Peer Review File

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<mark>Reviewer A</mark>

It is my pleasure to review this article. The authors reported a symptomatic case of pericardial cyst, presenting with hiccup. Authors suggested VATS for case of refractory hiccup under suspicious possible pericardial cyst. Congratulation for successful outcome, but this report has several concerns to be discussed.

In the literatures search, many articles or book already described association between pericardial effusion/ cyst and hiccup/singultus. Specific case report on hiccup-associated pericardial cyst seems not well found in internet archive, but old literatures might already describe about pericardial cyst with hiccup. I found similar recent references about cyst-associated hiccup as below.

1. Ungureanu D, Brătucu E, Daha C, Stefănescu AM, Debrețin M. Singultus rebel de cauză rară (Limfocel pleuro-pericardic compresiv cu evoluție lentă) prezentare de caz [Recessive hiccup of rare cause (compressive pleuro-pericardial lymphocele). Case report]. Chirurgia (Bucur). 2001 Nov-Dec;96(6):609-13. Romanian. PMID: 12737141.

2. Sabzi F, Faraji R. The Ruptured Pericardial Cyst to the Right Atrium: A Case Report. Iran J Parasitol. 2020 Jan-Mar;15(1):142-146. PMID: 32489387; PMCID: PMC7244842.

3. Haydari A, Sabzi F, Dabiri S, Poormotaabed A. Right Para Cardiac Pericardial Cyst. Multidiscip Cardio Annal. 2018;9(2):e68382. https://doi.org/10.5812/mcardia.68382.

In this case, dental procedure is thought to be causing factor of refractory hiccup, as described. We also can assume that dental procedure evoked hiccup possibly by vagal stimulation. What about the author's assumption of preexisting asymptomatic pericardial cyst, which came to accidentally provoke hiccup after dental surgery?

1) **Reply:** Thank you- we have included 3 more references pertaining to cases of other cystic lesions seemingly causing hiccups via mediastinal compression, and discussed these and their relevance in the introduction.

Changes in text: See Introduction, Page 4, Line 51.

Some researchers have been suggest anesthetic procedure can be treatment option for refractory hiccup, as below. Some comments on this phenomenon can be added, if needed.

1. Byun SH, Jeon YH. Treatment of Idiopathic Persistent Hiccups with Positive Pressure Ventilation -A Case Report-. Korean J Pain 2012;25:105-107. https://doi.org/10.3344/kjp.2012.25.2.105

2. Saitto, C, Gristina, G, Cosmi, EV. Treatment of hiccups by continuous positive airway pressure (CPAP) in anesthetized subjects. Anesthesiology, 1982;57;345.

3. Lierz, P, Felleiter, P. Anesthesia as therapy for persistent hiccups. Anesth Analg, 2002;95;494-495.

2) Reply: Thank you for the suggestion of this topic. We have incorporated this into the discussion. Changes in text: See Discussion, Page 8, Line 127.

In this case, radiologic evaluation study incidentally found pericardial cyst, abut with phrenic nerve. We can undoubtedly consider that chance between hiccup and cyst with phrenic nerve irritation.

Despite, suggested hypothesis of pericardial effusion-related symptomatic relief of hiccup seems not well proven, clear VATS images might be helpful for clinicians.

3) Reply: We have made VATS images clearer by inclusion of arrow labels in Figure 2B, as well as more

detailed discussion of the surgical procedure itself. Changes in text: See Figure 2B and Page 6, Line 84.

<mark>Reviewer B</mark>

The manuscript must be more concise and repetitions must be avoided carefully. *1) Reply: Thanks- we have made the manuscript more concise to avoid repetition.*

Figure 2B: provide an intraoperative image showing the relation between the phrenic nerve (including arrows) and the pericardial cyst.

2) Reply: We have modified Figure 2B with arrow labels. Changes in text: *See Figure 2B.*

<mark>Reviewer C</mark>

I think it is a technique that could help in some cases that have little space in the anterior The reviewer is honored to review an article about pericardial cyst possibly causing recurrent hiccups. This case report is only describing one case, but it is really interesting. There are several comments to be revised as follows:

1) The conclusion of the abstract is too long. Please shorten the conclusion.

1) **Reply:** Thank you- we have made the abstract conclusion more concise.

Changes in text: See Page 2, Line 35.

2) Approach of the VATS should be explained in more detail. Was it uni-portal or multi -portal?
2) Reply: Details of the VATS approach are now included.
Changes in text: See Page 6, Line 84.

<mark>Reviewer D</mark>

The authors have written an interesting case report describing a case report of a patient with recurrent hiccups that was found to have a pericardial cyst. This is a very interesting case that would be of interest of the readers of this journal.

Comments:

1- Can the authors describe how was the patient routinely monitored for his family history of arrhythmogenic right ventricular cardiomyopathy?

1) **Reply:** Thank you- we have added this to the text. **Changes in text:** See Page 5, Line 64.

2-In figure 2, can the authors use descriptors (arrows/arrowheads) to point out to the pericardial cyst in panel A, and the phrenic nerve in panel B?

2) *Reply:* We have adjusted the arrows on Figure 2. *Changes in text:* See Figure 2A and 2B.

3- I suggest the authors provide a figure with the histological microphotographs showing the histopathology of the pericardial cyst.

3) Reply: We have included a new figure showing histopathology. Changes in text: See Figure 3.

4-The authors described that no other cases of pericardial cysts related to recurrent hiccups has been reported. This information may be incorrect. A quick search in google revealed one case of a pericardial cyst with atypical symptoms of singultus (hiccups) and acid reflux (heartburn) [Iran J Parasitol. 2020 Jan-Mar;15(1):142-146.]. The authors should perform a more systematic search to provide a statement with more certainty.

5-The authors should review data of other cystic lesions (non-pericardial cysts) in the mediastinum that may

lead to recurrent intractable hiccups. Few case reports of other cystic mediastinal lesions leading to hiccups have been reported in the literature [e.g., Chirurgia (Bucur). 2001 Nov-Dec;96(6):609-13.].

4 and 5) Reply: Thanks. We have included three references of rare case reports on cystic lesions seemingly causing hiccups via mediastinal compression, and discussed these and their relevance in the introduction. *Changes in text*: See Introduction, Page 4, Line 51.