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Peer Review File

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Reviewer A

Comment 1: Please describe c stage. Did patient have lymph node metastasis before surgery?
Reply 1: The clinical stage of this patient was T1bN2M0. This patient had ipsilateral mediastinal and subcarinal lymph node metastases, thus the clinical N stage was cN2.
Changes in the text: We added the clinical stage of this patient (see Page 4, line 9, highlighted yellow part)

Comment 2: Please describe the reason adjuvant CTx followed by RTx. Is there evidence of RTx?
Reply 2: The International Adjuvant Lung Cancer Trial (IALT) confirmed the cisplatin-based chemotherapy brought both 5-y OS (45% vs. 40%, $p < 0.03$) and 5-y DFS (39% vs. 34%, $p < 0.003$) benefit comparing with observation in completely resected stage I-III NSCLC. LACE (a meta-analysis including 4584 patients) also verified the 5-y OS improvement (5.4% absolute benefit) by postoperative cisplatin-based chemotherapy. Furthermore, TREAT study showed that cisplatin/pemetrexed was less toxic regimen than cisplatin/vinorelbine with similar efficacy in completely resected stage IB-III NSCLC. Thus, patients could endure more cycles of chemotherapy with cisplatin/pemetrexed. A series of studies have demonstrated postoperative radiotherapy (PORT) conferred improved survival for stage III-pN2 NSCLC, especially for those with high metastatic mediastinal lymph node ratio (MLNR≥ 50%). In view of the pathological stage- III A (T1bN2) and uncertain excision-the positivity of highest resected mediastinal lymph node and a MLNR of 70%, the patient should be given postoperative CT and RT.
Changes in the text: We supplemented the reason of adjuvant chemotherapy and radiotherapy for this patient (see Page 4, line 16-24, Page 5, line 1-7, highlighted dark gray part) and related references (references: 11-19).

Comment 3: Please describe the reason treatment of Temozolomide. Is there evidence of Temozolomide?
Reply 3: Temozolomide (TMZ) was able to cross the blood-brain barrier (BBB).

Meta-analysis showed that the addition of TMZ to whole brain radiotherapy (WBRT) increased the overall response rate (ORR) of NSCLC patients with brain metastases comparing with WBRT alone. TMZ was initiated by the tertiary hospital for 1 cycle (TMZ 200mg d1-5).

Changes in the text: We added the related information (see Page 5, line 16-20, highlighted light gray part) and related references (reference: 20).

Comment 4: Please describe whether asymptomatic brain meta or not. If the patient was asymptomatic brain meta, why were you treat another systemic chemotherapy before whole brain.

Reply 4: The patient developed symptomatic brain metastases.

Changes in the text: We added the related contents. (see Page 5, line 12-13, highlighted dark yellow part).

Reviewer B

Ma et al reported a case with successful treatment using target therapy, radiotherapy and intrathecal chemotherapy in a patient of leptomeningeal metastasis with EGFR exon 20 insertion mutation.

Comment 1: However, it remains unclear which therapies have response to leptomeningeal metastasis. Only radiotherapy may work for leptomeningeal metastasis, and the conclusion in case report is not scientific.

Reply 1: Radical local treatment (WBRT with SIB) contributed to the good control of LM to a certain extent. Concurrent ITC with MTX 15mg, 6 times and Pemetrexed 10mg, once lead to CSF cytological negativity (12/19/2019). In the refractory LM setting, Pemetrexed 15mg 6 times delivered by intraventricular Ommaya reservoir with Anlotinib 10mg and Osimertinib 80mg daily make CSF cytology turn negative again (10/20/2020 and further extend the OS for 4 months.

Changes in the text: We supplemented the therapies contributed to the control of leptomeningeal metastasis. (see Page 11, line 7-10, 20-23, highlighted blue part).