CASE REPORT

18-Year Follow-Up After Coronary Stenting for Left Main Coronary Artery Lesions
A Case Report of Radiation-Induced Coronary Artery Disease

Junqin Bai, MD, Zhichao Dong, MD, Lifei Pan, MD, Xunlong Xia, MD and Bo Zhang, MD

Summary
The current treatment of radiation-induced coronary artery disease (RCAD) is comparable to that of generic coronary artery disease (CAD); however, the outcomes of these treatment measures have not been fully examined in RCAD. A 33-year-old woman, without conventional cardiovascular risk factors, presented with left main coronary artery (LMCA) lesions. At the age of 26, she received mediastinal radiation therapy (RT) to treat mixed cellularity Hodgkin lymphoma. One BiodivYsio 3.5 × 18 mm stent was implanted at the LMCA site. At the age of 38, the patient was treated by balloon dilatation because of approximately 50% in-stent stenosis. At the last follow-up in February 2018, when the patient was 51 years old, she no longer complained of chest pain. Coronary angiography showed no de novo or in-stenosis lesions, although optical coherence tomography showed mild neointimal proliferation, calcific plaque, small ruptured intima, and several uncovered struts. The experience of treating this case may shed some light on coronary stenting in coronary lesions caused by RCAD.

Key words: Radiotherapy, Percutaneous coronary intervention, Optical coherence tomography

Mediastinal radiation therapy (RT) is an effective treatment for Hodgkin lymphoma (HL), but it was found to be associated with increased risk of adverse cardiovascular events. The incidence of such events is increased in HL patients, especially in younger survivors who do not have traditional risk factors, because RT induces vascular endothelium damage, promotes inflammation, and accelerates atherosclerosis.1) So far, the long-term outcome of coronary stenting in radiation-induced coronary artery disease (RCAD) is not clearly understood, especially with respect to follow-up by optical coherence tomography (OCT). Here, we present a case of a patient who was treated with coronary stenting for left main coronary artery (LMCA) lesions following RT and describe the OCT analysis of the morphologic features of coronary stenting in the LMCA after an 18-year follow-up.

Case Report
A 26-year-old woman, without conventional cardiovascular risk factors, received mediastinal RT to treat mixed cellularity HL, with a cumulative radiation dose of 58 Gy (28 times, 38 days). The patient was referred to our institute in August 2000, at the age of 33, with a 1-month history of chest pain that was aggravated by effort. The baseline coronary angiogram showed significant eccentric stenosis at the middle of the LMCA. Percutaneous coronary intervention (PCI) was completed with implantation of one 3.5 × 18 mm BiodivYsio stent (a stent coated with phosphorylcholine polymer, Biocompatibles, Galway, United Kingdom) (Figure A and B). The patient was managed medically with the administration of aspirin (80 mg daily) and ticlopidine (0.25 g daily), with the ticlopidine treatment being withdrawn at the 12-month follow-up after discharge.

In June 2005, at the age of 38, the patient was admitted with a 6-month history of effort-related chest pain. The patient was treated by balloon dilatation with one 3.0 × 10 mm cutting balloon due to about 50% in-stent stenosis at the LMCA, and a further angiogram showed that the procedure had been successful (Figure C and D). In February 2006, a follow-up coronary angiogram showed no restenosis at the LMCA (Figure E). The patient was medically managed with aspirin (100 mg daily), clopidogrel (75 mg daily), atorvastatin (20 mg daily), and metoprolol (25 mg twice daily), with the clopidogrel treatment being withdrawn at the 12-month follow-up after cutting balloon dilatation.

The patient presented again in February 2018, at the age of 51, with atypical chest pain. Her coronary angiogram was found normal, without de novo or in-stenosis lesions at the LMCA. OCT showed mild homogeneous neointima, small ruptured intima, calcific plaque, and sev-
Figure. A: The baseline coronary angiogram in August 2000. B: One 3.5 × 18 mm BiodivYsio stent implanted. C: About 50% in-stent stenosis in June 2005. D: After balloon dilatation. E: Follow-up coronary angiogram in February 2006. F-H: Follow-up coronary angiogram and optical coherence tomography in February 2018.
should favor placement of one of the new drug-eluting doses (excess relative risk per Gray, 7.4%; 95% CI, 3.3-14.8%) among HL survivors. The onset of angina pectoris occurred early in our patient, only 7 years after radiation exposure, mainly because of the high doses of mediastinal irradiation (58 Gy). Infiltration of inflammatory cells into the area can be seen after doses as low as 5 Gy (Figure F-H). She has remained symptom free with the administration of aspirin (100 mg daily), atorvastatin (20 mg daily), and metoprolol (25 mg twice daily). The patient’s blood lipid levels were always normal, but levels of serum inflammatory cytokines including erythrocyte sedimentation rate (ESR), high sensitivity C-reactive protein (hs-CRP), and D-Dimer were determined to be higher in 2018 than normal (Table).

