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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 83733

Title: Synchronous endometrial and ovarian cancer: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03252941
Position: Editorial Board
Academic degree: MD
Professional title: Doctor, Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: Lithuania

Manuscript submission date: 2023-02-06

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-03-14 23:34

Reviewer performed review: 2023-03-17 12:57

Review time: 2 Days and 13 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Zilvic reported two cases of synchronous endometrial and ovarian cancer (SEOC) and performed review of the literature. After reading this manuscript, I think that this review is well organized and informative. Meanwhile, it is unclear what these case series add to the relevant field. The authors should clearly specify the novel findings and/or lessons obtained from their experience. In addition, I will list up some minor points below. 1. (p. 1, l.30) Also, OC with Endometrioid histology diagnosed under the sge og 50 …: Loss of mismatch repair, i.e., Lynch syndrome, is also associated with endometrial cancer. Authors should mention it. 2. (p.3, l.3) Next-generation sequencing was performed using uterine lavage and ovarian tissue samples. Please explain why endometrial cancer tissue was not used for sequencing. 3. (p.5, Table 1) Mutation profiles of two SEOC cases: This must be “Mutation profile of Case 2.” Mutation profiles of ovarian tissue and uterine lavage should be listed separately. 4. (p.5, l.21) ovary and uterus and still alive more than 2 years after treatment: more than 3 years. 5. (p.6) SEOC is misspelled as SEO at 3 places. 6. (p.7, l.2) GSK3beta/Axin complex is required for beta-catenin stabilization and translocation to nucleus: This is wrong. GSK3beta/Axin complex is

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required for beta-catenin phosphorylation and degradation. 7. (p.7, Figure 6) Arrow beneath AKT1 should be replaced with block, since AKT1 inhibits GSK3beta. 8. Mild grammar and spell check will be needed.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Cases*

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Title: Synchronous endometrial and ovarian cancer: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03252941
Position: Editorial Board
Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Lithuania

Manuscript submission date: 2023-02-06

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-05-07 08:37

Reviewer performed review: 2023-05-07 13:57

Review time: 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This manuscript was improved to some degree in the revised version, but there remain some problems to be settled. Major point: 1. In response to my previous comment, "Next-generation sequencing was performed using uterine lavage and ovarian tissue samples. Please explain why endometrial cancer tissue was not used for sequencing," you replied, "We didn't have possibility to take extra biopsies from uterine cancer tissue for NGS, as tumors were very small and patients didn't signed informed consent for extra biopsies from uterine tumors." However, I can read that at least case 1 underwent hysterectomy and NGS can be performed using pathological sample of the uterine corpus cancer. 2. In your reply to my comments, I found a description, "Uterine lavage shows molecular profile of endometrial as well as an ovarian cancer." Did you analyze molecular profiling of uterine lavage to investigate gene mutations in not only endometrial cancer but also ovarian cancer simultaneously? If so, analysis of uterine lavage may not be useful for the differential diagnosis between SEOC and metastatic cancer. 3. Please explain clearly why no mutations found in ovarian cancer and uterine lavage can lead to the diagnosis of SEOC in case 1. Minor points: 1. (p.3, l.12) Results: In our report patients with SEOC had an endometroid type histology with: endometrioid 2. (p.5, l.7) criteria by Ulbright and Roth for SEOC diagnostics may not always be appliable . When: applicable 3. (p.5, l.23) A 54-year-old, menopausal (gravida 0, para 0) women presented with lower abdominal: woman 4. (p.6, l.4) Hysterosocpy was performed because endometrial polyp was detected by ultrasound: Hysterescopy 5. (Figures 1 to 4) Site of cancer (endometrioid or ovarian) should be specified in figure captions. 6. (p.9, l.17) endometrial and Figure 4 shows ovarian tumor specimens. Peritoneal cytological: endometrium 7. (p.10, l.1) The patient underwent surgical staging: Please specify surgeries which this patient (case 2) underwent. Was the diagnosis of

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uterine corpus cancer without myometrial invasion possible without hysterectomy? Did the case 2 really not undergo hysterectomy? 8. (p.10, ll.13-15) In ovarian tissue sample, somatic mutations of PIK3CA and PTEN were detected. Moreover, tumor sample had a mutation in β-catenin gene CTNNB1: Do these two sentences mean these three genes were mutated in ovarian cancer tissue? If so, it should be described as follows: Somatic mutations of PIK3CA, PTEN, and CTNNB1 were detected in the ovarian cancer. Furthermore, in Table 1, "tissue mutation" should be replaced with "ovarian cancer mutation" in the headline. 9. (p.11, l.19) different clinical characteristics compared to patients with to EC or OC alone. SEOC is: different clinical characteristics compared to patients with EC or OC alone. SEOC is 10. (p.11, l.22) low-grade disease. The endometroid subtype of the primary tumors is the most: endometrioid 11. (p.11, l.26) The importance of distinguishing SEOC from either isolated endometrium or: endometrioid 12. (p.12, l.4) metastatic disease [1, 2, 4, 13]. Both patients in our report were diagnosed with low grade of: Delete "of." 13. (p.12, l.28) sequencing (NGS). Pairedbox gene 8 (PAX8) is a marker that can be useful in: Paired box 14. (p.13, l.12, l.21, l.23) SEO: SEOC 15. (p.13, l.17) and ARID1A gene mutations can be helpful for diagnostic of SEOC [16, 22-28]. Reijnen et al study: The study by Reijnen et al 16. (p.14, l.7) Figure 6: Figure 5 17. (p.14, ll.11-13) The numbers indicate TCGA published mutation data form uterine (right side data) and ovarian (left side data) cancers. Figure generated using PathwayMapper tool [22]: According to this explanation, ovarian cancer in case 1 represented mutations in PTEN, PIK3CA, and CTNNB1 genes which are reported to be very rare in SEOC according to the TCGA data (0.0%, 3.7%, and 1.2%, respectively). Is my speculation right?