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Carotid Artery Stenosis after Radiation Therapy in a Patient with Lung Cancer: A Case Report and Literature Review

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Abstract

We reported a case of carotid artery stenosis with stroke symptoms detected in a patient with lung cancer after radiotherapy. The patient was a 58-year-old male with a complaint of "a single episode of temporary amaurosis in the right eye for 10 minutes". The clinical diagnosis at admission, after consideration of the patient's age, medical history, and auxiliary examination results, was as follows: lung cancer; right common carotid artery stenosis; left common carotid artery stenosis; left vertebral artery stenosis; and right subclavian artery occlusion with right subclavian steal syndrome (Grade 3). Carotid angioplasty and stenting (CAS) were subsequently performed. During the 6-month follow-up, we observed no episode of temporary vision loss or other signs of stroke. Clinicians should pay great attention to delayed radiation-induced carotid stenosis. It is recommended that patients with a history of radiotherapy should undergo regular color Doppler ultrasound examination of the cervical region to diagnose, prevent, and treat RICS in an expedient fashion. This approach should improve survival rate and quality of life.

CASE REPORT

INTRODUCTION

Injury to blood vessels after radiation therapy remains a clinical problem in the field of radiation oncology (Weintraub *et al.* 2010). Patients with various malignancies are at risk of developing vascular diseases after radiation therapy (Russell *et al.* 2009). Radiation-induced carotid stenosis (RICS) is one such vascular disease encountered as a late complication of radiation therapy in patients with head or neck carcinoma (Chang *et al.* 2009; Xu & Cao 2014). As patients with carotid artery stenosis have increased risk for stroke, this specific complication should be borne in the minds of oncologists (Cheng *et al.* 2000).

In this rare case report, carotid artery stenosis with stroke symptoms was detected after radiation therapy in a patient with lung cancer. A brief literature review has been performed to explore the diagnosis and treatment of this complication. The report was exempted from ethics review by the First Hospital of Jilin University Ethics Review Board.

CASE REPORT

Patient Information

On April 11, 2018, a 58-year-old man presented to the Department of Neurology at the First Hospital of Jilin University reporting a one-time episode of temporary paroxysmal amaurosis in the right eye for 10 minutes which arose 7 days ago before admission. the symptoms was then resolved without treatment. The patient did not experience dizziness, headache, choking, or dysphagia. No limitation of physical activity was reported. The patient had been diagnosed with small-cell lung cancer seven years earlier. He underwent radiation therapy in 2011. The patient had no history of diabetes, hypertension, smoking, or alcohol abuse.

Clinical Findings

Physical examination at the time of admission revealed no significant abnormality. Blood pressure was 110/70 mmHg. The neurologic examination revealed no positive signs. No obvious abnormalities were detected by routine blood tests or measurements of blood coagulation, myocardial injury markers, preoperative infectious markers, liver function, blood lipid, blood glucose, anti-cardiolipin antibody, or male tumor markers. On April 9, 2018, magnetic resonance imaging (MRI) revealed no obvious abnormalities, while an ultrasound examination of the head and neck showed stenosis of the right common carotid artery (70–90%), occlusion at the origin point of the right subclavian artery with right subclavian steal syndrome (Grade 3),

