Author's response to reviews

Title: Isolated pineal region metastasis from lung adenocarcinoma with obstructive hydrocephalus: a case report

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Author's response to reviews: see over
Isolated pineal region metastasis from lung adenocarcinoma with obstructive hydrocephalus: a case report

Dear Editor,

The Journal of Medical Case Reports,

Thank you for your email of January 23, 2013, concerning our manuscript, “Isolated pineal region metastasis from lung adenocarcinoma with obstructive hydrocephalus: a case report”, and the valuable comments of the three reviewers. I attach herewith our revised manuscript, as well as our responses, point-by-point, to the reviewers’ comments.

We feel that the revised manuscript addresses all the concerns of the reviewers, and is significantly improved over the initial submission. We hope that you will now find it suitable for publication in the Journal of Medical Case Reports.

Thank you in advance for your kind consideration of this paper.

Yours sincerely,

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RESPONSE TO REVIEWER 1:

Dear Dr Vijay Hadda,

We wish to express our appreciation for your insightful comments, which have helped us significantly to improve the quality of our paper.

Comment 1: “Our present patient had adenocarcinoma, which seems to be a rare histological type associated with pineal metastasis.” May be written as “Our patient had adenocarcinoma, which seems to be a rare histological type associated with pineal metastasis.”

Response: We appreciate your comment. In accordance with your comment, we have changed the text from:

“Our present patient had adenocarcinoma, which seems to be a rare histological type associated with pineal metastasis.”

to

“Our patient had adenocarcinoma, which seems to be a rare histological type associated with pineal metastasis.”

Comment 2: “Most cases of pineal metastases are asymptomatic, and are diagnosed by autopsy [2, 3].” May be written as “Most cases of pineal metastases are asymptomatic, and are diagnosed during autopsy [2, 3].”

Response: We appreciate your comment. In accordance with your comment, we have changed the text from:

“Most cases of pineal metastases are asymptomatic, and are diagnosed by autopsy [2, 3].”

to

“Most cases of pineal metastases are asymptomatic, and are diagnosed during autopsy [2, 3].”
Comment 3: The usual features of the pineal tumours are related to visual field, Hypo-pituitarism (Diabetes Insipidus, Hypothyroidism etc). Authors should mentioned that whether this patient had these.

Response: We appreciate your comment on this point. Accordingly, we have added the following text to the Case presentation section: “On admission to our hospital, neurological examination of the patient revealed no abnormalities, including evidence of visual disturbance; in addition, there were no features of hypopituitarism, such as secondary central diabetes insipidus or hypothyroidism. The standard blood workup also revealed no abnormalities.”

Comment 4: Authors have also mentioned levels of CEA values which were elevated. Authors should discuss the usefulness of this test in such setting.

Response: We appreciate your comment on this point. Accordingly, we have added the following text to the Discussion section: “This patient was elderly and had a primary lung tumor with elevated serum CEA levels, although it was not diagnosed preoperatively, both of which are consistent with the diagnosis of metastasis to the pineal region.”

Comment 5: Did patient received corticosteroids during pre-operative?

Response: We thank you for your comment. No, the patient did not receive corticosteroids prior to surgery, as there was no evidence of hypopituitarism.

Comment 6: “The mechanism underlying the development of pineal metastasis is only partially understood; Ortega et al. suggested hematogenous spread to the pineal body through the posterior chroidal arteries [7]. According to Toner et al. [8], the pineal gland is excluded from the blood-brain barrier, and is thus a more vulnerable site for hematogenous metastasis from distant tumors.” May be rephrased “The mechanism underlying the development of pineal metastasis is partially understood. Ortega et al. suggested hematogenous spread to the pineal body through the posterior chroidal arteries [7]. Since the
pineal gland is excluded from the blood-brain barrier, it is more vulnerable site for hematogenous metastasis from distant tumors [8].”

Response: In accordance with your comment, we have changed this to “The mechanism underlying the development of pineal metastasis is partially understood. Ortega et al. suggested hematogenous spread to the pineal body through the posterior choroidal arteries [7]. Since the pineal gland is excluded from the blood-brain barrier, it is more vulnerable site for hematogenous metastasis from distant tumors [8].”

Comment 7: “In this context, Kashiwagi et al. described that one of the contributory factors was the special histological characteristics of the pineal body, namely, the numerous sinusoidal vessels with no perivascular glial sheets which increases the vascular permeability [3].” This statement may also be put together with suggested mechanisms/risk factors causing isolated pineal metastases.

Response: In accordance with your comment, we have added the following text to this section: “In this context, Kashiwagi et al. described, in relation to the mechanism of development of pineal metastasis, that one of the contributory factors was the special histological characteristics of the pineal body, namely, the numerous sinusoidal vessels with no perivascular glial sheets, which increases the vascular permeability [3].”

