Cerebral Embolism Caused by Thrombus in the Pulmonary Vein Stump after Left Lower Lobectomy: A Case Report and Literature Review

Abstract:
Cerebral embolism after left upper lobectomy caused by a thrombus in the pulmonary vein stump (PVS) is a serious complication. However, it is unclear if cerebral embolism can develop after other types of lobectomy. We present a case of a 68-year-old man with cerebral embolism after left lower lobectomy with a longer PVS than normal. There were no clinically suspected sources for the thrombus except for the PVS. This thrombus seemed to have formed in the PVS. The endovascularly removed thrombus contained scattered nuclear debris around neutrophils, suggesting a physiological response caused by tissue injury.

Key words: stroke, endovascular thrombectomy, lung cancer

Introduction
Cerebral embolism after lung cancer surgery is a rare and serious complication, developing in approximately 0.4% of cases (1). However, it is a serious complication. Cerebral embolism develops after left upper lobectomy (LUL), which consistently leaves a longer pulmonary vein stump (PVS) than other types of lobectomy. It has been reported that a thrombus in the vein stump can cause cerebral embolism (1, 2). In contrast, cerebral embolism caused by a thrombus in the vein stump after left lower lobectomy (LLL) has not been reported to our knowledge. Although some theories about the mechanism of thrombus formation have been proposed, this has not been investigated in detail.

We herein report the case of a patient with cerebral embolism after LLL with a longer PVS than normal.

Case Report
A 68-year-old man was referred to the Department of General Thoracic Surgery of our hospital because of an abnormal shadow on chest computed tomography (CT). His medical history included hypertension and end-stage renal failure owing to hypertensive nephrosclerosis that had been treated with hemodialysis. He had a smoking history of 20 pack-years. He had no history of cerebrovascular disease, atrial fibrillation (AF), or heart disease. Chest CT to investigate the cause of his chronic anemia incidentally detected two part-solid ground-glass nodules (13 mm in S8 and 5 mm in S9). The ground-glass nodules grew slightly during the follow-up period, which led to a diagnosis of lung cancer [cT1bN0M0-stage IA as defined by the 7th Edition of TNM classification (TNM7) of lung cancer] (3). Video-assisted thoracoscopic LLL was performed three years and two months after his first visit. The pathological diagnosis of...
both tumors was lepidic adenocarcinoma (pT1bN0M0-stage IA as defined by the TNM7 of lung cancer) (3).

At 27 hours after the surgery, the patient was referred to the Department of Cerebrovascular Medicine with consciousness disturbance [Glasgow Coma Scale, 8 points (E2V2M4)], conjugate deviation of the eyes to the left, right complete hemiplegia, and mixed aphasia. The patient’s score on the National Institutes of Health Stroke Scale (NIHSS) was 24. Blood tests showed that his brain natriuretic peptide level was 124.6 pg/mL (normal, <18.4 pg/mL), and the D-dimer level was 2.6 μg/mL (normal, <1.0 pg/mL). Electrocardiography displayed a sinus rhythm. Carotid ultrasonography displayed no meaningful stenosis in the bilateral carotid artery. Head CT displayed a hyperdense middle cerebral artery (MCA) sign, which suggested acute middle cerebral artery infarction (Fig. 1A). Because he was a postoperative patient, tissue plasminogen activator was not administered. On cerebral angiography, the left MCA was found to be interrupted in the middle of the horizontal region, and the distal artery was not visible (Fig. 1C). The thrombus was endovascularly removed using the Penumbra System, which is a mechanical thrombectomy device, and successful recanalization (thrombolysis on the cerebral infarction scale, 2b) was achieved (Fig. 1D).

The endovascularly removed thrombus was subjected to a histopathological analysis. The thrombus consisted of two parts: the first part contained many neutrophils trapped within a dense laminar fibrin network, together with red blood cells (RBCs) and platelets (Fig. 2A and B). Nuclear debris was scattered around the neutrophils (Fig. 2C). The second one contained many RBCs entrapped within a subtle mesh-like fibrin network (Fig. 2D). Platelets were also trapped within the fibrin network, with fewer neutrophils. The thrombus structure was more similar to that of a freshly formed thrombus than an organized longstanding thrombus. There were no cholesterol clefts or foamy cells, suggesting that the thrombus had not been formed by atherosclerosis.