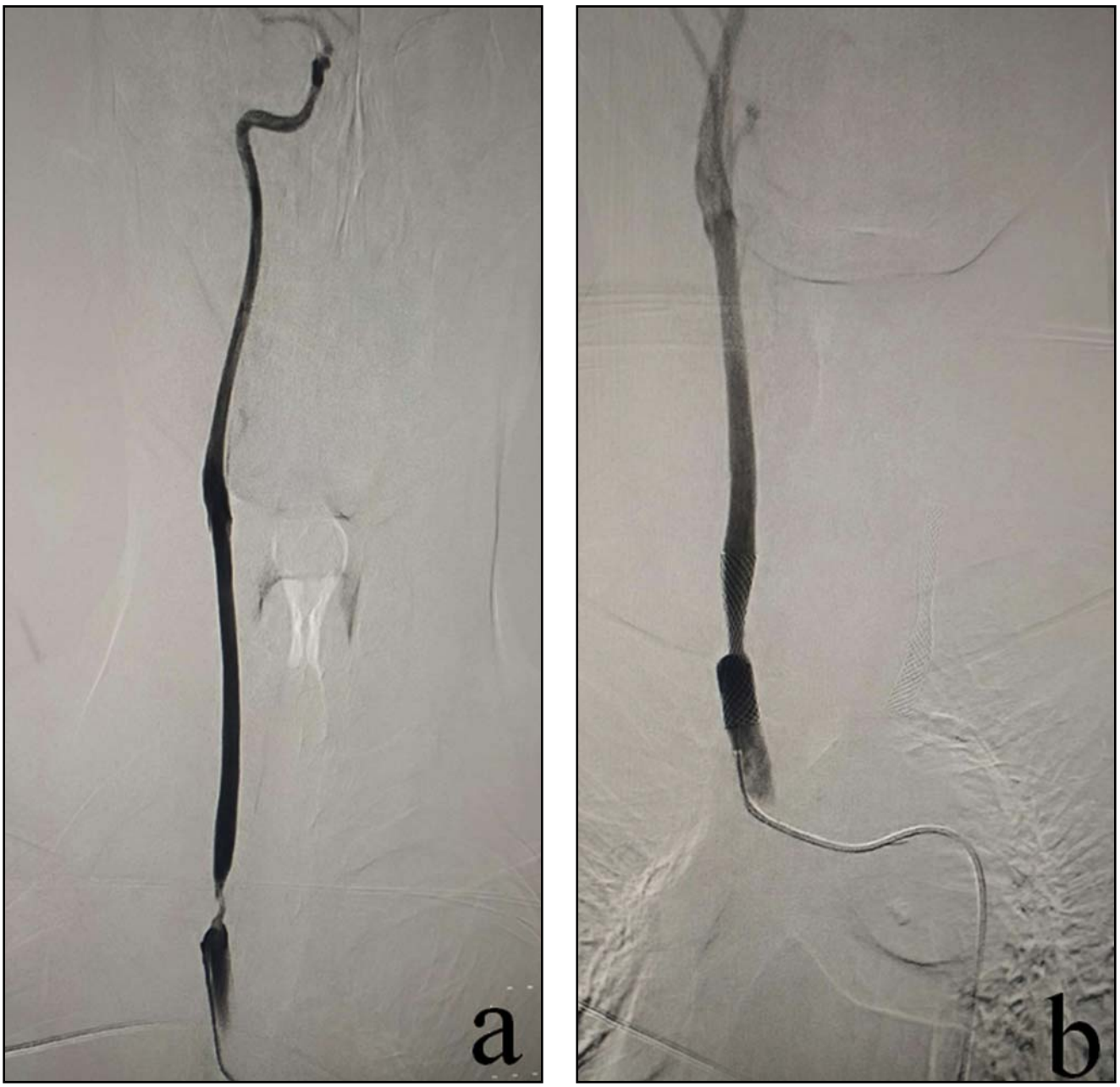

Fig. 1. Right common carotid angiography before (a) and after (b) stenting.

