

Review Response:

Reviewer #1: Comments to the authors This submission by Yousuf and colleagues from the j overwork of Missouri addresses the development of what looks like a benign hepatic cyst but is related to the VO shunt drainage area bro g walled off to form what they call a hepatic pseudocyst

Major comments

1. case description did the patient at age 49 still have the original VP shunt placed at age 7 Yo?

Response: Patient had the same shunt placed since 7 years old ago. Change made to the manuscript.

2. Why was a hepatobiliary scan performed?

Response: The hepatologist wanted to rule out sphincter of Oddi dysfunction and hepatobiliary leak for any other possible cause of the cyst or fluid collection.

3. Under treatment you claim a partial hepatectomy- I really doubt that you did any substantive hepatic parenchyma resection re word please.

Response: The operative report stated under the procedures performed robotic liver cyst fenestration with partial hepatectomy. We also reconfirmed from liver transplant surgeon who performed this procedure. He is one on listed author in this manuscript and well renowned surgeon in our liver transplant center.

4. When was the follow up act performed- how many weeks postop. ***Follow-up CT scan was done 5 weeks postop.***

5. Please describe in much more detail how the Cust was fenestrated- don't you really mean marsupialised. After it was opened widely. OR. Was only a small entrance to the cyst made. Ideally one would have opened the wall of the cyst unroofing it as widely as possible to "marsupialise" the cyst wall.

Response: Fenestration was done and not marsupialization of the cyst. Provided additional description of the process in the manuscript.

6. Discussion paragraph starting with "The management". (see why you number the pages and lines?) you say a CT guided biopsy? Why not a simple aspiration of cyst content and culture? Two sentences later you say "internalization" I assume that means marsupialising the cyst?

Response: From the literature review we determined that CT-guided biopsy is done to rule out malignancy and obtain fluid samples.

7. From my read of the presentation, he had no symptoms of hydrocephalus or increased intracranial pressure. That suggest that the absorption of CSF fluid from the intact cyst was enough to prevent obstruction of CSF drainage. Therefore how do you explain the increasing suspend. Also I rather doubt that this cyst led to abdominal distension. it appears to me that he has quite a bit of visceral fat. I am having problems relating his symptoms to this cyst.

Response: Yes, the patient had no symptoms of hydrocephalus and intracranial pressure. The cyst was noted incidentally on imaging. On further evaluation was found to have what appeared to be errant positioning of the shunt and the reason for cyst formation. After expert view of the case between Hepatology, Neurosurgery and Transplant Surgeon, the decision was made for shunt repositioning and cyst fenestration. The patient was having abdominal distention aside from the presence of the visceral fat and upon palpation in the right upper quadrant he had pain.

Minor comments

1. authors please in the future number the pages and ideally the lines in an axe ding order makes communication between reviewer and editor and authors.

Response: Page Number and Lines added.

2.4th sentence of Introduction please expand for the reader how pulmonary emboli develop based the the presence of an intravascular foreign body.

Response: Adjustment and mechanism of PE with further clarification added. Also added new reference. (Wu D, Guan Z, Xiao L, Li D. Thrombosis associated with ventriculoatrial shunts. Neurosurg Rev. 2022;45(2):1111-22.)

Reviewer #2: COMMENTS TO AUTHORS: Manuscript NO: 82468 Title: Cerebrospinal Fluid Liver Pseudocyst: A Bizarre Long-term Complication of Ventriculoperitoneal Shunt REVIEW: The liver cysts caused by VP shunts was described in this article. As a rare condition, this report may also be valuable. However, there are several problems, particularly major problem is in the Discussion section. The majority of the discussion is a summary of the literature, and the discussion of the authors' own case is neglected. As a result, the Conclusion section is a summary about previous reports, and authors fails to highlight the strengths of the authors' report.

1. An important role of case reports is to present hypotheses on matters that are not yet known. I think the authors would like to emphasize that the present case experienced a rare disease, hepatic CSF, and that it was treated with robotic surgery. Thus, in the conclusion section, I

suggest you to propose, for example, "We suggest that abdominal ultrasound be performed every 3 months for the first 2 years for early detection of hepatic CSF" or "Robotic surgery is the best treatment for hepatic CSF for early discharge from the hospital, but there are limited facilities available to try it, and the cost is also a problem. (on page 4 in abstract section)

Response: Thanks for your suggestions. Authors agree that we use robotic surgery as a tool for the management of hepatic CSF cyst. We added comments on it in the conclusions. Authors do not want to suggest use of ultrasound every 3 months for 2 years for early detection of hepatic CSF cyst especially in asymptomatic patients. This is a long term complication of VPS, and we think it will be unreasonable to recommend it especially when there is lack of available data. However once hepatic pseudocyst identified incidentally on imaging, it is reasonable to monitor cyst size with ultrasound in 1-2 year for planning of surgical vs conservative management in asymptomatic patients especially in those patients with increasing cyst size.