Electrocardiographic monitoring displayed no AF after
surgery, and transthoracic echocardiography, transesophageal echocardiography, and venous ultrasonography displayed no thrombus. Contrast-enhanced chest CT showed a left inferior pulmonary vein (LIPV) stump, with a length of 1.4 cm, in which no thrombus was found (Fig. 3). There were no other suspected sources; however, anticoagulant therapy with heparin was started owing to the possibility of a cerebral embolism. On the day after thrombus removal, the neurological function was dramatically improved (NIHSS score, 4 points). Magnetic resonance imaging displayed a high-signal intensity area in the left basal ganglion on fluid-attenuated inversion recovery (Fig. 1B) and no low-intensity area on T2-star-weighted imaging. Magnetic resonance angiography demonstrated that the left MCA did not have any interruptions. Three days after thrombus removal, his NIHSS score was 0. The patient had no major complications, was discharged from our hospital, and continued taking warfarin (3 mg/day). The patient has since been followed up as an outpatient and has not experienced a recurrence of a cerebral embolism for three years and five months since the last episode.

Discussion

This is a rare case of cerebral embolism after lung cancer surgery. The following are the known causes of embolic stroke: cardiogenic, arteriogenic, paradoxical, and cancer-associated embolisms (4). In our present case, cerebral embolism was presumably caused by a thrombus in the PVS because there were no other suspected sources, and electrocardiographic monitoring detected no AF after surgery. Our case suggested that two factors contributed to thrombus formation in the PVS: length and inflammation.

Although eight cases of cerebral embolism caused by a
Figure 3. Left inferior pulmonary vein stump after left lower lobectomy. (A, B) Contrast-enhanced chest computed tomography showed a left inferior pulmonary vein stump with a length of 1.4 cm (arrow). No thrombus remained in the left inferior pulmonary vein stump. The arrowhead indicates the right atrium.

Table. Summary of Patients with Cerebral Embolism Caused by a Thrombus in the Pulmonary Vein Stump after Lobectomy.

<table>
<thead>
<tr>
<th>Ref</th>
<th>Age</th>
<th>Sex</th>
<th>Type of lobectomy</th>
<th>Postoperative period</th>
<th>Risk factors of cerebrovascular disease</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>66</td>
<td>M</td>
<td>LUL</td>
<td>18 months</td>
<td>Smoking history, cancer*</td>
<td>Conservative therapy</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>M</td>
<td>LUL</td>
<td>7 years</td>
<td>HL, smoking history</td>
<td>Anticoagulation therapy</td>
</tr>
<tr>
<td>7</td>
<td>46</td>
<td>F</td>
<td>LUL</td>
<td>6 months</td>
<td>Not reported</td>
<td>Surgical removal of pulmonary vein thrombus, anticoagulation therapy</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>M</td>
<td>LUL</td>
<td>2 days</td>
<td>Smoking history</td>
<td>Endovascular removal of thrombus, anticoagulation therapy</td>
</tr>
<tr>
<td>1</td>
<td>70</td>
<td>M</td>
<td>LUL</td>
<td>1 day</td>
<td>HT, DM, HL</td>
<td>Anticoagulation therapy</td>
</tr>
<tr>
<td>1</td>
<td>68</td>
<td>M</td>
<td>LUL</td>
<td>9 days</td>
<td>HL</td>
<td>Not reported</td>
</tr>
<tr>
<td>1</td>
<td>55</td>
<td>M</td>
<td>LUL</td>
<td>3 days</td>
<td>None</td>
<td>Not reported</td>
</tr>
<tr>
<td>9</td>
<td>77</td>
<td>F</td>
<td>LUL</td>
<td>8 days</td>
<td>Not reported</td>
<td>Anticoagulation therapy</td>
</tr>
<tr>
<td>This study</td>
<td>68</td>
<td>M</td>
<td>LLL</td>
<td>1 day</td>
<td>HT, DM, CKD, smoking history</td>
<td>Endovascular removal of thrombus, anticoagulation therapy</td>
</tr>
</tbody>
</table>

(*) maxillary, oropharyngeal, tongue cancer.


