Reviewer #1:

Comments： Kindly expound on the epidemiology of splenic malignancies, that can confirm its rarity and therefore would warrant a multidisciplinary discussion. The case summaries were elaborate and described the clinical presentation very well. Maybe, an additional review of literature on how to diagnose clinically and pathologically these rare splenic tumors can be included. The roles of each member of the MDT should also be highlighted since the manuscript basically reports the importance of an MDT.

Response： thank you for you insightful advice. First of all, we added the literature review in the title of our manuscript. And we also added a brief literature review in discussion section showing like bellows :

Line 14/Page 9:

While the MDT meeting is a regularly scheduled discussion of patients, comprising professionals from different specialties, such as surgeons, medical and radiation oncologists, radiologists, pathologists and nurse specialists[15]. MDT was first appeared in 1970's in America known as tumor boards to discuss cases by a group of specialists[16]. MDT meetings were set up to give specialists the opportunity to update new developments in disease diagnosis and give the patient most suitable treatment[17]. MDT management has been broadly applied in cancer

management and recommended as best practice by professional guidelines[18]. MDT meeting can be involved in every stage of clinics, and associated with precise diagnosis, initial management plans, higher rates of treatment, shorter time to treatment after diagnosis , and better survival. Basically, for some rare disease diagnosis is the most challenging problem. With the help of MDT meetings, For case 1, we surgeons and emergency physicians believed that spleen rupture was secondary to blunt trauma. During the MDT discussion, our pathologist pointed out that spontaneous splenic rupture of LCA is not uncommon, reaching as high as 32% [19].

Line21/page 10:

For the patient, MDT meeting can benefit patients suffering from rare disease, when the diagnosis is not easy to make like case 2. Meanwhile, MDT management can reduce the time from diagnosis to treatment. For physicians present several advantages that it can improve communication between MDT members, give doctors opportunity for education and to keep up to date with new developments, and improve the job satisfactions as well[20].

Reference:

15 Kurpad R, Kim W, Rathmell WK, Godley P, Whang Y, Fielding J, Smith L, Pettiford A, Schultz H, Nielsen M, Wallen EM, Pruthi RS. A multidisciplinary approach to the management of urologic malignancies: does it influence diagnostic and treatment decisions? *Urologic oncology* 2011; **29**(4): 378-382 [PMID: 19576797 DOI: 10.1016/j.urolonc.2009.04.008]

16 Gross GE. The role of the tumor board in a community hospital. *CA: a cancer journal for clinicians* 1987; **37**(2): 88-92 [PMID: 3102006 DOI: 10.3322/canjclin.37.2.88]

17 Patkar V, Acosta D, Davidson T, Jones A, Fox J, Keshtgar M. Cancer multidisciplinary team meetings: evidence, challenges, and the role of clinical decision support technology. *International journal of breast cancer* 2011; **2011**: 831605 [PMID: 22295234 PMCID: 3262556 DOI: 10.4061/2011/831605]

18 Planchard D, Popat S, Kerr K, Novello S, Smit EF, Faivre-Finn C, Mok TS, Reck M, Van Schil PE, Hellmann MD, Peters S, Committee EG. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology : official journal of the European Society for Medical Oncology* 2018; **29**(Suppl 4): iv192-iv237 [PMID: 30285222 DOI: 10.1093/annonc/mdy275]

19 Neuhauser TS, Derringer GA, Thompson LD, Fanburg-Smith JC, Miettinen M, Saaristo A, Abbondanzo SL. Splenic angiosarcoma: a clinicopathologic and immunophenotypic study of 28 cases. *Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc* 2000; **13**(9): 978-987 [PMID: 11007038 DOI: 10.1038/modpathol.3880178]

20 Taylor C, Sippitt JM, Collins G, McManus C, Richardson A, Dawson J, Richards M, Ramirez AJ. A pre-post test evaluation of the impact of the PELICAN MDT-TME Development Programme on the working lives of colorectal cancer team members. *BMC health services research* 2010; **10**: 187 [PMID: 20587062 PMCID: 2914033 DOI: 10.1186/1472-6963-10-187]

Reviewer 2#

Comments 1-11, 13 and 14:

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes 3 Key words. Do the key words reflect the focus of the manuscript? Yes 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Yes 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes

Response 1-11, 13 and 14:

Thank you for your recognition of his work.

Comments 12: Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented?

Is the style, language and grammar accurate and appropriate? No. Paper needs Improvement.

Response 12:

thank you for you insightful advice. First of all, we added some topic sentence to improve the readability of our manuscript . And we also added a brief literature review in discussion section showing like bellows :

Line 6/page 11:

What is more, MDT discussion is necessary for treatment. The postoperative MDT conference for Case 2 saw a debate regarding the diagnosis. One idea considered the tumor as angiosarcoma, and the other regared it as HS.

Line 14/Page 9:

While the MDT meeting is a regularly scheduled discussion of patients, comprising professionals from different specialties, such as surgeons, medical and radiation oncologists, radiologists, pathologists and nurse specialists[15]. MDT was first appeared in 1970's in America known as tumor boards to discuss cases by a group of specialists[16]. MDT meetings were set up to give specialists the opportunity to update new developments in disease diagnosis and give the patient most suitable treatment[17]. MDT management has been broadly applied in cancer management and recommended as best practice by professional

guidelines[18]. MDT meeting can be involved in every stage of clinics, and associated with precise diagnosis, initial management plans, higher rates of treatment, shorter time to treatment after diagnosis , and better survival. Basically, for some rare disease diagnosis is the most challenging problem. With the help of MDT meetings, For case 1, we surgeons and emergency physicians believed that spleen rupture was secondary to blunt trauma. During the MDT discussion, our pathologist pointed out that spontaneous splenic rupture of LCA is not uncommon, reaching as high as 32% [19].

