Long-term Survival Associated with Crizotinib in a Lung Cancer Patient with a Pulmonary Artery Embolism

Qian Shen, Xiao-Qi Dong, Jian-Ying Zhou

Department of Respiratory Diseases, The First Affiliated Hospital of College of Medicine, Zhejiang University, Hangzhou, Zhejiang 310003, China

To the Editor: Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a common complication in cancer patients, and the overall risk of VTE in patients with a malignancy was 7-fold as high as that for patients without cancer.[1] Herein, we report a case of long-term survival associated with crizotinib in an anaplastic lymphoma kinase (ALK)-positive lung cancer patient with a pulmonary artery embolism.

A 48-year-old female was referred to our hospital in September 2014 due to chest distress for 2 months. The patient had an unremarkable medical history and had no specific family history except for penicillin allergy. The chest computer tomography (CT) revealed soft-tissue shadows in the right upper lung [Figure 1a] with enlargement of the hilar and mediastinal lymph nodes. In addition, thrombosis was seen in both the superior vena cava and the right pulmonary artery [Figure 1b and 1c]. Magnetic resonance imaging of the brain demonstrated an abnormal signal in the left frontal lobes, indicating possible metastases. Initial laboratory workup revealed the followings:

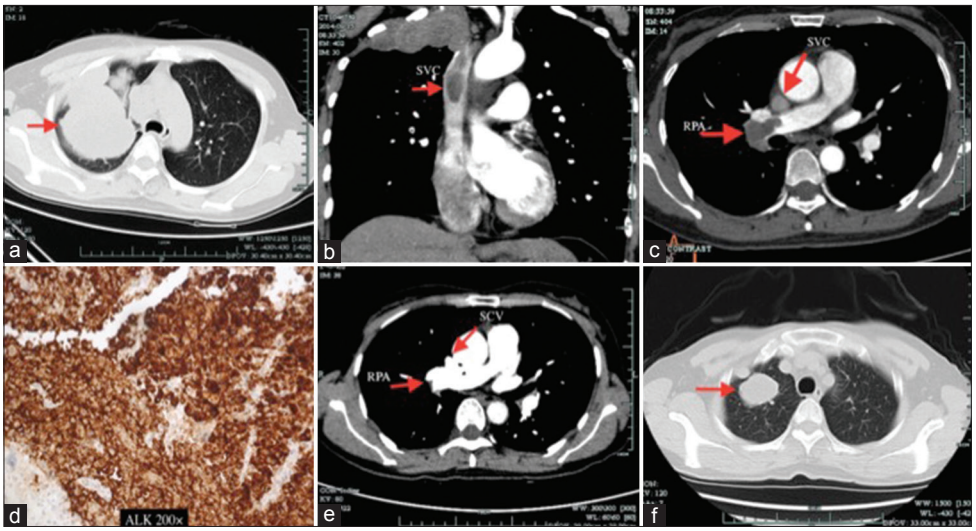

Figure 1: Chest CT revealed soft-tissue shadows in the right upper lung (arrow; a). CTA showed the thrombi in SVC (arrow; b). CTA showed the thrombi in the RPA (left arrow) and SVC (right arrow; c). ALK was positive with ICH/VANTANA (×200; d). CTA showed the thrombi in the pulmonary artery (left arrow) and superior vena cava (right arrow) disappeared after 1 year (e). Chest CT showed the lesion reduced after therapy for 3 years (f). CT: Computer tomography; CTA: CT angiography; RPA: Right pulmonary artery; SVC: Superior vena cava; ALK: Anaplastic lymphoma kinase.

white blood cell count, 11 × 10^9/L; D-dimer, 24,360 μg/L. Other biomarkers were normal.

