

## Response to Reviewers' Comments

Reviewer: 1

Page 5- Fig 2. The percentage of positive cells is important to be considered for IHC and its impact on the clinical managements 2-Page 6. Fig 3. The percentage of positive cells is important to be considered for IHC and its impact on the clinical managements The diverse expression pattern is remarkable in this figure.

Thank you very much for your comment. Just as you said, the percentage of positive cells is important to be considered for IHC. The percentage positive for CK20 is about 25%. expressed as CK20(+) The percentage positive for CDX2 is about 80%. expressed as CDX2(++++)

This has been added as “Figure 3. The tumor cells from the seminal vesicle were positive for CDX-2 (++++)(A) and CK20 (+)(B)”

Reviewer: 2

1. Avoid short forms in abstract or mention them completely first. Mention complaints and presentation followed by past history.

Thank you very much for your comment. We have revised all the short forms in abstract and adjusted the order of the history of present illness and past illness .

This has been added as “Subsequent investigations included a positron-emission tomography (PET) and computed tomography (CT) imaging confirmed the very unusual diagnosis of a solitary tumour at the left seminal vesicle. Laparoscopic left-sided vesiculectomy was carried out. Histological analysis with immunohistochemistry showed positivity for caudal type homeobox 2 (CDX-2) and negative for cytokeratin7 (CK7)” (Page 3, line

41-46)

This has been added as “A 46-year-old man presented with recurrent episodes of painless haemospermia. This was not associated with any lower urinary tract symptoms. He had a past medical history of ileal tumor at the terminal ileum with solitary mesenteric lymph node metastasis on presentation, and underwent partial ileectomy and lymphadenectomy 4 years ago” (Page 3, line 37-41)

## 2. Expand the Introduction in terms of tumors of seminal vesicles and metastasis to it.

Thank you very much for your comment. We have added some information on seminal vesicles and metastasis to it in the discussion section.

This has been added as “Primary adenocarcinoma of the seminal vesicles (SV) are rare and approximately only 60 cases have been reported in the literature [5]. Seminal vesicle metastasis from other organs are even rare. It has been reported only in renal cell carcinoma, hepatocellular carcinoma, and colon adenocarcinoma [6,7,8], which are all case reports” (Page 7, line 142-146)

## 3. T4N1M1. The tumor was already M 1 with a retroperitoneal mass. Provide the complete details. One statement mentions ‘hemicolectomy’ and other ‘ilectomy’. Use consistent terminology.

Thank you very much for your comment. Sorry, the retroperitoneal mass is actually the solitary mesenteric lymph node metastasis. No distant metastasis (T4N1M0). The patient just performed partial ilectomy and lymphadenectomy without hemicolectomy in his past illness history.

This has been added as “He had a past medical history of ileal tumor at the terminal ileum with solitary mesenteric lymph node metastasis on presentation, and underwent partial ileectomy and lymphadenectomy 4 years ago” (Page 5, line 88-90)

## 4. Use generic names of drugs in treatment with full forms. (esp first time)

Thank you for your comment. We have revised the generic names of drugs in treatment.

This has been added as “The patient subsequently received adjuvant radiochemotherapy (intensity-modulated radiotherapy combined with Capecitabine)”(Page 7, line 130-131)

5. It will be better to put presentation and clinical details first, followed by past history and investigations to arise interest in reading.

Thank you very much for your comment. We have changed the order, put presentation and clinical details first, followed by past history and investigations.

This has been added as “**Chief complaints** A 46-year-old man presented to our urology outpatient clinic with recurrent episodes of painless haematospermia.**History of present illness** This was not associated with any lower urinary tract symptoms. He had initially been treated with several courses of oral antibiotics for almost three months but did not work. This patient denied prior trauma or genitourinary tract infection.**History of past illness** He had a past medical history of ileal tumor at the terminal ileum with solitary mesenteric lymph node metastasis on presentation, and underwent partial ileectomy and lymphadenectomy 4 years ago. This was followed by adjuvant capecitabine chemotherapy and intraperitoneal infusion chemotherapy with 5-Fluorouracil (5-FU). The patient had an uneventful recovery and had been on remission since. His tumor markers including carcinoembryonic antigen (CEA), Alpha-Fetoprotein (AFP), human chorionic gonadotropin (HCG), and lactate dehydrogenase (LDH) nadir within normal range following his treatment.”(Page 5, line 80-95)

## 6. What was the status of tumor margins ? Was it R0 or R1 resection due to its proximity with ureter ?

Thank you very much for your comment. Intraoperative frozen sections showed negative tumor margins. So, it was R0 resection.

