Author’s response to reviews

Title: Diabetes insipidus and panhypopituitarism as a first presentation of silent adenocarcinoma of lung: a case report and literature review

Authors:
Sirinart Sirinvaravong (sirinart.sir@mahidol.ac.th;sirinart.oh@gmail.com)
Peeradon Vibhatavata (p_wipatavut@hotmail.com)
Paweeha Chunharojrith (paweharo@hotmail.com)
Porruchak Cheunsuchon (pcheunsuchon@gmail.com)
Sutin Sriussadaporn (sutin.sri@mahidol.ac.th)

Version: 1 Date: 25 Jul 2019

Author’s response to reviews:

Dear the editor and reviewers,

Reference number: BEND-D-19-00184

Thank you for your letter and constructive comments concerning our manuscript entitled “Diabetes insipidus and panhypopituitarism as a first presentation of silent adenocarcinoma of lung: a case report and literature review: Reference number: BEND-D-19-00184”. We studied your comments carefully and made corrections with yellow highlights in the manuscript which we hope to meet with your approval. We answered your questions and comments in details in the following texts.

Replies to questions and comments:
Answer to Yasir Elhassan (Reviewer 1):

This case reported by Sirinvaravong et al is interesting, but similar cases of pituitary metastasis from occult lung malignancy have been numerously reported.

Some specific criticism:

Comment 1: As this is a case report AND literature review, the methods of literature search should be described (key words, platforms searched etc.)

Reply: We have added methods of literature search in the revised manuscript as below (background section, line 59-63, page 4-5)

“In this article, we report a rare case of pituitary metastasis from adenocarcinoma of the lung who first presented with central diabetes insipidus and panhypopituitarism, without known evidence of the primary malignancy. A literature review was performed. A search of the literature was performed on the PubMed and Ovid Medline databases. The initial search string used was “Pituitary AND Metastas.*” References cited in the articles identified by our original search were also assessed for relevance. Most of the papers identified were case studies and case series; those in languages other than English were excluded.”

Comment 2: The English needs some review prior to publication.

Reply: Thank you for your comment on the language. In response to this, we have had the entire manuscript edited and proofread by a professional medical editor who is a native English speaker. All changes and corrections made are indicated using Track changes.

Comment 3: Line 106: describing "hypogonadotrophic hypogonadism" in a postmenopausal woman is odd as all are "hypogonadal". Maybe say "inappropriately low gonadotrophins”.

Reply: We have corrected the term “hypogonadotrophic hypogonadism” to “inappropriately low gonadotropins” according to your suggestion in the revised manuscript as below (case presentation section, line 111, page 8):

“Pituitary hormonal profiles (Table 1) showed inappropriately low gonadotropins, low plasma adrenocorticotropic hormone (ACTH) level, low morning serum cortisol level that did not respond to cosyntropin stimulation indicating secondary adrenal insufficiency”
Answer to Olcay Evliyaoglu, MD (Reviewer 2):

I have reviewed the manuscript entitled 'Diabetes insipidus and panhypopituitarism as a first presentation of silent adenocarcinoma of lung: a case report and literature review'. In this report a 72 years old woman presented with panhypopituitarism due to pituitary metastases due primary adenocarcinoma of lung. Isolated pituitary metastases of the primary lung tumor can be interesting. This manuscript can be published after the revisions below made:

Comment 1: In the case report section; serum osmolality should also be given. Serum osmolality is assumed > 300mOsm/kg before giving desmopressin.

Reply: We thank the reviewer for the kind suggestion. Serum osmolality of the patient was 325 mOsm/kg prior to administration of desmopressin. We have added this information in the revised manuscript as below (case presentation section, line 91, page 7)

“At the first hour after admission, she had polyuria with urine output of 300 mL/hour (6.7 mL/kg/hour). Laboratory test results were serum sodium 160 mmol/L; potassium 3.9 mmol/L; chloride 125 mmol/L; bicarbonate 24 mmol/L; creatinine 1.4 mg/dL. Serum osmolality was 325 mOsm/kg. Her urine specific gravity was 1.002 without proteinuria or glucosuria.”

Comment 2: In discussion section; although the most common site for metastases is posterior pituitary, in the presented case anterior pituitary is also involved. Involvement of the both parts of the pituitary should be discussed. Why are both sites involved, what is the risk factors for this patient?

Reply: We would like to thank the reviewer for raising an interesting point of discussion. Metastatic involvement of the anterior pituitary lobe mostly results from direct spreading from the posterior pituitary and is associated with a larger area of the extending posterior pituitary lesion. In addition, tumor in posterior lobe or stalk may potentially compromise a blood supply of the anterior lobe, resulting in ischemic infarct. Thus, involvement of the anterior pituitary in our patient could be explained by the effect of large metastatic volume in the posterior pituitary as well as damage to the vascular supply through the stalk as demonstrated by unidentifiable stalk on MRI. We have inserted this discussion point into the revised manuscript as below (Discussion section, line 170-174, page 13).

“Metastases to the anterior pituitary mostly originate via direct spreading of metastatic foci from the posterior pituitary (1) and associate with a larger area of the extending posterior pituitary lesion. In addition, tumor in posterior lobe or stalk may potentially compromise a blood supply of the
anterior lobe, resulting in ischemic infarct (4). Thus, involvement of the anterior pituitary in our patient could be explained by the effect of large metastatic volume in the posterior pituitary as well as a damage to the vascular supply.”

We really hope these modifications can meet with your approval. Thank you very much.

Yours Sincerely,

Sirinart Sirinvaravong, MD

Division of Endocrinology and Metabolism, Department of Medicine
Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand
Email: Sirinart.sir@mahidol.ac.th