Author’s response to reviews

Title: Metastatic malignant melanoma with neuroendocrine differentiation – report of a rare case and review of the literature

Authors:

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Author’s response to reviews:

Dr. Itzhak Brook, editor
Journal of Medical Case Reports
Stockholm, February 4th 2020

Dear Dr. Brook,

Please find attached our re-revised case report JMCR-D-19-00769 entitled “Metastatic malignant melanoma with neuroendocrine differentiation – report of a rare case and review of the literature” by Carl Christofer Juhlin, Jan Zedenius and Felix Haglund.

Thank you for your remarks. We note that no additional referee comments were raised regarding our previous revision, but instead a number of editorial queries have been added.

In this re-revised version, we have again scrutinized the patient’s medical records and listed parameters suggested when available. Changes to the main text have been carried out to meet the suggestions proposed by the editor, and are marked up in yellow in the re-revised version. Changes from the previously revised version are now implemented without color highlight, to facilitate the reading. The specific responses to the comments raised by the editor follow below:

Editorial comment:

“Your manuscript "Metastatic malignant melanoma with neuroendocrine differentiation – report of a rare case and review of the literature" (JMCR-D-19-00769R2) has been assessed by our reviewers. Although it is of interest, we are unable to consider it for publication in its current form. The reviewers have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in Journal of Medical Case Reports. Their reports, together with any other comments, are below. Please also take a moment to check our website at https://www.editorialmanager.com/jmcr/ for any additional comments that were saved as attachments."
If you are able to fully address these points, we would encourage you to submit a revised manuscript to Journal of Medical Case Reports."

Reply: Thank you for your comments. We did not find any additional comments from the two original reviewers, but instead a number of editorial remarks. We have now revised our manuscript a second time as according to the suggestions of the editor. Please see our answers below. Please note that this patient was originally referred to our department as a pathology consult case, and most initial clinical work-up was performed in outside hospitals in which we lack access to the medical charts. However, we do have access to medical files from when the patient was subsequently admitted to our department for oncological treatment. We have therefore implemented all suggestions from the editor whenever possible to do so and hope for your understanding.

1. The case report should include past medical, social, environmental, family and employment history.

Reply: The additional, departmental clinical information from our hospital that was retrievable for us has been retrieved through the medical charts and added to the case presentation as suggested. The patient's past medical history, as presented in the manuscript, consisted of hypertension, benign prostatic hyperplasia, polycythemia vera and duodenal ulcers. The patient was born in Iraq and arrived in Sweden in 2002. He was previously employed as a medical secretary but retired at the time of admission. His previous social history is largely unknown, but he was married, and he had three children (two sons and one daughter) according to previous medical files. This information has now been added to the manuscript.

2. What medications was the patient receiving prior to diagnosis? Did the patient smoke, and/or consume alcohol?

Reply: Following a medical chart review, we could conclude that the patient at the time of initial admission received metoprolol, 100 mg daily as well as aspirin, 75 mg daily. He had a history of smoking, but ceased tobacco use 15 years prior to the current admission. The patient did not consume alcohol. This information has now been added to the manuscript.

3. Give detailed physical and neurological examination on admission. What was the pulse, blood pressure and temperature, on admission?

Reply: For reasons explained above, we had limited access to admission data as this is foremost a pathology consult case in which tissue slides originally were sent to us for review. This process also includes a brief recap of the patient's medical history as well as assorted radiological information. From our records, we did manage to recover some information regarding the second admission when the patient was admitted to us for chemotherapy and external irradiation.

Upon admission to our hospital, the patient was confined to wheelchair and in considerable pain from the groin region. The groin was investigated, and a 20 mm enlarged lymph node was palpable – and was assumed part of the patient’s disseminated disease. The patient had substantial bilateral pitting edema over the lower extremities but was without dyspnea. He had no fever or symptoms indicating an infection. No neurological examination was performed. The blood pressure was measured several times during the hospitalization, but was 123/89 mm Hg shortly after admission, with a pulse rate of 113 and
a saturation of 93% without oxygen supply. This information has now been implemented in the manuscript as suggested.

4. Give the doses of all medications that were given and their doses.

Reply: Besides the chemotherapy treatment, the patient was administered fentanyl (75 micrograms/hours, transdermal administration) against his back pain, ondansetron (4-8 mg intravenously) against chemotherapy-induced nausea and sodium phosphate laxatives against morphine-instigated constipation. The patient was also administered furosemide intravenously (20-40 mg) when needed. This information has now been implemented in the manuscript as suggested.

5. Give all results of laboratory findings (i.e. CBC, liver and renal functions), urinalysis, serology, microbiology etc.

Reply: The patient was in palliative treatment following the dissemination of the tumor. Considering the state of the patient, few broad laboratory investigations were launched, and hence only limited data is available. No serologies or microbiological testing was performed at admission. At admission in our hospital, the hemoglobin count was 170 gram/L (reference: 134-170), the erythrocyte count was 5,5(x1012) (reference: 4,2-5,7), the leukocyte count was 8,0(x109) (reference: 3,5-8,8) and the thrombocyte count was 117(x109) (reference 145-348). Liver parameters were mostly normal (aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, bilirubin), except for hypoalbuminemia (24 g/L, reference: 34-45). Renal function was not impaired, as evident by a normal plasma creatinine and a calculated glomerular filtration rate (GFR) of 75 mL/min (reference: &gt;60 mL/min). This information has now been implemented in the manuscript as suggested.

6. Were any radiographic and other scans done? Show a representative X ray and scans.

Reply: As outlined in the manuscript, a CT scan performed in an outside hospital was performed in which malignant disease was first noted. These radiographies were sent for second opinion at our radiology department, in which we concurred in the former diagnosis of largely disseminated disease. Unfortunately, no scans from this period are kept in our own records. We have now added an image of a representative plain radiology scan displaying the pathological hip fracture from which the metastatic melanoma was diagnosed and included it in a revised Figure 2. Consequently, the internal image order (A-G) has shifted, and the figure legend as well as the manuscript text have both been edited to match this change.

7. Was an autopsy performed, and what were the findings?

Reply: No autopsy was performed. This information has now been added to the manuscript.

8. Discussion – add a paragraph at the beginning of the Discussion that summarizes the case and describes what is unique in this case compared to what is available in the literature.

Reply: The suggested paragraph has been added.
9. The Discussion is too short and superficial. Please briefly review the literature discussing diagnosis and treatment. The Conclusion section should be separate and include the lessons learned from the presented case. It is currently too short and superficial.

Reply: The literature has been previously reviewed as detailed in the manuscript, and as the number of reports on this infrequent disease entity is scarce, we unfortunately cannot add additional studies covering the subject. Nevertheless, we have made some additions to the Discussion and Conclusion sections as suggested and hope for your understanding in this matter.

We thank the editor for improving our manuscript once more. We hope that you will find the above-suggested additions of sufficient quality to warrant publication.

Best regards,

Carl Christofer Juhlin, MD, Associate Professor
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