Comment 8: While discussing the role of serum tumour markers, authors should also mentioned other tumour markers such as beta-hCG, lactate dehydrogenase (LDH) and placental alkaline phosphatase for differentiation of primary vs metastatic pineal tumour.

Response: We appreciate your comment on this point. Accordingly, we have changed the following text from:

“～, while other serum tumor marker levels were within normal limits.”

To

“～while the serum levels of other tumor markers such as lactate dehydrogenenase (LDH)
and human chorionic gonadotropin (HCG) were within normal limits.”

And we have added the following text to the Discussion section: “In addition, our present patient did not show any elevation of the serum LDH or HCG levels, which enabled us to rule out germ cell tumor, the most frequently occurring primary tumor of the pineal gland [9].”

We agree with the reviewer that additional information on “placental alkaline phosphatase” would be valuable. We regret, however, that we did not measure this marker.

Comment 9: Hanada et al. reviewed 33 cases of metastatic pineal tumors diagnosed in life, and 6 patients underwent neuroendoscopic third ventriculostomy for hydrocephalus, which resulted in good control in all cases [13]. The message of the statement is not clear, please rephrase it.

Response: In accordance with your comment, we have changed the sentence to “Hanada et al. reviewed the clinical data of 33 patients with metastatic pineal tumors diagnosed during life [13]; six of these patients underwent neuroendoscopic third ventriculostomy for hydrocephalus, with good control obtained in all the six patients.”

Thank you again for your comments on our paper. We trust that you will find our revised manuscript suitable for publication in the Journal of Medical Case Reports.
RESPONSE TO REVIEWER 2:

Dear Dr Takefumi Saito,

We wish to express our appreciation to you for your insightful comments, which have helped us significantly to improve the quality of paper.

**Comment 1:** In “Case presentation of the paper”, Magnetic resonance imaging (MRI) of the brain revealed a tumor in the pineal region measuring 25 cm in diameter. I guess that 25 cm is 25 mm.

**Response:** We appreciate your observation. Indeed it was 25 mm; we apologize for our error and have corrected “25 cm” to “25 mm”.

We wish to thank you again for your comment. We trust that you will find our revised manuscript suitable for publication in the *Journal of Medical Case Reports*. 
RESPONSE TO REVIEWER 3:

Dear Dr Neetu Jain,

We wish to express our appreciation to you for your insightful comments on our paper. We feel that the comments have helped us significantly to improve the quality of our paper.

Comment 1: In case presentation part of the report, the writer has mentioned that they did a tumour biopsy via neuroendoscopy, I would like them to give reasons why did not they resect the tumour. This would have helped them to get larger specimen for histopathology as well. In the discussion part they have mentioned that they could obtain only small fragments of tumour.

Response: Thank you for your insightful comment; we appreciate your concern on this point. We considered that neuroendoscopic tumor biopsy rather than surgical removal of the tumor would be more appropriate for this case; we elected to perform the minimally invasive procedure because, preoperatively, the present patient had begun to show progressive worsening of the level of consciousness.

Comment 2: It would be worthwhile to discuss the differential diagnosis of the pineal gland tumors and pineal gland metastasis in more detail.

Response: Accordingly, we have added the following text to the Discussion section: “In addition, our present patient did not show any elevation of the serum LDH or HCG levels, which enabled us to rule out germ cell tumor, the most frequently occurring primary tumor of the pineal gland [9].”

Comment 3: The reference for the statement “Hanada et al. reviewed 33 cases of metastatic pineal tumors diagnosed in life…….” in the discussion part of the report is wrongly stated.

Response: Accordingly, we have changed this to “Hanada et al. reviewed the clinical data of
33 patients with metastatic pineal tumors diagnosed during life [13]; six of these patients underwent neuroendoscopic third ventriculostomy for hydrocephalus, with good control obtained in all the six patients.”

Comment 4: The authors have not gone into details of hormonal effects of pineal metastasis and their management.

Response: We thank you for your comment on this point. We think that the major hormonal effect of pineal metastasis is hypopituitarism. Therefore, we have added the following text to the Case presentation section: “~there were no features of hypopituitarism, such as secondary central diabetes insipidus or hypothyroidism.”

Comment 5: Authors need to recheck the references(ref no 13)

Response: We appreciate your comment on this point. We regret that our expression of references no 12 and no 13 was contrary. Therefore, we have revised the references as follows:


Thank you again for your comments on our paper. I hope that you will find our revised manuscript suitable for publication in the Journal of Medical Case Reports.