Acute limb ischemia of the lower extremity associated with left upper lobe surgery for primary lung cancer

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ABSTRACT
Thrombosis formation in the pulmonary vein stump after pulmonary lobectomy has recently been reported to be an extremely rare cause of arterial embolism. We herein report the first case series of acute limb ischemia encountered after video-assisted thoracoscopic left upper lobectomy or left upper division segmentectomy for primary lung cancer. The patients underwent embolectomy, and their perioperative courses were uneventful. It should be recognized that the pulmonary vein stump can cause acute limb ischemia after pulmonary lobectomy. (J Vasc Surg Cases and Innovative Techniques 2018;4:83-6.)

Key words: Multidetector computed tomography; Perioperative; Left upper lobectomy

Acute limb ischemia (ALI) can result from various causes, and emboli originate from the heart in >80% of cases. Thrombosis formation in the pulmonary vein (PV) stump after pulmonary lobectomy has recently been reported as an extremely rare cause of acute arterial embolism. To our knowledge, however, no cases of ALI of the lower extremities encountered after surgery for primary lung cancer have been reported in the English literature.

We herein report the first case series of ALI encountered after left upper lobectomy (LUL) or left upper division segmentectomy for primary lung cancer. The patients provided written consent for the publication of the case reports.

CASE REPORTS

Case 1. A 64-year-old man underwent video-assisted thoracoscopic left upper division segmentectomy. The pathologic stage of the lung cancer was IA (T1bN0M0). He had a history of hypertension and smoking. Three days after surgery, he complained of severe intermittent claudication on his left calf but did not report any paresthesia, paralysis, or rest pain. On Doppler flowmetry, the posterior tibial and dorsal pedal arteries were detected. Multidetector computed tomography (MDCT) showed occlusion of the left popliteal artery (Fig 1, A). MDCT also showed a remnant of the long stump of the left superior PV (LSPV) without thrombosis (Fig 1, B and C). Subsequently, urgent embolectomy was performed with local anesthesia. His perioperative course was uneventful, and he was discharged with a continuation of anticoagulant therapy (ACT) with warfarin. A pathologic examination revealed that the explanted thrombus was composed of aggregated red blood cells and fibrin-thrombocytic components with no involvement of any mural components of blood vessels or carcinoma cells.

Case 2. A 68-year-old man underwent video-assisted thoracoscopic LUL for lung cancer (pT1aN1M0; pathologic stage IIA). He had a history of smoking. Three days after surgery, he complained of hypoesthesia and paresis in both legs. On Doppler flowmetry, neither the posterior tibial nor dorsal pedal arteries were detected. MDCT showed a remnant stump of the LSPV without thrombosis (Fig 2, A), and his plasma D-dimer level had increased to 4.0 μg/mL. MDCT also showed occlusion of the terminal aorta and bilateral common iliac artery (Fig 2, B). Subsequently, emergent embolectomy was performed with direct oral anticoagulant (DOAC). Postoperative MDCT showed that no stenotic lesions remained (Fig 2, C).

Case 3. A 72-year-old man underwent video-assisted thoracoscopic LUL for lung cancer (pT1bN0M0; pathologic stage IA). He had a history of early gastric cancer. One year after surgery, contrast-enhanced computed tomography (CECT) revealed thrombosis at the remnant of the stump of the LSPV, and his plasma D-dimer level had increased to 3.5 μg/mL. Subsequently, ACT with DOAC was started. As the thrombus on LSPV disappeared after ACT had been administered for about 1.5 months, ACT was discontinued. However, 17 months after LUL, CECT revealed recurrent thrombosis at the remnant stump of the LSPV (Fig 3, A), so ACT was restarted. At the same time, he became aware of severe intermittent claudication on his left calf, and ultrasound examination showed occlusion of the left popliteal artery. Urgent embolectomy was performed with local...
anesthesia, and intraoperative angiography showed occlusion of the left popliteal artery (Fig 3, B). His perioperative course was uneventful, and he was discharged with continuation of ACT with DOAC.