This has been added as “This was followed by an uneventful laparoscopic transperitoneal complete excision of the left SV. Intraoperative frozen sections showed negative tumor margins.”

(Page 6, line 122-123)

## 7. Mention the stain used and magnification for the images.

Thank you for your comment. We mentioned the stain used and magnification in the caption of the figures.

This has been added as “ HE staining 400x magnification , CDX2 staining 400x magnification ” (in PPT)

## 8. What is the follow up of this patient and current status ?

Thank you very much for your comment. The patient has been alive with multiple metastasis and is now receiving palliative chemotherapy with cetuximab.

This has been added as “The patient has been alive with multiple metastasis and is now receiving palliative chemotherapy with cetuximab.”

(Page 7, line 139-140)

9. One statement mentions 'laparoscopic resection' and other 'excision biopsy'. Be consistent. It is not mentioned in case discussion that the plan was excision biopsy.

Thank you very much for your comment. Actually, the patient underwent laparoscopic transperitoneal complete excision of the left seminal vesicle for both diagnostic and curative purposes .

This has been added as "Under general anaesthetics a prophylactic left-sided ureteral stent was inserted due to anticipated close tumour proximity to the ureter. This was followed by an uneventful laparoscopic transperitoneal complete excision of the left SV."

(Page 6, line 120-123)

10. Discussion needs minor corrections for syntax.

Thank you very much for your comment. We have made some corrections for syntax in the discussion section.

11. Mention few atypical tumors and any mentioned metastasis to seminal vesicles (in literature) to enhance the discussion about this atypical metastasis to seminal vesicle.

Thank you very much for your comment. We have mentioned that Seminal vesicle metastasis from other organs are extreme rare.

This has been added as "Seminal vesicle metastasis from other organs are even rare.It has been reported only in renal cell carcinoma,hepatocellular carcinoma,and colon adenocarcinoma [6,7,8] ,which are all case reports"

(Page 7, line 142-146)

Science editor:

(1) The "Author Contributions" section is missing. Please provide the author contributions;

Thank you very much for your comment. We have provided the author contributions.

This has been added as "**Author contributions:** Cheng XB ,Lu ZQ and Li JS collected the clinical data. Cheng XB researched literature and wrote the manuscript. Wayne Lam and Yiu MK reviewed and edited the manuscript. All authors have read and approve the final manuscript."

(Page 2, line 19-21)

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Thank you very much for your comment. We have provided the original figure documents and arranged the figures using Powerpoint.

(3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Thank you for your comment. We have provided the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references.

This has been added as

1 **Reynolds I**, Healy P, Mcnamara DA. Malignant tumours of the small intestine.

*Surgeon* 2014; **12**: 263-270 [PMID: 24637026 DOI: 10.1016/j.surge.2014.02.003.]

2 **Dabaja BS**, Suki D, Pro B, Bonnen M, Ajani J. Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. *Cancer* 2004; **101**: 518-526 [PMID: 15274064 DOI: 10.1002/cncr.20404.]

3 **Talamonti MS**, Goetz LH, Rao S, Joehl RJ. Primary cancers of the small bowel: analysis of prognostic factors and results of surgical management. *Arch Surg* 2002; **137**: 564-70; discussion 570-1 [PMID: 11982470 DOI: 10.1001/archsurg.137.5.564.]