2. Was there any infection? Did you use antimicrobials? Was cyst drainage performed? What day was the surgery performed? How did his/her symptoms change as a result of those treatments? Case presentation is poor.

Response: No cyst fluid samples were collected given it was clear fluid without noticeable pus, blood or pseudomembrane in cyst cavity concerning for infectious etiologies. There was no leukocytosis, fever or signs of sepsis. Patient did not require antibiotics. Patient felt better after the procedure.

3. You have described intestinal bacteria and superficial bacteria. Can you provide a discussion of the route of infection? (on page 8 line 27-30 in Discussion section).

Response: We have added mechanism of pathogenesis and predisposing risk factors discussion under relevant section.

4. Were the characteristics of the authors' cases similar to those previously reported? Are they atypical? Discussion for your own cases is necessary. Please describe it. (in Discussion section)

Response: We have added a new paragraph of our case discussion and addressed this comment

5. The authors' cases have a considerably longer time to symptom onset than the previously reported cases. Please discuss the reasons. Consideration of their own cases is necessary. (in Discussion section)

Response: We have added a new paragraph of our case discussion and addressed this comment

6. Since you are performing robotic surgery, which is the most advanced treatment, please describe why you used it in this case and its advantages over conventional methods. Has the choice of robotic surgery had a positive outcome for the authors' case? (in Discussion section)

Response: We have added a new paragraph of our case discussion and addressed this comment

7. Please discuss the characteristics of cases that are spontaneously absorbed (cases that may avoid unnecessary treatment). (on page 10 line 23)

8. “The physician dependent treatment plan had similar outcomes in both groups of patients, except that the self-absorbing cysts took longer to resolve (about 9 months vs immediately after surgical procedure)[8].” This representation contains ambiguity. The reader of this paper will not read references 1-27 in as much detail as the authors. Therefore, the description needs to be changed so that it can be understood by those who have not read Refs. 1-27. (on page 10 line 24-26)

Response to comment 7 and 8: We have provided our prospective and observation from previously published data about comment 7,8. We believe systematic review of previous published data will be useful to detained answer of comments 7 and 8. Detailed discussion of these comments is beyond scope if this case report. We have added following statement. “Most of the cysts (12 out of 15 case studies) showed near complete or complete resolution of hepatic CSF pseudocysts with either surgical or ultrasound guided drainage, however clinical characteristics and etiology of cysts are variable with no specific differences in clinical variables^[2-28]. Large prospective studies are required to further investigate clinical characteristic of patients who will benefit surgical vs conservative approach for spontaneous resolution of hepatic CSF pseudocysts. Rare nature of hepatic CSF pseudocyst is predominant roadblock for conducting prospective studies.”

9. An important role of case reports is to present hypotheses on matters that are not yet known. What hypothesis would the authors like to propose to neurosurgeons, hepatologists and liver surgeons through this case? Suggestions for site of VP shunt tip? Methodologies for early detection? Advantages of robotic surgery?

Response: We addressed above comments in discussion under relevant paragraphs.

Minor 1. The first abbreviation you describe in your abstract should be spelled out. (“CSF” on page 4 line 4 in abstract section).

Response: Done. Spelt it out.

2. Are you saying that small hepatic CSFs do not present neurological symptoms? (in Core Tip section).

Response: It may cause neurologic symptoms due to impairment of drainage that usually happens due to high pressure in the larger size cysts. Hydrocephalus may get worse if there is catheter malfunction as well.

3. The following sentence in “chief complaints” should be included in "History of present illness": “A 49-year-old man with history of intellectual disability due to congenital hydrocephalus status post (s/p) bilateral VP shunt placement at 3 months and 7 years of age, presented with progressively worsening dyspnea on exertion, abdominal discomfort/distention and bilateral lower extremity swelling associated with pain, erythema, and drainage.”

Response: we have made changes as suggested.

4. There is no text in "History of present illness", only a subtitle.

Response: we have made appropriate changes.

5. The following sentence in “History of past illness” should be included in "History of present illness": ”Patient denied abdominal pain, nausea, vomiting, diarrhea, or constipation.”

Response: we have made changes as suggested.

6. Since the chief complaint describes a feeling of dyspnea, vital signs such as oxygen level and respiratory rate are also required. Also, since the patient is reported to have drainage from the lower extremities, we will need to know the body temperature. (on page 7 line 11).

Response: we have made changes as suggested.

7. Can you provide laboratory findings of hepatic cystic fluid? (on page 7 line 16).

Response: Unfortunately No cyst fluid samples were collected.

