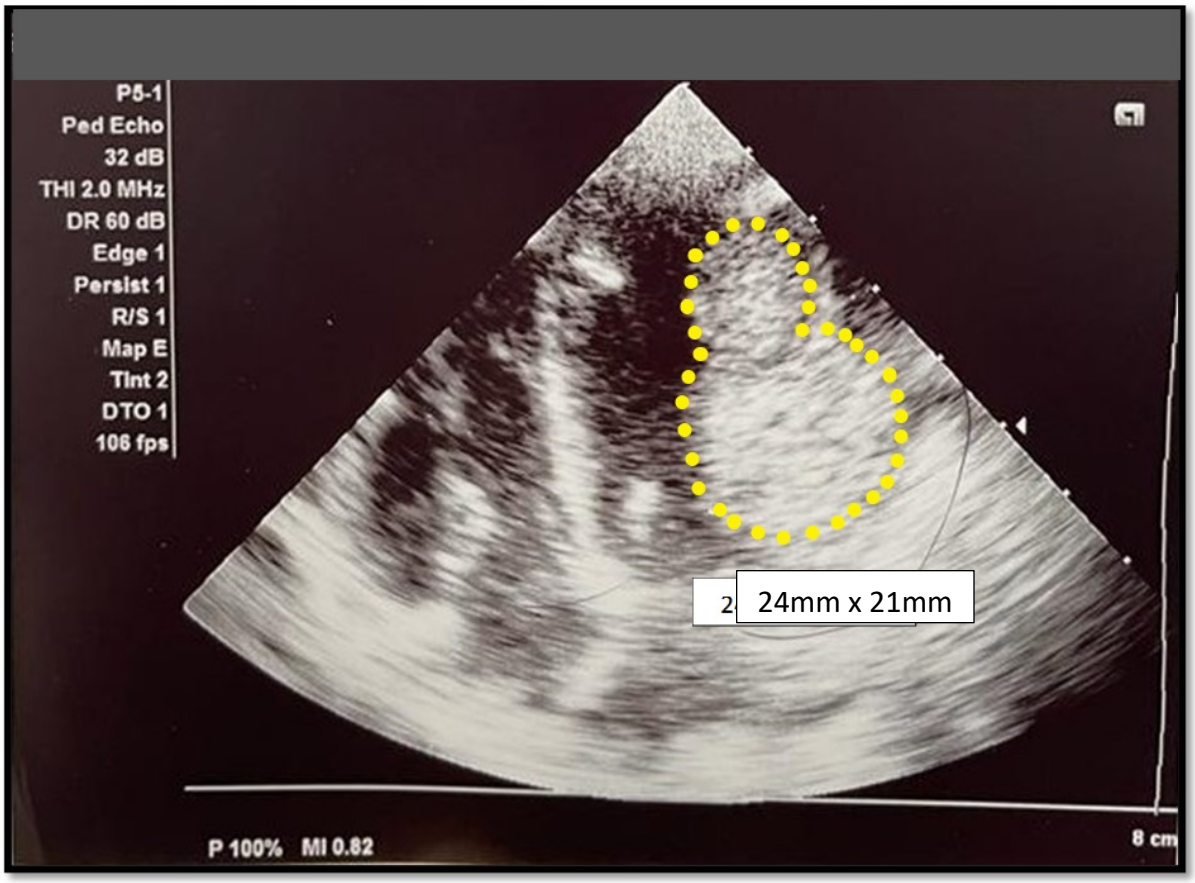


Figure 4: Echo finding of the cardiac tumour, size 24mm x 21mm, sessile tumour.

-Reason for conservative management added on (see Page 5 line 125-127)

Comment 3:

This case report is interesting and has many unique features. The literature review portion of this case report is not novel and other studies with more patients have shown similar results. The novel conclusions can be drawn from the patients age and cardiac tumor as an insighting factor for prompt diagnosis, which is rare.

Reply 3:

-Additional information added as per suggestion. The mean age for the onset usually at 2 years old, while in our case, she presented early at the age of 1 year old.

Changes in the text: (all changes in red):

-We have modified our text as advised (see Page 9 line 207-209)

***All figures in this article are original.**