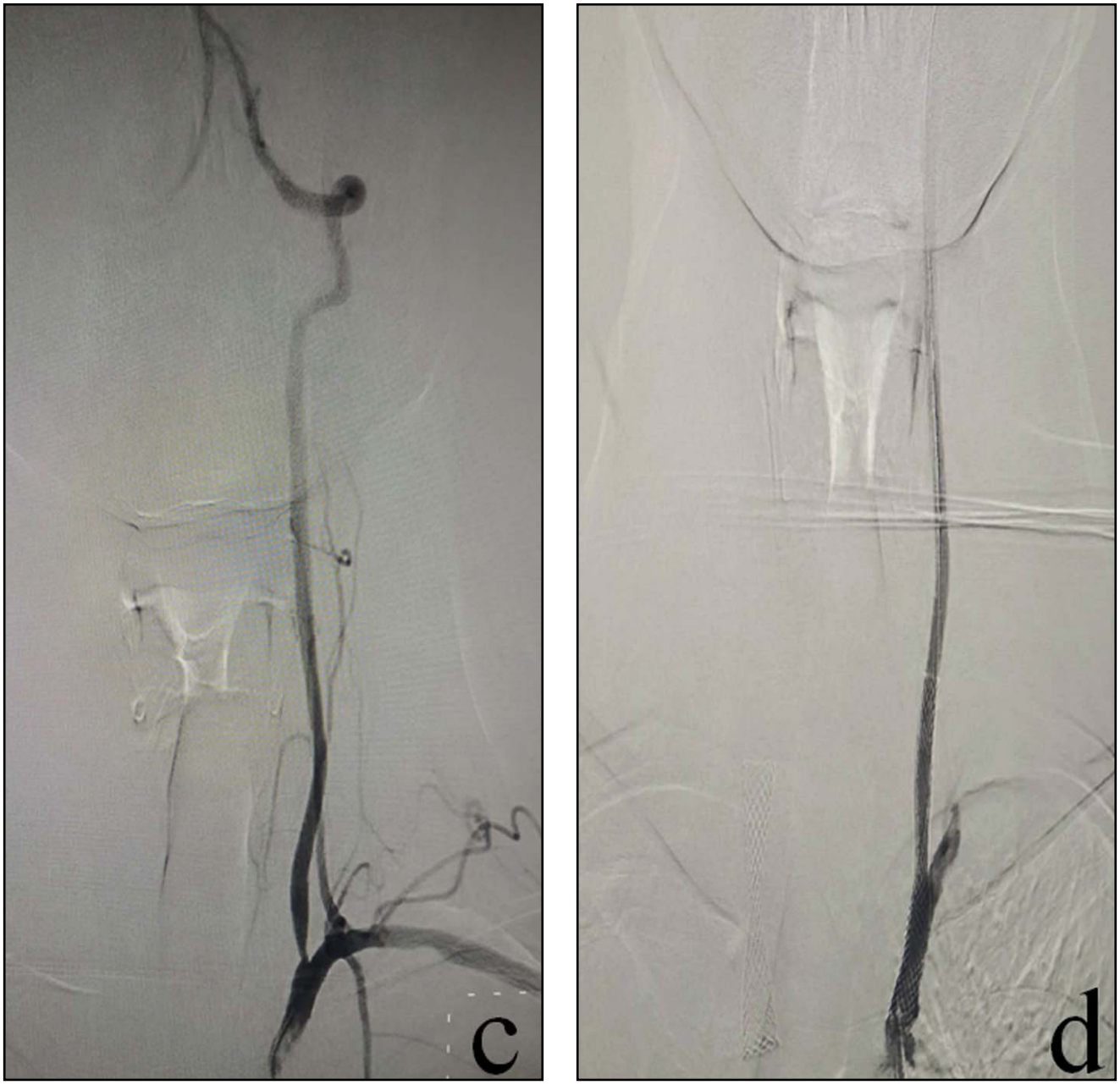

Fig. 2. Left vertebral artery angiography before (c) and after (d) stenting.

and left-side stenosis of the vertebral artery (50–69%). Whole-cerebral angiography revealed occlusion at the origin point of the right subclavian artery, severe stenosis at the origin point of the right common carotid artery, severe stenosis of the left vertebral artery, mild stenosis of the left common carotid artery, and right subclavian steal syndrome (Grade 3).

Diagnostic Assessment

The patient had a history of lung cancer and radiation therapy. According to his physical examination, medical history, and auxiliary examinations, the clinical diagnosis at admission was as follows: lung cancer; right common carotid artery stenosis; left common carotid artery stenosis; left vertebral artery stenosis; right subclavian artery occlusion with right subclavian steal syndrome (Grade 3).