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16 Gross GE. The role of the tumor board in a community hospital. *CA: a cancer journal for clinicians* 1987; **37**(2): 88-92 [PMID: 3102006 DOI: 10.3322/canjclin.37.2.88]

17 Patkar V, Acosta D, Davidson T, Jones A, Fox J, Keshtgar M. Cancer multidisciplinary team meetings: evidence, challenges, and the role of clinical decision support technology. *International journal of breast cancer* 2011; **2011**: 831605 [PMID: 22295234 PMCID: 3262556 DOI: 10.4061/2011/831605]

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19 Neuhauser TS, Derringer GA, Thompson LD, Fanburg-Smith JC, Miettinen M, Saaristo A, Abbondanzo SL. Splenic angiosarcoma: a clinicopathologic and immunophenotypic study of 28 cases. *Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc* 2000; **13**(9): 978-987 [PMID: 11007038 DOI: 10.1038/modpathol.3880178]

Reviewer 3#

Comments: SPECIFIC QUESTION. IN THE SECOND CASE, PREOPERATIVIELY MALIGNANCY WAS SUSPECTED. STILL THE AUTHORS WENT IN FOR LAP SURGERY. HOW WAS THE SPECIMEN TAKEN OUT? WHAT WAS THE CHANCE OF TUMOUR SPILLAGE? HOW WAS IT ADDRESSED.\?

Response: we are sorry we missed some important information here. In case 2, histiocytic sarcoma was firstly misdiagnosed as Kasabach-Merritt syndrome based on the symptom of thrombocytopenia as well as the CT imaging features of splenic angioma. Meanwhile, splenectomy is the best choice to diagnose, cure KMS, and ameliorate thrombocytopenia. We have added these details in Line 9/page7 showing like this: To diagnose, cure KMS, and ameliorate thrombocytopenia, splenectomy can be a better choice [5, 6].

Although laparoscopic surgery has developed a lot in hepatobiliary, gastroenterology, urology, as well as gynecology, how to avoid the implantation metastasis of malignant tumor in abdominal cavity, port site or incision is still a problem. The standard procedure is the use of protective bags for tissue retrieval. In case 2 , once the spleen was completely freed, we put the specimen in to a protective bag, and pull out the bag from a 5cm incision using the reflexed bag to isolate the specimen from the incision.

Reference:

5 Tang JY, Chen J, Pan C, Yin MZ, Zhu M. Diffuse cavernous hemangioma of the spleen with Kasabach-Merritt syndrome misdiagnosed as idiopathic thrombocytopenia in a child. *World journal of pediatrics : WJP* 2008; **4**(3): 227-230 [PMID: 18822934 DOI: 10.1007/s12519-008-0042-6]

6 Dufau JP, le Tourneau A, Audouin J, Delmer A, Diebold J. Isolated diffuse hemangiomatosis of the spleen with Kasabach-Merritt-like syndrome. *Histopathology* 1999; **35**(4): 337-344 [PMID: 10564388 DOI: 10.1046/j.1365-2559.1999.00726.x]

Reviewer #3:

Comments 1. In Figure 1, post-operative CT image should be deleted. 2. In case 2, pre-operative CT image should be indicated as Figure.

Response: thank you for your kindly advices here. To make our figure more precise, a rearrangement of figures were made. With your kindly advice, firstly we have deleted the post-operative CT Scan and change former figure 1 to a new figure (Figure 2 in revised manuscript). Secondly, we have isolated the IHC results of case 1 as a separate figure (Figure 1 in revised manuscript). The following text is the new figure indication in paper and the revised figure legend:

Line 15/page 5:

The patient accepted an emergency splenectomy. Accidently, the immunohistochemical pathology demonstrated the tumor cell was $CD34^{+}$/ERG^{+}/$CD31^{+}$/$CD8^{+}$/$CD68^{+}$/$lysozyme^{+}$/$F8^{+}$, sox-10^{-}/S-100^{-}, $P53^{local+}$, and Ki-$67^{(+,\ 5\text{-}10\%)}$ (Figure 1 and Table 1). Based on the positivity of both endothelial (CD34, ERG, and Cd31) and histiocytic markers (CD68, CD8, Lysozyme, and F8), she was ultimately diagnosed with a ruptured littoral cell angiosarcoma (LCAS)(Figure 1).

Line 20/page 6:

with a CT value of 48Hu and showing gradual enhancement (Figure 2, the arrow indicated the mass in spleen). A general lymph node

ultrasonic…

Line 1/page 17:

Figure 1. HE and immunohistochemical characteristics of case 1.

For LCAS , the tumor contains perivascular sinus-like heterocysts with dark nucleus and multiple mitotic phase in HE staining. As for immunohistochemical phenotype analysis, the tumor cells are CD31 positive, while CD68 is focal positive. Furthermore, it is found that typical endothelial markers CD34 and ERG are positive and perivascular expressed in LCAS. However, these two markers positively express only in normal vascular endothelial cell (black arrow) rather than perivascular cells. The Ki-67 index is 5-10%.

Figure 2. Abdominal computed tomography (CT) angiograph scan of case 2

Pre-operational CT scan revealed splenomegaly, and a tumor (size 6.0*5.7 cm, white arrow indicates the tumor) with CT value 48Hu showing gradually enhanced.

Figure 3. HE and immunohistochemical characteristics of case 2.

The tumor of case 2 contained plenty of large cells with abundant blue cytoplasm with binucleated and trinucleated cell, which is coincidence with the characteristic of HS. As for immunohistochemical phenotype analysis, tumor cells are CD31 positive, while CD68 is general positive in case 2. The Ki-67 index is 15-20%.