

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61547

Title: Long-term survivor of metastatic squamous-cell head and neck carcinoma with occult primary after cetuximab-based chemotherapy – a case report.

Reviewer's code: 03210360

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-22 01:17

Reviewer performed review: 2021-02-26 08:32

Review time: 4 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The authors presented a rare case of a 42-year-old female patient suffered from metastatic squamous-cell head and neck cancer with occult primary with lymph node and bone metastases. The patient was treated with cetuximab plus platinum-fluorouracil chemotherapy achieving complete remission (CR). Ten years after cancer diagnosis she is still alive and in good performance status representing an exceptional case. This is an interesting Case Report. Before resubmitting the article, some information should be added as follows.

1. In the Figure 1, arrows should be added to point out the representative swollen lymph nodes you mentioned.
2. In the Section of Imaging examination, the compression of the right renal artery and osteolyses of the third and fifth lumbar vertebral bodies should be presented in the figure for the reader of Journal.
3. The authors did not find out the primary lesion by Gastroscopy, coloscopy, and bronchoscopy. The blood system should also be considered as one of the sources of primary lesions. PET-CT examination would be very helpful for discovery of primary lesions.

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



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manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes. 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Yes. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? No. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes. 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes. 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? Yes. 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? Yes. 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61547

Title: Long-term survivor of metastatic squamous-cell head and neck carcinoma with occult primary after cetuximab-based chemotherapy – a case report.

Reviewer's code: 00070823

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-20 08:00

Reviewer performed review: 2021-02-26 15:15

Review time: 6 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting and rare case. In this case report, authors show that even cetuximab-based therapy has the potential to succeed in long-term survival of advanced squamous-cell head and neck carcinoma. This phenomenon has good clinical significance for similar patients. Before acceptance, the authors are supposed to address the following questions: (1) Treatment is effective, but more specific treatment details should be described for reference. For example, what is the dose of chemotherapy and what is the target area of radiotherapy. (2) The data before and after treatment should be compared. The images of lymph nodes after treatment should be provided, and the situation of lymph node regression should be reflected by data. (3) Did the patient have a genetic test?

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61547

Title: Long-term survivor of metastatic squamous-cell head and neck carcinoma with occult primary after cetuximab-based chemotherapy – a case report.

Reviewer's code: 05834099

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-23 13:23

Reviewer performed review: 2021-03-02 15:54

Review time: 7 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

In this case report, the author reported that the patient with primary occult carcinoma in head and neck carcinoma could survive for long term. As you reported, unknown primary carcinoma in head and neck is poor prognosis, and it is difficult to control progression. The author could control the unknown primary carcinoma in head and neck by Extreme regimen. However, in accordance with TNM Classification of Malignant tumors -8th edition, unknown primary carcinoma with p16 positive was regarded as p16 positive oropharyngeal cancers. Not surprisingly, p16 positive oropharyngeal cancer has good prognosis for chemotherapy. First of all, the author should correct this.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61547

Title: Long-term survivor of metastatic squamous-cell head and neck carcinoma with occult primary after cetuximab-based chemotherapy – a case report.

Reviewer's code: 05604310

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-19 11:55

Reviewer performed review: 2021-03-11 22:35

Review time: 20 Days and 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors reported a case report of patient with cancer of primary unknown who underwent cetuximab-based therapy and archived long-term survival. The patient is still alive after ten years after the initiation of palliative chemotherapy. The authors proposed that this case is an exceptional case. They also suggested that biomarker analyses are warranted to predict the response of chemotherapy. Although the manuscript has some interesting points, the reviewer has following concerns. 1. Although it was reported that the patient achieved complete response after four cycles of chemotherapy, no figures showing the response to chemotherapy were not represented. 2. The details of treatment course were not described especially with regard to chemotherapy. Which platinum agent was used, cisplatin or carboplatin? How many courses of chemotherapy were conducted? 3. The standard regimen for cancer of primary unknown is carboplatin plus paclitaxel. Meanwhile, cetuximab-based therapy which is targeted to head and neck cancer was successful in this case, suggesting the usefulness of site-specific therapy. The advantage of site-specific therapies over empirical chemotherapy is still controversial (Hayashi H, et al. J Clin Oncol. 2019 Mar 1;37(7):570-579.). This should be discussed more. 4. The authors mentioned the value of biomarker analyses. However, whole genome sequence or gene expression analysis was not conducted. This limitation should be described. 5. Further English proofing may be needed. For example, "ECOG 0" should be "ECOG PS 0" (Page 7, Line 19).

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61547

Title: Long-term survivor of metastatic squamous-cell head and neck carcinoma with occult primary after cetuximab-based chemotherapy – a case report.

Reviewer's code: 03210360

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-19

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-04-07 07:00

Reviewer performed review: 2021-04-07 07:11

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript addressed my concerns and improved after revision. I have no more comments on the manuscript.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61547

Title: Long-term survivor of metastatic squamous-cell head and neck carcinoma with occult primary after cetuximab-based chemotherapy – a case report.

Reviewer's code: 05604310

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-19

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-04-12 13:04

Reviewer performed review: 2021-04-18 01:09

Review time: 5 Days and 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript has been revised well.