Letter

FOLFOX-containing chemotherapy as a potential cause for pneumothorax

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To the Editor:

I read with great interest the article published by Yang et al. (1) entitled ‘pneumothorax after bevacizumab-containing chemotherapy: a case report’. The authors reported an interesting case of a patient with lung metastases from colorectal cancer who developed spontaneous pneumothorax 7 days after the second cycle of chemotherapy. The patient in that case was treated with a combination of bevacizumab and FOLFOXIRI (5-fluorouracil, leucovorin, oxaliplatin and irinotecan).

Yang et al. reasonably postulated that bevacizumab was the cause of the pneumothorax, based upon two reasons. Firstly, gastrointestinal perforations in patients with underlying malignancy had been reported following treatment with bevacizumab (2). Secondly, a large Phase III trial which looked into FOLFOXIRI as a first-line chemotherapy had not reported any cases of pneumothorax (3).

We recently encountered a lady with a newly diagnosed Stage III colon cancer. She presented with severe dyspnea and fever, 1 month after completing 12 cycles of FOLFOX (5-fluorouracil, leucovorin, oxaliplatin) chemotherapy regime. Her symptoms did not improve with intravenous (IV) antibiotics and she required high concentrations of oxygen to maintain saturations >94%. Computed tomography examination of (CT) chest revealed extensive fibrotic changes in the lungs. The rapid onset of fibrotic changes in the lungs had led us to believe that she had pulmonary fibrosis secondary to FOLFOX therapy and she was started on IV methylprednisolone. She responded remarkably well to the corticosteroid therapy and continued to improve clinically and radiologically. Interestingly, a repeat CT scan showed that she had developed a spontaneous pneumothorax. This subsequently resolved after 5 days of chest drainage. She was not a smoker and did not have a history of lung disease or pulmonary metastases. She was not treated with any other chemotherapeutic agents apart from the FOLFOX chemotherapy.

Based on the Title and Discussion in Yang et al’s article, it seems as though the authors had completely dismissed FOLFOXIRI as the cause of the pneumothorax. Both bevacizumab and FOLFOXIRI had never been reported to cause pneumothorax prior to 2011. I believe that it is not unreasonable to speculate that FOLFOXIRI could have been partially responsible for the development of pneumothorax in Yang et al’s case. There have been several case reports on FOLFOX or oxaliplatin-containing chemotherapy causing rapid and extensive fibrosis in the lungs.

It is important to consider that patients with severe lung fibrosis are at an increased risk of developing secondary spontaneous pneumothorax. Rupture of the lung due to underlying lung fibrosis may lead to a persistent defect in the visceral pleural and subsequently, a bronchopleural fistula may form (5). Yang et al. proposed that the main cause of spontaneous pneumothorax in their cases was due to the weakening of the local structures following tumor shrinkage and necrosis. Therefore, it will not be unreasonable to consider that treatment with FOLFOXIRI in their case could have potentially contributed to the development of pneumothorax. This is due to the fact that FOLFIRI may have also been involved in tumor regression and necrosis. We postulate that pneumothorax can develop following injury to the bronchial tree and pleural space from the underlying pulmonary fibrosis.

The authors rightly concluded that pneumothorax secondary to bevacizumab is rare. Since the article was published in 2011, there have only been three reported cases of bevacizumab-related pneumothorax in the literature (6–8). Nevertheless, we should be aware of the pulmonary complications secondary to chemotherapy as they are often associated with a significant risk of mortality and morbidity. A written consent has been obtained from the patient prior to submission of this letter.

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Conflict of interest statement

None declared.

References


