

Response to Reviewer 00723857:

Thank you for your encouraging and constructive comments on our paper. We have revised our paper according to your suggestions.

Response to Reviewer 00503260:

We appreciate the careful reading of our manuscript and valuable suggestions. We have carefully considered your comments and have revised the manuscript accordingly. Our responses to your comments are as follows:

Comment 1): “Therefore, I doubt that the reasons why NK/T-cell lymphoma associated with SIADH has not been reported until now are due to the rarity of NK cell lymphoma or due to publication bias. Therefore, the authors should describe the specialty of SIADH due to NK cell lymphoma (for example, pathogenic mechanism, etc.).”

Response: We appreciate your advice and agree with your observation and suggestion. NK cell lymphomas belong to mature T-cell lymphomas; however, separate research regarding NK cell lymphomas with SIADH is scarce. Regretfully, we could not find further details regarding SIADH due to NK cell lymphomas.

Comment 2) There is no description to suggest that this patient suffered from SIADH in Abstract. Therefore, the authors should briefly add the evidences to suggest SIADH in Abstract.

Response: Thank you for your suggestion. We have revised the Abstract accordingly.

Comment 3) The speed of decreased serum sodium is very important. Therefore, the authors should indicate serum sodium levels before admission.

Response: Thank you for your comments. Unfortunately, serum sodium levels before admission were not available. The initial serum sodium (137.6 mmol/L) after admission is provided in our paper.

Comment 4) Because no data in the endocrinology department (plasma osmolality, urine osmolality, blood pressure, renal function and adrenal

function) were found, it is impossible for me to make a definite diagnosis of SIADH. Therefore, the authors should indicate the raw data.

Response: We appreciate your valuable suggestion. Unfortunately, adrenal function was not detected. Urine osmolality was previously mentioned in our paper; following your advice, we have also added plasma osmolality, blood pressure, and renal function.

Comment 5) Reduced renal sodium excretion is not consistent with the definition of SIADH. The authors should explain why renal sodium excretion decreased.

Response: Thank you for your comment. On one hand, the patient had intermittent fever after admission, and her temperature fluctuated between 36°C and 39.3°C, accompanied by heavy sweating. She did not show congestive heart failure before hyponatremia. On the other hand, renal sodium secretion (20 mmol/L) was assayed only one time after fluid restriction and administration of sodium chloride. It would have been preferable had we examined renal sodium earlier and performed the test one more time; unfortunately, this was not the case.

However, we appreciate your kind help and consideration.

Response to Reviewer 02714171:

Thank you for your encouraging and constructive comments on our paper.

Response to Reviewer 03704412

Thank you for your encouraging and constructive comments on our paper.

Comment 1) Can the authors comment on any link between NPC and NK/T cell and concomitant SIADH development?

Response: We appreciate your valuable suggestion. EBV is closely associated with the development of malignant tumors, including nasopharyngeal carcinoma and lymphomas, and in very rare cases, it can lead to NK/T-cell lymphoma. Unfortunately, we could not find further information regarding a

link between NPC and NK/T cell and concomitant SIADH.

Comment 2) Are there any known genetic alterations behind NK/T cell lymphoma and SIADH? This should be discussed.

Response: Thank you for your constructive comment. As mentioned in the manuscript, lymphoma is one of the causes of SIADH. Unfortunately, we could not find any known genetic alterations behind NK/T cell lymphoma and SIADH. This needs to be studied further.

Comment 3) The patient was found to be EBV positive. Are there any specific organs where the viral integration was detected?

Response: We appreciate your valuable suggestions. Virus infection in other organs could not be determined from clinical manifestations. According to the patient's status, we did not perform other biopsy, so there were no specific organs where the viral integration was detected.

Response to Reviewer 00071178

Thank you for your valuable suggestions. We have carefully considered your comments and have revised the manuscript accordingly.

Comment 1) Case presentation section is quite long. I think it should be shortened.

Response: Thank you for your constructive comment. We shortened the case presentation accordingly.

Comment 2) The authors wrote the discussion section very long, but they did not comment on the tables. I think a paragraph should be prepared for the results of the table presented by 33 patients.

Response: Thank you for your valuable suggestion. We shortened the discussion section and added some comments on the tables.

Comment 3) Unnecessary information about the pathogenesis of lymphoma should be removed from the discussion section.

Response: We appreciate your advice. We deleted some unnecessary text.

Response to Reviewer 00123524

We appreciate the careful reading of our manuscript and valuable suggestions. We have carefully considered your comments and have revised the manuscript accordingly. Our responses to your comments are as follows:

Comment 1) The abstract does not inform readers about the clinical picture that made SIADH a likely diagnosis or the time frame of the clinical events that led to the patient's demise.