DISCUSSION

ALI is any sudden decrease in limb perfusion causing a potential threat to limb viability. It can be due to various causes, such as atrial fibrillation, old myocardial infarction, cardiac tumor, atheroembolism, aortic aneurysm, arteriosclerosis, and a hypercoagulable state.1 These patients had no history of heart disease, such as atrial fibrillation, and lacked an identifiable embolic source from the aorta to the peripheral artery on MDCT. Regarding the pathologic findings, no mural components of blood vessels were found to be involved in the explanted thrombus. Xiromeritis et al11 collected 104 cases of acute arterial obstruction by tumor embolus and reported that the major origins of tumor embolus were primary or metastatic lung cancer invading the PV or left atrium and spreading to the systemic circulation. Furthermore, 80% of arterial embolisms from lung cancer were caused by manipulation during the perioperative period.12 However, these patients suffered from small lung cancer (T1: tumor size ≤30 mm), and the explanted embolus included no neoplastic cells.

In 1989, Seki et al13 reported the first case of left femoral artery thrombosis after LUL in the Japanese literature and speculated that the thrombus had originated from the PV stump, although PV thrombus was not proved. Recently, cases of arterial embolism after pneumectomy have been attracting attention. Ohtaka et al14 evaluated the frequency of thrombus formation in the PV stump in 193 patients after pulmonary lobectomy. All of the patients with thrombus had undergone LUL, and 13.5% of those who had undergone LUL developed thrombus in the PV stump. PV thrombus was confirmed on the basis of the imaging findings of one of these cases. Because of the lack of any other obvious causes of embolism, we also speculated that the thrombus that formed on the LSPV caused ALI in the other cases.

Thrombosis formation in the PV stump after pneumectomy has recently been reported as an extremely rare cause of acute arterial embolism.2-10 Including the current cases, most of these patients underwent LUL, and two patients (17%) underwent left upper division segmentectomy. Although the brain, kidney, and spleen are frequent sites of embolism, the limbs are relatively rarely afflicted by embolism, and these are the first cases of ALI caused by PV thrombus after pneumectomy for primary lung cancer to be reported in English. On limiting our evaluation to the 60 patients undergoing

Fig 1. Computed tomography (CT) images obtained at the onset of acute limb ischemia (ALI). A, CT angiography image of lower extremities. The arrow indicates the short-segment occlusion of left popliteal artery. B, CT angiography showing the remnants of the long stump of the left superior pulmonary vein (LSPV). C, Axial image showing the stump of the LSPV. There was no thrombus in the stump of the LSPV. The arrow indicates the stump of the LSPV.
LUL for lung cancer in our institute from April 2012 to March 2017, 2 cases (3.3%) were complicated with ALI postoperatively. This incidence might suggest that there were more unreported or unrecognized cases complicated by ALI due to PV thrombus. In nine cases (75%), PV thrombus was confirmed in an imaging study. The duration from lung resection to arterial embolism ranged from 2 days to 7 years (median time, 18 days), and after limiting our evaluation to the cases without confirmation of PV thrombosis, the average duration was <4 days. PV thrombosis may start as soon as lung resection has been performed, as its development depends on the morphology of the PV stump. Therefore, although the postoperative follow-up of lung cancer is usually performed using plain computed tomography (CT), CECT should be performed at least once for LUL relatively early after surgery, although there is no consensus concerning when CECT should be performed. To avoid missing early-onset embolism cases. CECT should be performed within a few days after LUL, although with this timing, small, slow-growing thrombi may be missed. Intraoperative or postoperative transesophageal echocardiography may also be helpful for screening for PV thrombus. Blood tests such as D-dimer or fibrinogen/fibrin degradation products might also be useful for screening for thrombosis, although the D-dimer and fibrinogen/fibrin degradation product levels in all patients with PV thrombus were within the normal reference ranges at 2 years of follow-up.14

Although endovascular intervention may expand the range of therapeutic options for ALI, we elected to perform embolectomy because the patients seemed to suffer from embolism. The patients recovered, and their postoperative courses were uneventful. Ohtaka et al14,15 pointed out that the LSPV stump is significantly longer than the stumps of other veins and suspected that this relatively long PV stump might have contributed to thrombus formation. The lengths of the PV stumps in these cases measured using postoperative CT were 27 mm, 17 mm, and 20 mm, lengths that were equivalent to Ohtaka’s measurements. Dividing the LSPV in the pericardium to form a shorter stump might reduce the risk for PV thrombus. However, it might not be practical to perform such a procedure for all patients because of its complicated and invasive nature. Practically, ACT seems to be the only prophylactic treatment for PV thrombus. As in most previous cases, these patients were all treated with ACT. Of note, whereas the PV thrombosis of case 3 disappeared with ACT, it recurred on ACT cessation. This suggests that patients with PV thrombus should receive lifetime ACT. Although there is no consensus concerning how long ACT should be performed, we plan to continue ACT permanently, as long as it is possible, because recurrence can cause fatal cerebral or renal embolism.