8. Abbreviation “IV” for intravenous injection? Inappropriate.

Response: we have made changes as suggested.

9. The following finding is unnecessary because it duplicates the finding of the abdominal CT: “however revealed a large 18 x13 x13.5 cm hepatic cyst in the right lobe of liver”(on page 7 line 26).

Response: Will need to keep this as this was the first time the incidental finding of cyst was noted.

10. Are lower extremity cellulitis and liver cysts related? At this time, no evidence (for example, history or examine findings) has been presented that they are related, so please provide the evidence. (on page 8 in FINAL DIAGNOSIS sub section).

Response: These are two separate entities. We don't think they are inter-related.

11. Is an abdominal ultrasound radiological modalities? (on page 9 line 12-14)

Response: No, it is not. We rephrase the sentence.

12. I believe that culture testing usually perform with cyst fluid. Did you perform culture testing with biopsy tissue? (on page 9 line 9-10).

Response: Unfortunately, No cyst fluid samples were collected. That's why No culture testing was done. Pathology report concluded no evidence of neoplastic cyst and likely benign cyst.

13. Describe the characteristics of the recurrent cases. (On page 10 line 26-28)

14. "In case of infected pseudocysts, antibiotics therapy followed by interval replacement of a new VP shunt catheter is a reasonable approach." Were the authors' cases accompanied by infection? If not, this sentence should be moved to the Discussion section, not the Conclusion section. (on page 11 line 7-9 in Conclusion section)

Response: In our case, pseudocyst was not infected. We removed it from conclusions. We talked about it in discussion.

Re-review response:

1. The authors responded to my points as follows: No cyst fluid samples were collected given it was clear fluid without noticeable pus, blood or pseudomembrane in cyst cavity concerning for infectious etiologies. There was no leukocytosis, fever or signs of sepsis. Patient did not require antibiotics. Patient felt better after the procedure. However, this case is complicated by cellulitis of the lower leg. Did the cellulitis improve without the use of antimicrobials? Do you want to describe the cellulitis of the lower leg as a congestive dermatitis caused by compression of the inferior vena cava due to a huge abdominal cyst, not infection, and that it improved as the cyst shrank? As it stands, cellulitis of the lower leg is listed as a diagnostic name, but it is not described in the discussion and its role in this paper is unclear.
 - a. **The cellulitis was just part of the diagnosis process as a separate entity unrelated to hepatic pseudocyst. The patient's cellulitis was treated with antibiotics (clindamycin 300 mg QID for 7 days) with complete resolution on follow up. There was no congestive dermatitis due to compression of the inferior vena cava due to a huge abdominal cyst. We do not think there was an infective process of pseudocyst thus limited need of antibiotics in discussion. Cellulitis was secondary process and we don't think our main focus is to describe cellulitis in this case report.**

2. Are you saying that small hepatic CSFs do not present neurological symptoms? (in Core Tip section). Authors Response: It may cause neurologic symptoms due to impairment of drainage that usually happens due to high pressure in the larger size cysts. Hydrocephalus may get worse if there is catheter malfunction as well. I recommend that this discussion be included in the text along with the references cited.
 - a. **The neurological symptoms of the cyst have been stated in the discussion. On page 9, second paragraph lines 252-256 we discuss the neurological symptoms that are primarily noted in pediatric patients and less likely in adults.**

3. "The physician dependent treatment plan had similar outcomes in both groups of patients, except that the self-absorbing cysts took longer to resolve (about 9 months vs immediately after surgical procedure)[8]." This representation contains ambiguity. The reader of this paper will not read references 1-27 in as much detail as the authors. Therefore, the description needs to be changed so that it can be understood by those who have not read Refs. 1-27. (on page 10 line 24-26) Authors Response: We have provided our prospective and observation from previously published data about comment 7,8. We believe systematic review of previous published data will be useful to detailed answer of comments 7 and 8. Detailed discussion of these comments is beyond scope of this case report. We have added

following statement. "Most of the cysts (12 out of 15 case studies) showed near complete or complete resolution of hepatic CSF pseudocysts with either surgical or ultrasound guided drainage, however clinical characteristics and etiology of cysts are variable with no specific differences in clinical variables[2-28]. Large prospective studies are required to further investigate clinical characteristic of patients who will benefit surgical vs conservative approach for spontaneous resolution of hepatic CSF pseudocysts. Rare nature of hepatic CSF pseudocyst is predominant roadblock for conducting prospective studies." I would like to point out on "The physician dependent treatment plan". I would like a more detailed explanation of the physician dependent treatment plan for the reader.

- a. Added additional information to help explain the physician dependent treatment plan.**