Response: We appreciate your valuable suggestion. We have revised the manuscript accordingly.

Comment 2) I could find at least one case report of SIADH caused by NK lymphoma: <http://en.tumorsci.org/index.php/tumor/article/view/1427>

Response: Thank you for this useful comment. Previously, we did not find a case report in Chinese of SIADH caused by NK lymphoma. We have added the suggested reference to our manuscript. Our manuscript contains a review of literature regarding cases of lymphoma with concomitant SIADH, while the case report in Chinese does not contain. Additionally, the international influence of the case report in Chinese is lower than that published in Pubmed.

Comment 3) The authors should consider the possibility that the limited number of case reports of SIADH in patients with lymphoma is due to the fact that it is already widely known and described in textbooks that lymphomas are a cause of SIADH. Therefore there would be little interest in publishing case reports of already known phenomena.

Response: We appreciate your comment. On one hand, NK/T cell lymphoma is an uncommon type of non-Hodgkin lymphoma, which is known to be a cause of SIADH. As SIADH has atypical clinical manifestations, it is difficult to detect. Moreover, NK/T cell lymphoma with concomitant SIADH is relatively rare, and the relationship between NK/T cell lymphoma and SIADH was still not clear. Thus, we considered it useful to present a case and literature review that further explores NK/T cell lymphoma and SIADH.

Comment 4) “One year prior, she had traveled to Europe and ate local food including sausage and fish”. I don’t see how that information could be relevant for the current case report whose purported novelty relates to an unusual cause of SIADH.

Response: Thank you for your question. The history of her travel was mentioned to describe the possibilities we considered during attempts to identify the cause of the fever, such as typhoid or brucellosis.

Comment 5) The authors should report the size and consistency of the lymph node that was palpated below the left jaw of the patient because large lymph nodes are known to be associated with increased cancer risk.

Response: We are grateful for your advice. We added the size and consistency of the lymph node in the manuscript.

Comment 6) I don’t understand why the authors performed a PET scan and so many other tests before proceeding with the biopsy of the enlarged submandibular lymph node that was identified during physical examination early on. That biopsy would be the most obvious approach in a patient with fever of unexplained origin and an easily accessible large lymph node.

Response: We are grateful for your comments. We suggested to the patient that biopsy should be completed first. However, due to the patient’s family wishes, priority was given to those noninvasive approaches, and biopsy of the enlarged submandibular lymph node was postponed.

Comment 7) The patient was treated with vinorelbine, a vinca alkaloid known to be a cause of SIADH. Because the patient’s hyponatremia was closely associated in time with the administration of that drug, wouldn’t it be more likely attributed to it than to the patient’s lymphoma? In the discussion section the authors state that SIADH was discovered before she received chemotherapy, however that sentence is in clear disagreement with the information reported that described the occurrence of hyponatremia after chemotherapy on day 10.

Response: We appreciate the careful reading of our manuscript and valuable

suggestions. We are sorry for not indicating the chronological order clearly. The patient's SIADH occurred before the use of chemotherapy. We revised this part in the manuscript, and thus SIADH might be attributable to lymphoma.

Comment 8) It seems that the clinical management of the severe episode of hyponatremia was poor. If patients with severe hyponatremia and decreased level of consciousness are not hypovolemic, they should receive hypertonic (3%) saline aimed at increasing sodium levels within the next few hours but not exceeding 10 mEq/L increase in 24h. It makes no sense to give a patient with decreased level of consciousness oral salt capsules in face of such severe hyponatremia not only because the patient is at risk of aspiration but because it could compromise the control over the rate of correction of hyponatremia. The level of consciousness of patients improve dramatically with increases between 3 and 7 mEq/L of sodium and faster rates of correction of the hyponatremia may incur in osmotic demyelination, a life-threatening complication. The very limited information provided by the authors, stating that after 2 days, the patient's sodium level "gradually" increased to 126.5mmol/L is not enough for readers to be reassured that the patient's hyponatremia was managed correctly.

Response: Thank you for your detailed suggestion. We apologize for the confusion caused and have revised this part carefully to introduce the case more clearly. Although the patient developed lethargy, she could be awakened and could take the drugs orally when she was awake. Additionally, the rate of the recovery of serum sodium was under control (8.6 mmol/L per day). Thus, the possibility of the aspiration and developing osmotic demyelination appears to be low.

Comment 9) P.8 "... whether hyponatremia was recurrent could not be determined". That sentence suggests that the patient's sodium level was not followed up during hospitalization after an episode of severe hyponatremia, which is very worrisome.

Response: We appreciate your valuable suggestion. Because of the death of the patient, further detection of her serum sodium was infeasible. However, after the occurrence of SIADH, the patient's serum sodium was carefully monitored and hyponatremia was not recurrent.