*Fig 2.* Computed tomography (CT) images obtained at the onset of acute limb ischemia (ALI) and after embolectomy. **A,** Axial image showing the stump of the left superior pulmonary vein (LSPV). There was no thrombus in the stump of the LSPV. The arrow indicates the stump of the LSPV. **B,** CT angiography image of lower extremities at the onset of ALI. The arrow indicates the short-segment occlusion of terminal aorta and bilateral common iliac arteries. **C,** CT angiography image of lower extremities after embolectomy.
CONCLUSIONS

We herein describe the first case series of ALI encountered after pneumectomy for primary lung cancer. It should be recognized that the PV stump after pulmonary lobectomy can cause ALI.

The authors thank Dr Brian T. Quinn for providing critical comments on the manuscript.

REFERENCES

1. O’Connell JB, Quiñones-Baldrich WJ. Proper evaluation and management of acute embolic versus thrombotic limb ischemia. Semin Vasc Surg 2009;22:10-6.

2. Asai K, Mochizuki T, Iizuka S, Momiki S, Suzuki K. Pulmonary vein stump thrombus: an early complication following upper division segmentectomy of the left lung. Gen Thorac Cardiovasc Surg 2014;62:244-7.

3. Asteriou C, Barbetakis N, Efstathiou A, Kleontas A, Tsilikas C. Renal artery thrombosis following lobectomy for lung cancer. Case Rep Oncol 2010;3:208-11.

4. Ichimura H, Ozawa Y, Nishina H, Shiotani S. Thrombus formation in the pulmonary vein stump after left upper lobectomy: a report of four cases. Ann Thorac Cardiovasc Surg 2014;20(Supp1):613-6.

5. Manabe S, Oshima Y, Nakano M, Fujii T, Maehara T, Nitta K, et al. Renal infarction in a patient with pulmonary vein thrombosis after left upper lobectomy. Case Rep Nephrol Dial 2014;4:103-8.

6. Schwalm S, Ward RP, Spencer KT. Transient ischemic attack in a patient with pulmonary vein thrombosis after left upper lobectomy for squamous cell lung cancer. J Am Soc Echocardiogr 2004;17:487-8.

7. Ohira S, Doi K, Okawa K, Matsushiro T, Yaku H. Surgical removal of extensive left pulmonary vein stump thrombus after pulmonary lobectomy: a rare cause of acute cerebral embolism. Ann Thorac Surg 2013;96:e135-6.

8. Nagaoka E, Yano M, Sugano T, Miyamoto T. Thrombus in the left superior pulmonary vein after left upper pulmonary lobectomy. J Thorac Cardiovasc Surg 2008;135:709-10.

9. Ohtaka K, Hida Y, Kaga K, Iimura Y, Shina N, Muto J, et al. Pulmonary vein thrombosis after video-assisted thoracoscopic left upper lobectomy. J Thorac Cardiovasc Surg 2012;143:63-5.

10. Gual-Capllonch F, Teis A, Palomeras E. Pulmonary vein spontaneous echocontrast and stroke after pulmonary lobectomy. J Clin Ultrasound 2013;41:321-2.

11. Xiromeritis N, Klonaris C, Papas S, Valsamis M, Bastounis E. Recurrent peripheral arterial embolism from pulmonary cancer. Case report and review of the literature. Int Angiol 2000;19:79-83.

12. Gómez JR, Vañó J, Luengo L, Escuder J, Castellote M, Ros S, et al. Tumor embolism after pneumonectomy for primary pulmonary neoplasia. Ann Vasc Surg 1995;9:199-203.

13. Seki M, Endo M, Kidani M, Kobayashi H, Sato H, Noto T. A rare case of left atrial thrombus after left upper pulmonary lobectomy. [in Japanese]. Nihon Kyobu Geka Gakkai Zassi 1989;37:1371-5.

14. Ohtaka K, Hida Y, Kaga K, Kato T, Muto J, Nakada-Kubota R, et al. Thrombosis in the pulmonary vein stump after left upper lobectomy as a possible cause of cerebral infarction. Ann Thorac Surg 2013;95:1924-8.

15. Ohtaka K, Hida Y, Kaga K, Takahashi Y, Kawase H, Hayama S, et al. Left upper lobectomy can be a risk factor for thrombosis in the pulmonary vein stump. J Cardiothorac Surg 2014;9:5.

Submitted Nov 9, 2017; accepted Dec 21, 2017.