Therapeutic Intervention

The patient underwent carotid angioplasty and stenting (CAS) of the right common carotid artery (Figure 1) and the left vertebral artery (Figure 2). Favorable dilation was achieved after stenting. During the operation, a detached plaque was found in the umbrella-shaped filter (Figure 3). Pathological examination of the exfoliated tissue retrieved from the umbrella-shaped filter revealed platelets, red blood cells, numerous fibrin deposits and white blood cells, and local changes in thrombosis homogenization (Figure 4). These pathological results confirmed the preprocedural diagnosis

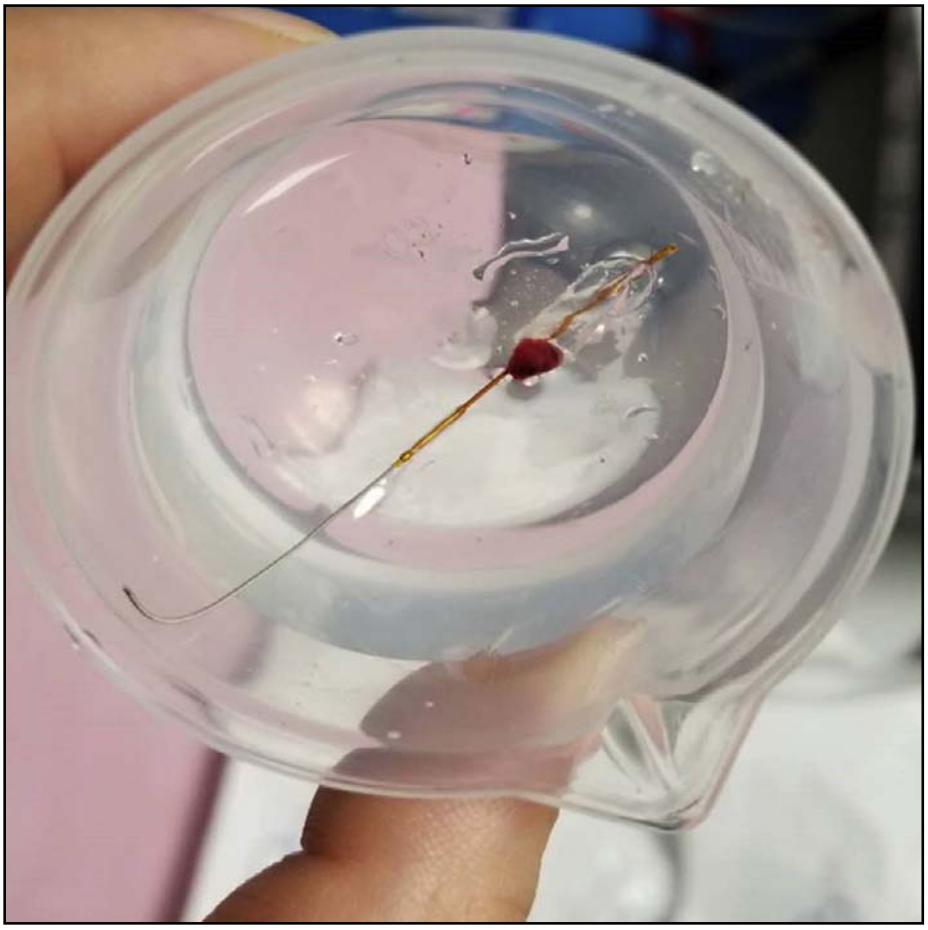

Fig. 3. A detached plaque was found in the umbrella-shaped filter.

of RICS. The postprocedural evaluation showed that the residual stenosis rate was less than 30%.

Follow-up

At the time of discharge, the patient was prescribed aspirin 100 mg QD, clopidogrel 75 mg QD, and atorvastatin 20 mg QD. Over the 6-month follow-up period, there was no episode of temporary vision loss or other stroke signs.

