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Reviewer A

The authors report a rare case with LCNEC of the lung treated well with perioperative chemo-immunotherapy. Because LCNEC is rare, this manuscript is worth publishing. However, there are some points to be revised. Additionally, I think English proof reading is necessary.

1. In line 71-73, they described "Based on the above results and some information not presented, this patient was diagnosed with III A clinical stage (T4N1M0)." Please describe the detailed information.
Reply 1: Thank you for your kind remind. This patient's maximum tumor diameter was 10.1 cm（T4）, with a few lymph nodes enlarged around left bronchus (N1), but without any distant metastasis(M0). This patient was diagnosed with stage III A, T4N1M0.
Changes in the text: see Page 2, line 50; Page 3, line 52.

2. In line 80-81, "Neoadjuvant efficacy reached partial remission (PR) and met the surgical indication." What is the indication for surgical resection? Down staging after neoadjuvant therapy? If so, please mention the "yc" stage.
Reply 2: Thank you for your question. After 2 cycles of chemo-immunotherapy, tumor diameter reduced from 10.1cm to 6.3cm, which successfully reduced the tumor size. The yc stage is ycT3N1M0. With the evaluation of thoracic surgeons, the tumor could be resectable. Then the patient was advised to undergo surgery. We added these information in the paper.
Changes in the text: see Page 4, line 66-71.

3. In line 83, they described the postoperative pathology. How about lymph node metastasis? What is the "yp" stage?
Reply 2: Thanks. The postoperative pathology showed that lymph nodes all were negative. The yield pathological stage was ypT1bN0M0. We had added these important informations according your recommends.
Changes in the text: see Page 4, line75,80.

4. In line 88-89, they continued the adjuvant chemo-immunotherapy. If the tumor resected completely, they had an option without continuation of chemo-immunotherapy after the operation. Please discuss the reason why you decided to continue chemo-immunotherapy after the operation.
Reply 4: Thank you for your question. In clinical, 2-3 cycles of chemotherapy are conducted before surgery. It is suggested to carried out chemotherapy for total 4 cycles during perioperative

stage. And in this case postoperative pathology showed 2 focal residual lesions in tumor bed, thus, we continued 2 cycles of chemo-immunotherapy after surgery.

Reviewer B

The case showed by authors is very interesting and concerns pre- and postoperation immunochemotherapy. This kind of treatment is rarely used. The pathological remission grade after this therapy was IIB grade left residual tumor cell <10%. It is spectacular effectiveness.
I agree with the authors that there are no clinical trials in this direction.
In my opinion a case concerns combined LCNEC with component of squamous cell carcinoma (after neoadiuvant therapy). CK5/6 positive means that it was squamous cell carcinoma diagnosed by based fine needle (line 69).
Reply 1: Thank you for your question. In this case, only focal positive of cytokeratin 5/6 in fine needle sample, while other squamous cell carcinoma markers, such as p40, p63, were negative. We invited pathologists to review the samples again. They were agreeed that there had no enough evidence to identify squamous cell carcinoma exiting in the slids.
Changes in the text: see Page 3, line 56-57.

Line 71-72 What authors mean by „and some information not presented…"?
Reply 2: We are sorry for the careless expression. That means we did not show the image of bone, brain, adrenal gland or other organs, which all did not show the evidence of distant metastasis. We had deleted this sentence and highlighted there was no other distant metastasis.
Changes in the text: see Page 3, line 52.

Line 84 The authors showed that neuroendocrine differentiation was 5%. According to WHO, the both criteria of combined LCNEC: neuroendocrine markers expression on a level 10% and morphological features for LCNEC have to be met.
According to WHO criteria the combined LCNEC is LCNEC with components of adenocarcinoma, squamous cell carcinoma, or spindle cell carcinoma, and/or giant cell carcinoma. The authors presented combined LCNEC with component of large cell carcinoma. That excludes diagnosis of combined LCNEC.
There are no information about the second component of combined LCNEC. I suggest a consultation of the histopathological material from fine needle and postoperative material. It is needed to correct diagnosis.

Reply 3: Thank you for the careful and useful reminding. The WHO diagnosis criteria of LCNEC taken chromogranin, synaptophysin、CD56 as immunohistochemical markers. One positive marker is enough if the staining is clear in more than 10% of the tumor cells. The pathologists reviewed the pathological slides. Tumor bed size was 7.5 * 4 cm, see 2 focal residual carcinomas, size 0.6 * 0.3 cm(without CD56 positive cell) and 0.5 * 0.4 cm(with 15%

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CD56 positive cell)respectively. If taken together, CD56 positive cell in 2 lesions was about 5%. Their diagnosis was large-cell neuroendocrine carcinoma. We had amended this in the paper. As we all known, tissue heterogeneity existed among the tutor lesions. And the neoadjuvant therapy might affect the proportion of neuroendocrine expression in different tumor cells. we discussed this question in the discussion section.

As to combined LCNEC, the pathologists considered that the evidence for the diagnosis of squamous cell carcinoma was insufficient as we replied above.

Changes in the text: see Page 4, line 75-80， Page 6, line 103-109