

Dear Reviewers:

Thank you for your comments concerning our manuscript entitled “ Cerebral infarction and pulmonary embolism occurred in patient with NSCLC after applying bevacizumab combined with chemotherapy : A case report” (Manuscript NO.: 70587). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Responds to the reviewer’s comments:

Reviewer #1:

1. In the background section of Abstract, bevacizumab was modified to anti-VEGF monoclonal antibody.
2. In the case summary section of Abstract and History of present illness section of case presentation, evaluation of the curative effect was PR according to RECIST 1.1 standards.
3. In the history of present illness section of case presentation, endobronchial ultrasound-guided transbronchial lung biopsy was difficult to obtain and was not performed due to the presence of diffuse small lesions within the left lung.

4. Therapeutic purposes are added in the treatment section of case presentation, the patient developed distant metastatic disease and was unable to be cured; therefore, systemic treatment was the goal in his palliative care plan.

5. In the discussion section, non-infective endocarditis is modified to infiltrating endocarditis, the ECG and color doppler echocardiography of the discussed patient showed no obvious abnormalities. The advantages of MRI and CTA in the diagnosis of acute ischemic stroke were discussed (MRI of the head is advantageous in detecting early cerebral infarction as it can accurately assess brain tissues at risk of infarction and exclude certain diseases that exhibit stroke-like characteristics, such as tumors. MRI of the head using diffusion imaging is better than CT, and neurovascular imaging is very important for acute ischemic stroke. Magnetic resonance angiography (MRA) and CTA can be used to assess extracranial and intracranial large vessels in order to determine the presence of embolism or hypoxemia in ischemic stroke as well as the potential source of the flow.)

6. In the last paragraph of discussion section, pleural effusion of the left lung increased during maintenance therapy, indicating that the patient had disease progression at the time of these thromboembolic events.

7. In the discussion section, some further discussion are added on prophylactic anticoagulation in patients with advanced lung cancer around the available possible models for this and their applicability to lung cancer (The prediction models used for VTE risk assessment of cancer patients include the Khorana score, PROTECHT score, COMPASS-CAT score and CONKO score. These models have been developed and validated in patients with ambulatory lung cancer [17].

Khorana score is currently the most validated chemotherapy-related VTE risk assessment model, which is a reliable model based on five clinical and laboratory parameters. It is suitable for the VTE risk assessment of patients undergoing lung cancer chemotherapy and can be used to customize anticoagulant thrombosis prevention in such patients [18]. However, The Khorana score may not be sensitive enough to identify high-risk lung cancer patients. Verso et al has shown that the PROTECHT score is more advantageous than the Khorana score in distinguishing patients at high risk of VTE [19]. Meanwhile, COMPASS-CAT score is able to accurately distinguish high-risk and low-risk VTE patients [20]. It is more sensitive in predicting the VTE risk of lung cancer patients compared to that of the Khorana, PROTECHT, and CONKO models and may be more suitable for thrombosis prevention in lung cancer patients receiving anti-tumor therapy, however, further verification is needed.).

Review#2:

Comments: This is a good case report and will be a good addition to safety profile of bevacizumab. It is a well written manuscript and you have narrated the clinical history and findings in a comprehensive way. Case is discussed very well with good support of references.

Answer: Thanks for your comments.

Thank you and best regards

Yours sincerely

Liang Hong