Anticoagulation therapy with low-molecular-weight heparin (LMWH) was administered (4100 U i.h. q12h). Although the clinical diagnosis was lung tumor, anticoagulation treatment was stopped 12 h before pulmonary puncture biopsy. The pathological

Access this article online	
Quick Response Code:	Website: www.cmj.org
	DOI: 10.4103/0366-6999.221265

Address for correspondence: Dr. Jian-Ying Zhou, Department of Respiratory Diseases, The First Affiliated Hospital of College of Medicine, Zhejiang University, Hangzhou, Zhejiang 310003, China
E-Mail: zjyhz@zju.edu.cn

Received: 11-08-2017 **Edited by:** Ning-Ning Wang
How to cite this article: Shen Q, Dong XQ, Zhou JY. Long-term Survival Associated with Crizotinib in a Lung Cancer Patient with a Pulmonary Artery Embolism. Chin Med J 2018;131:111-2.

diagnosis confirmed the presence of an adenocarcinoma; the immunohistochemical results were positive for both thyroid transcription factor-1 and Ki-67 and negative for both p63 and wild-type epidermal growth factor receptor (EGFR), while the ALK was positive with ICH/VANTANA [Figure 1d]. Crizotinib was used as an initial therapy (250 mg p.o. bid), combined with the anticoagulation treatment with LMWH.

After 2 months of therapy, CT demonstrated that the thrombi in the right pulmonary artery and superior vena cava were notably reduced. According to the guidelines, the LMWH was used for 3 months; the index of the coagulation function returned to normal, and LMWH was replaced by warfarin (3 mg p.o. qd). One year later, the CT angiography revealed that the thrombi in the right pulmonary artery and superior vena cava had completely disappeared [Figure 1e], and the lesion was smaller than before. The warfarin treatment was stopped after one and half years, and no thrombosis-related events have occurred to date. Evaluation of crizotinib as a first-line therapy showed a partial response and disappearance of intracranial lesions. The duration of progression-free survival was 23 months. In September 2016, the intracranial metastasis progressed and was treated with a gamma knife. The patient was on consolidation therapy with oral crizotinib and remained stable until October 18, 2017, during the follow-up period [Figure 1f].

Patients with lung cancer are at a particularly high risk for VTE when compared to patients with other tumor types and have a worse prognosis.[2] The current article suggests that a K-ras gene mutation was involved in the pathophysiology of tumor-associated thrombosis;[3] Lee *et al.*[4] suggested that EGFR mutations and ALK rearrangements were not associated with VTE development. To treat the cancer-associated thrombosis, the favored option is LMWH.[5] The therapy using crizotinib was effective for the patient and led to a satisfactory quality of life and prolonged survival time. This case indicates the possibility that targeted therapy for adenocarcinoma-driven genes combined with anticoagulant therapy can be one of the protocols to improve the prognosis of advanced lung-cancer patients with thromboses.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s)/patient's guardians has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients/patient's guardians understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Blom JW, Doggen CJ, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. JAMA 2005;293:715-22. doi: 10.1001/jama.293.6.715.
2. Kourelis TV, Wysokinska EM, Wang Y, Yang P, Mansfield AS, Tafur AJ, *et al.* Early venous thromboembolic events are associated with worse prognosis in patients with lung cancer. Lung Cancer 2014;86:358-62. doi: 10.1016/j.lungcan.2014.10.003.
3. Corrales-Rodriguez L, Soulières D, Weng X, Tehfe M, Florescu M, Blais N, *et al.* Mutations in NSCLC and their link with lung cancer-associated thrombosis: A case-control study. Thromb Res 2014;133:48-51. doi: 10.1016/j.thromres.2013.10.042.
4. Lee YG, Kim I, Lee E, Bang SM, Kang CH, Kim YT, *et al.* Risk factors and prognostic impact of venous thromboembolism in Asian patients with non-small cell lung cancer. Thromb Haemost 2014;111:1112-20. doi: 10.1160/TH13-11-0956.
5. Easaw JC, Shea-Budgell MA, Wu CM, Czaykowski PM, Kassis J, Kuehl B, *et al.* Canadian consensus recommendations on the management of venous thromboembolism in patients with cancer. Part 2: Treatment. Curr Oncol 2015;22:144-55. doi: 10.3747/co.22.2587.