DISCUSSION

Patients with RICS usually have relatively few risk factors for atheromatous plaque formation, relatively young age, and severe stenosis (Shichita *et al.* 2009). Although the clinical features of the patient in this study were generally typical of those diagnosed with RICS, his age was 58 years, which is younger than that of most patients with general atherosclerotic stenosis (Koo 2015). Additionally, the onset time was seven years after radiation therapy. Lam *et al.*. analyzed 71 patients after radiation therapy and 51 patients who were newly diagnosed with nasopharyngeal carcinoma, who had not yet undergone radiation therapy. The results of the study revealed that 78.9% of patients in the radiation therapy group had carotid stenosis, but only 21.6% of the patients in the non-radiation therapy group were affected ($p < 0.01$). Two-thirds of the patients in the radiation therapy group gradually developed > 50% stenosis, while none of the patients in the non-radiation group developed > 50% stenosis (Lam *et al.* 2001). RICS may occur within 1 to 2 years after the end of radiation therapy, and the likelihood of RICS increases with prolonged survival (Zureik *et al.* 2000). The time interval between the end of radiation and stenosis is an important factor for RICS (Fernandez-Alvarez *et al.* 2018). Cheng *et al.* reported that the risk of RICS in patients who received more than five years of treatment was 8.5 times higher than in patients who had received under five years of treatment (Cheng *et al.* 2000). In summary, the radiation therapy history of the patient presented here is consistent with his diagnosis of RICS. Furthermore, the post-procedural pathological examination of exfoliated tissue showed visible platelets, a large amount of fibrin, numerous white blood cells, some red blood cells, and local changes in thrombotic homogenization. There was no macrophage cell infiltration or evidence of lipid components, which is typical of atherosclerotic stenosis. Finally, the lesions in blood vessels were severely stenotic, which cannot be explained by the formation of a general atherosclerotic plaque. Generally, atherosclerotic plaques that were not induced by

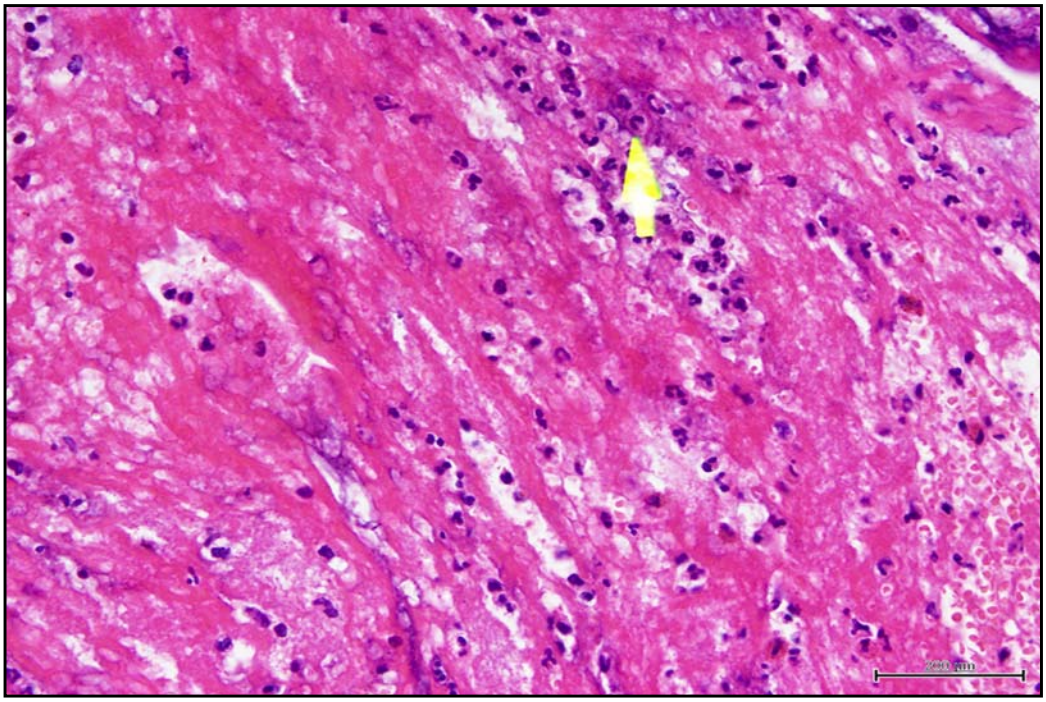

Fig. 4. Microscope slide with exfoliated tissue from the umbrella-shaped filter (H&E, ×100).

radiation therapy have thin fibrous caps and large lipid cores, with inflammatory cell infiltration, intraplaque hemorrhage, ulcers, and neovascularization at the base of the plaque (Fokkema *et al.* 2012b). A cross-sectional histopathological study of endometrial plaques showed that compared to the plaques characteristic of atherosclerotic stenosis, RICS plaques have fewer signs of inflammation, more fibrin tissue, less macrophage infiltration, and smaller lipid cores. RICS is always limited to the area that has been treated with radiation. The lesion dose not appear in the typical area, which is more stable than the atherosclerotic lesion (Fokkema *et al.* 2012b). For the case reported here, patient age (relatively young), stenotic characteristics, and the results of pathological analysis were consistent with RICS.

