Cerebral infarction after drug-eluting bead bronchial arterial chemoembolization due to the mechanical force-mediated opening of an errant passage

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To the Editor: Drug-eluting bead bronchial arterial chemoembolization (DEB-BACE) has been proven to be a feasible and well-tolerated treatment option for patients with non-small cell lung cancer (NSCLC) who are ineligible for or refuse to receive standard chemotherapy. Here, we report a rare complication of multiple cerebral embolic infarcts, mainly in the posterior cerebral circulation, in a patient with squamous cell lung cancer who was performed with DEB-BACE. To our knowledge, this complication has rarely been reported in patients with NSCLC undergoing DEB-BACE. Approval was obtained from our Institutional Review Board and patient for the publication of this case report.

A 78-year-old woman with primary squamous cell lung cancer (cT4N0M0, stage IIIA) without a tumor driver gene mutation presented to our clinic and had not undergone chemotherapy due to a poor Karnofsky performance score. The patient has provided consent to receive DEB-BACE. Selective bronchial angiography showed that the left bronchial artery had a common origin from the descending aorta, with slight tortuousness and significant distal tumor staining. The bronchial arteriogram also clearly revealed the absence of collateral circulation between the bronchial artery and other systemic arterial vessels and the absence of a shunt between the bronchial artery and pulmonary vessels [Figure 1A]. The left bronchial artery was embolized using Embosphere (300-500 µm, Hengrui Medicine, Jiangsu, China) that had been preincubated with nedaplatin (Xiansheng Medicine, Jiangsu, China) 20 mg for 30 min. During the embolization procedure, each Embosphere injection induced a cough with bloody sputum. We stopped the injection procedure due to the worsening of the symptoms after the injection of one-third of the planned dose. The patient immediately exhibited aphasia, dyskinesia, and right-side motor weakness; she was transferred to the intensive care unit (ICU) and was intubated. A brain

computed tomography (CT) scan showed multifocal hypodensities in the cerebellum, and the condition in the left cerebellum was worse 6 h later [Figure 1B]. A brain magnetic resonance imaging (MRI) showed multifocal infarcts in the cerebellum and cerebrum after 5 days [Figures 1C and 1D]. The patient became comatose (Glasgow Coma Scale 6) after 12 h. She was treated with intravenous hydration, strict glucose control, and anti-platelet therapy. Continuous telemetry did not reveal cardiac arrhythmia. Her mental status returned to the baseline after 36 h, and she was transferred to a normal ward. After 4 weeks, the motor weakness improved, and myodynamia improved to Grade III; however, aphasia persisted. The patient is currently continuing to receive rehabilitation therapy.

Severe neurological complications due to BACE with microspheres or polyvinyl acetate (PVA) include spinal artery and cerebrovascular embolism. The patient described here is a rare patient diagnosed with squamous cell lung cancer to experience embolic strokes after DEB-BACE. As shown in the study by Boushy *et al*, ^[2] dogs undergoing embolization with glass microspheres smaller than 200 μm develop hind leg paralysis. Experimental studies revealed a bronchopulmonary anastomosis of 25 to 50 μm in healthy human lungs. ^[3] Therefore, the use of microsphere particles larger than 300 μm does not provoke any off-target embolization when administered through the normal microcirculation.

From the perspective of vascular anatomy, a pathway from the bronchial artery to the intracranial artery should exist in this case. Knight *et al*^[4] proposed five possible mechanisms, including (a) the presence of collateral circulation between the bronchial artery and systemic arterial vessels (vertebral arteries), (b) an arterial-arterial shunt between the bronchial and vertebral arteries at the level of the lung, (c) an anomalous origin of the vertebral arteries, (d) an intracardiac shunt (the most common type is the right-to-left shunt),

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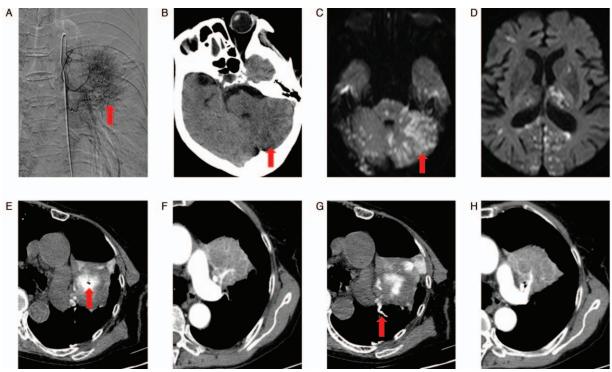


Figure 1: Related images of this patient before and after the DEB-BACE procedure. (A) The left bronchial angiography showed a tortuous artery and significant distal tumor staining. The red arrow shows the lesion. (B) A brain CT scan showed multifocal hypodensities (darker area) in the left cerebellum 6 h after DEB-BACE. The red arrow shows the lesion. (C) Diffusion-weighted MRI showed multiple infarcted areas (white dots) in the cerebellum 5 days after DEB-BACE. The red arrow shows the lesion. (D) Diffusion-weighted MRI showed multiple infarcted areas (white dots) in the cerebrum 5 days after DEB-BACE. (E) Pairs of new cavities appeared in the center of the lesion 6 h after DEB-BACE. The red arrow shows the cavity. (F) This image was captured 20 days before the DEB-BACE procedure, and no cavity was observed in the lesion. (G) A new vessel silhouette appeared 6 h after DEB-BACE. The red arrow shows the vessel silhouette. (H) This image was captured 20 days before the DEB-BACE procedure, showing the left trunk of the pulmonary artery. CT: Computed tomography; DEB-BACE: Drug-eluting bead bronchial arterial chemoembolization; MRI: Magnetic resonance imaging.

and (e) shunting between the pulmonary arterial and pulmonary venous microcirculation. However, in our patient, we were able to exclude all the aforementioned possibilities, based on the evidence obtained from the bronchial artery angiogram and echocardiogram.

Here, we would like to highlight a phenomenon that occurred during the embolization procedure. This patient coughed and produced bloody phlegm each time the microspheres were injected, and she had never coughed up bloody phlegm before. A clear causal relationship exists between the injection process and the cough. The chest CT scan has taken 6 h after symptom onset, which showed some unusual phenomena compared with the chest CT that took 20 days before the procedure. First, pairs of cavities appeared in the center of the lesion [Figure 1E and 1F]. Second, high-density areas in the lesion were observed due to the stasis of contrast material, and a vessel silhouette emerged, which was presumed to be the pulmonary vein based on the pulmonary artery image captured before the procedure [Figure 1G and 1H]. Thus, we hypothesized that lung cancer led to hypertrophy, tortuous bronchial arteries, and the possible formation of multiple unvisualized anastomoses between the bronchial arteries and pulmonary veins or a latent vessel loop that functioned as an arteriovenous shunt. [5] During the injection, mechanical forces disrupted the unvisualized anastomoses or loop, which opened errant emboli passages through the pulmonary vein and allowed off-target embolization of the intracranial arteries. We recommend an increase in the injection pressure during the bronchial arterial angiography to 150 pounds per square inch (psi) or higher to mimic the mechanical forces (in this case was 100 psi), gentle management and being alert to coughing, particularly coughing with bloody sputum, during the embolization procedure, to prevent or avoid this potentially fatal complication.

Conflicts of interest

None.

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