4 **Rompoteaux P**, Gagnière J, Gornet JM, Coriat R, Baumgaertner I, Lecomte T, Afchain P, Zaanen A, Pocard M, Bachet JB, Bonichon-Lamichhane N, Bouché O, Faucheron JL, Forestier J, Lecaille C, Manfredi S, Tougeron D, Terrebbonne E, Chehimi M, Villing AL, Sarda C, Legoux JL, Benamouzig R, Aparicio T. Resection of small bowel adenocarcinoma metastases: Results of the ARCAD-NADEGE cohort study. *Eur J Surg Oncol* 2019; **45**: 331-335 [PMID: 30501999 DOI: 10.1016/j.ejso.2018.11.012.]

5 **Sollini M**, Silvotti M, Casali M, Giovanardi F, Zadro A, Froio A, Erba PA, Versari A. The role of imaging in the diagnosis of recurrence of primary seminal vesicle adenocarcinoma. *World J Mens Health* 2014; **32**: 61-65 [PMID: 24872954 DOI: 10.5534/wjmh.2014.32.1.61.]

6 **Matsuzaki K**, Yasunaga Y, Fukuda S, Oka T. Seminal vesicle metastasis of renal cell carcinoma. *Urology* 2009; **74**: 1017-1018 [PMID: 19589576 DOI: 10.1016/j.urology.2009.04.058.]

7 **Gong L**, Zheng M, Li Y, Zhang W, Bu W, Shi L, Zhang W, Yan H. Seminal vesicle metastasis after partial hepatectomy for hepatocellular carcinoma. *BMC Cancer* 2011; **11**: 111 [PMID: 21443783 DOI: 10.1186/1471-2407-11-111.]

8 **Hsu YL**, Lin IC, Tung CL. 18F-FDG PET/CT of Seminal Vesicle Metastasis From Ascending Colon Adenocarcinoma. *Clin Nucl Med* 2017; **42**: 138-139 [PMID: 28005644 DOI: 10.1097/RLU.0000000000001519.]

- 9 **Meng MV**, Werboff LH. Hematospermia as the presenting symptom of metastatic malignant melanoma of unknown primary origin. *Urology* 2000; **56**: 330 [PMID: 10925109 DOI: 10.1016/s0090-4295(00)00634-8.]
- 10 **Kavoussi LR**, Schuessler WW, Vancaille TG, Clayman RV. Laparoscopic approach to the seminal vesicles. *J Urol* 1993; **150**: 417-419 [PMID: 8326567 DOI: 10.1016/s0022-5347(17)35498-8.]
- 11 **Nakanoko T**, Koga T, Taketani K, Hirayama Y, Yoshiya S, Minagawa R, Kai M, Kajiyama K, Maehara Y. Characteristics and Treatment Strategies for Small Bowel Adenocarcinoma in Advanced-stage Cases. *Anticancer Res* 2015; **35**: 4135-4138 [PMID: 26124367]
- 12 **Howe JR**, Karnell LH, Menck HR, Scott-Conner C. The American College of Surgeons Commission on Cancer and the American Cancer Society. Adenocarcinoma of the small bowel: review of the National Cancer Data Base, 1985-1995. *Cancer* 1999; **86**: 2693-2706 [PMID: 10594865 DOI: 10.1002/(sici)1097-0142(19991215)86:12<2693::aid-cnrcr14>3.0.co;2-u.] (Page 9-10, line 190-232)

(4) The “Case Presentation” section was not written according to the Guidelines for Manuscript Preparation. Please re-write the “Case Presentation” section, and add the “FINAL DIAGNOSIS”, “TREATMENT”, and “OUTCOME AND FOLLOW-UP” sections to the main text, according to the Guidelines and Requirements for Manuscript Revision;

Thank you very much for your comment. We have rewritten the “Case Presentation” section, and added the “FINAL DIAGNOSIS”, “TREATMENT”, and “OUTCOME AND FOLLOW-UP” sections to the main text, according to the guidelines and requirements for manuscript revision.



(5) Please upload the primary version (PDF) of the Informed Consent Form (Surgical procedures or other) that has been signed by the patients in the study, prepared in the official language of the authors' country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc. Example: Download our sample of signed informed consent-Case report, at <https://www.wjgnet.com/bpg/GerInfo/287>.

Thank you very much for your comment. We have uploaded the primary version of the Informed Consent Form that has been signed by the patients to the system