The severity of RICS is affected by many factors, such as age, dose of radiation administered, time interval after radiation therapy, and traditional atherosclerotic factors (e.g., smoking, hyperglycemia, hypertension, hyperlipidemia) (Shichita *et al.* 2009; Lam *et al.* 2001). The specific mechanism underlying RICS is not well understood, but most researchers believe that the mechanism of injury includes the following factors. First, radiation therapy directly damages endothelial cells. Second, vessels supplying the artery may be damaged and/or occluded, resulting in ischemic necrosis. The loss of elastic tissue and muscle fibers then leads to fibrosis. These factors may accelerate the progression of atherosclerosis (Weintraub *et al.* 2010; Chang *et al.* 2009). Sano *et al.* conducted a study that included clinical imaging and histological analysis of RICS. The results showed a high incidence of vulnerable plaques in patients with RICS. Although the cause of this difference is not clear, it may be related to the progression of RICS (Sano *et al.* 2015).

During the first 10 years of RICS, direct damage to the intima results in the progression of stenosis. Subsequent intimal proliferation may then result in more fibrotic, stable plaques. However, during the subsequent pathological phase (typically observed after 10 years), vasotrophic dysfunction caused by indirect injury may lead to the development of intra-plaque hemorrhages. The presence of such hemorrhages may result in the gradual transformation of a stable plaque into a vulnerable plaque (Sano *et al.* 2015). In the case reported here, we found evidence of tissue shedding and instability during the stenting procedure. These factors are considered to be related to the progression of RICS.

RICS is commonly caused by radiation therapy for nasopharyngeal carcinoma, but there are few reports of RICS after lung cancer. Although the incidence of RICS is often related to the dose of radiation administered, (Fernandez-Alvarez *et al.* 2018; Abayomi 2004) in this case, severe vascular stenosis followed a single session of radiation therapy. Furthermore, it has been reported that RICS is commonly found in the common carotid artery, internal carotid artery, and the extracranial artery (Shichita *et al.* 2009; Abayomi 2004). However, for this reported case, we found that the subclavian artery and vertebral artery were also involved, which suggested that blood vessel screening for such patients should not be limited to the common carotid arteries, the extracranial arteries, and the internal carotid arteries. This clinical phenomenon should be considered by clinical practitioners to facilitate the early diagnosis and treatment of RICS.

Regarding the treatment of RICS, both carotid endarterectomy (CEA) , carotid angioplasty and stenting (CAS) are viable revascularization techniques. Patients undergoing CEA had more temporary cranial nerve injury, but stent restenosis and advanced cerebrovascular disease in patients with CAS were higher (Fokkema *et al.* 2012a). Huang *et al.* (2013) reported there were no significant differences in mortality, transient cerebral ischemia, stroke and harmful cerebrovascular events after 5 years of follow-up after CEA or CAS. For patients with high complications and high risk, CAS is a reasonable alternative to CEA. CAS can be performed safely with no increased morbidity or restenosis in Neck radiation therapy(XRT) patients Compared with non-XRT patients (Ravin *et al.* 2015). Carotid angioplasty and stenting (CAS) provides a new treatment for this type of patient and is approved by the American Stroke Association guidelines (Ravin *et al.* 2015). The treatment of the effect of the stent for this case was good.

CONCLUSION

Clinicians should include delayed RICS in their differential diagnosis. It is recommended that patients with a history of radiation therapy should undergo regular cervical color Doppler ultrasonography in for the expedient diagnosis and treatment of RICS. This approach will improve quality of life and the rate of survival. At the same time, the risk factors for RICS as well as the mechanism underlying this condition remain to be elucidated. Further long-term studies are needed.

DECLARATION OF INTEREST

The authors have no personal or financial affiliations to disclose.

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