Thrombus in the PVS have been reported to date (Table) (1, 5-9), all of these cases occurred after LUL. This is because LUL consistently leaves a longer PVS (median length of 1.7 cm) than other types of lobectomy, allowing blood congestion to occur easily (2). In contrast, the median length of the LIPV stump in LLL is 0.5 cm, and blood congestion is less likely to occur (2). In our case, the LIPV stump was 1.4 cm in length, which is longer than the median length and appears to have been one of the causes of thrombogenesis in this patient.

The dominant view is that blood congestion is the main cause of thrombogenesis (10, 11). Regarding AF, which causes thrombogenesis by blood congestion, it is widely known that the risk of thromboembolic complications is very low when cardioversion is performed without anticoagulants within 48 hours of AF onset (12). This means that a thrombus that causes embolic complications is seldom formed by only blood congestion within 48 hours of AF onset. Our patient developed a cerebral embolism 27 hours after lobectomy, and in some patients, cerebral embolisms have been reported to develop in the early postoperative period, which suggests that not only blood congestion but other factors may also contribute to thrombogenesis of the vein stump.

The pathological findings of the removed thrombus suggested that inflammation at the PVS also contributed to
thrombus formation. The first part of the removed intracerebrovascular thrombus contained many neutrophils trapped in a dense laminar fibrin network, together with RBCs and platelets. The thrombus consisted of fewer RBCs and more white blood cells than the typical thrombus (13-15). In this case, platelet aggregation and leukocyte recruitment at the thrombus suggested endothelial injury at the PVS. Thrombus formation was likely to be caused by the physiological response to tissue injury after surgery, and a recent study suggested that immune cells, such as neutrophils, play an important role in thrombus formation (16). The second part of the thrombus contained fewer white blood cells than the first part and included many RBCs and fibrins, which are typically seen in thrombi caused by blood congestion (13-15). This part of the thrombus is therefore likely to have been formed by blood congestion.

No method for preventing cerebral embolism after lobectomy has been established. We reported a case of thrombus reformation in the PVS after cerebral embolism after LUL for lung cancer. Thrombus reformation was seen even though the patient had already been treated with preventative antiplatelet therapy (17). Anticoagulation therapy should be considered in order to prevent thrombus formation in the PVS. However, as bleeding complications after lobectomies can be fatal, administering anticoagulation therapy to all patients after lobectomy for the prevention of cerebral embolism is controversial (1). Anticoagulation therapy should therefore be considered for only high-risk patients. These patients may be selected according to the CHADS2/CHADS2-VASc score (18, 19), which is a criterion for cardiogenic cerebral embolism. This score may also be used to predict the risk of cerebral embolism after lobectomy, as blood congestion is also associated with it.

The characteristics of PVS seem to be important for estimating the risk of cerebral embolism after lobectomy. As previous studies and our case suggested that a longer PVS may contribute to thrombus formation (2), anticoagulation therapy should be considered in patients with a longer PVS, not limited to LUL. In addition, the choice of operative procedure may also be important for estimating the risk of cerebral embolism after lobectomy. The inflammatory response to endothelial injury also seems to contribute to thrombus formation (11, 16). The degree of inflammation may be affected by the operative procedure, such as thoracotomy versus thoracoscopic surgery and automatic versus manual sutures. However, such factors have never been investigated thoroughly. Further studies are expected to address these issues.

In conclusion, this is the first case of a cerebral embolism presumably caused by a thrombus in the PVS after LLL for lung cancer. The thrombus might have been formed in the LIPV stump due to the relatively long PVS and tissue injury caused by surgery in the early postoperative period.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

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