| Characteristic | 2000 | 2005 | 2006 | 2018 |
|---------------|------|------|------|------|
| Blood lipid   |      |      |      |      |
| TC (mmol/L)   | 3.49 | 3.37 | 3.43 | 4.05 |
| TG (mmol/L)   | 0.75 | 1.05 | 1.07 | 2.26 |
| LDL-C (mmol/L)| 2.24 | 2.10 | 2.11 | 2.05 |
| HDL-C (mmol/L)| 0.92 | 1.08 | 1.02 | 1.24 |
| Inflammatory index | | | | |
| ESR (mm/h)    | 44   |      |      |      |
| hs-CRP (mg/L) | 8.03 |      |      |      |
| D-Dimer (ug/L)| 2190 |      |      |      |

TC indicates total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; and hs-CRP, high sensitivity C-reactive protein.

The involved artery in our patient is the LMCA, in agreement with the findings that radiation-induced coronary artery lesions tend to be proximal or ostial, close to the radiation field. In our patient, in-stent stenosis and subsequent cutting balloon angioplasty demonstrates the higher rate of in-stent restenosis and revascularization of the target vessel following placement of a bare metal stent in HL survivors. When PCI is indicated, decision-making should favor placement of one of the new drug-eluting stents as the safer modality in these patients. Our patient is doing well after cutting balloon angioplasty, and the routine coronary angiogram at the 18-year follow-up further indicated that PCI with stent placement is one safe modality in this patient population. The first-in-man OCT analysis in a young patient with RCAD showed that the plaque had fibrous characteristics and some lipid components, indicating an overlap of RCAD with age-related atherosclerosis. To the best of our knowledge, our case is the first reported OCT analysis of RCAD at the long-term follow-up of a patient following coronary stenting. The fact that the OCT showed no significant luminal narrowing, with mild homogeneous neo-intima, small ruptured intima, calcific plaque, and several uncovered struts, underscores the importance of secondary prevention of CAD, including long-term active antiplatelet and lipid-lowering therapy in this patient population, despite the lack of common cardiovascular risk factors.

**Discussion**

A previous study found a four- to seven-fold higher risk for coronary artery disease (CAD) in individuals who had received higher-dose RT, compared with the general population. CAD may develop 5-20 years after radiation exposure, and it initially tends to be asymptomatic. The experience of treating this case may shed some light on coronary stenting in coronary lesions caused by RCAD, even LMCA.

**Conclusion**

In cases of RCAD, PCI with coronary stenting and extension of long-term antiplatelet and statin therapy should be considered when feasible, as is the case for patients who are at higher risk of developing atherosclerosis. The treatment of this case may shed some light on coronary stenting in coronary lesions caused by RCAD, even LMCA.

**Disclosure**

Conflicts of interest: None.

**References**

1. Taunk NK, Haffty BG, Kostis JB, Goyal S. Radiation-induced heart disease: Pathologic abnormalities and putative mechanisms. Front Oncol 2015; 5: 39.
2. van Nimwegen FA, Schaaepveld M, Janus CP, et al. Coronary artery disease after Hodgkin lymphoma treatment: 40-year disease risk. JAMA Intern Med 2015; 175: 1007-17.
3. van Nimwegen FA, Schaaepveld M, Cutrer DJ, et al. Radiation dose-response relationship for risk of coronary heart disease in survivors of Hodgkin lymphoma. J Clin Oncol 2016; 34: 235-43.
4. DeZorzi C. Radiation-induced coronary artery disease and its treatment: A quick review of current evidence. Cardiol Res Pract 2018; 2018: 8367268.
5. van Rosendaal AR, Daniëls LA, Dimitriu-Leen AC, et al. Different manifestation of irradiation induced coronary artery disease detected with coronary computed tomography compared with matched non-irradiated controls. Radiother Oncol 2017; 125: 55-61.
6. Cuomo JR, Sharma GK, Conger PD, Weintrab NL. Novel concepts irradiation-induced cardiovascular disease. World J Cardiol 2016; 8: 504-19.
7. Cuomo JR, Javaheri SP, Sharma GK, Kapoor D, Berman AE, Weintrab NL. How to prevent and manage radiation-induced coronary artery disease. Heart 2018; 104: 1647-53.
8. Caro-Codón J, Jiménez-Valero S, Galeote G, Sanchez-Recale A, Moreno R. Radiation-induced coronary artery disease: Useful insights from OCT. Int J Cardiol 2016; 202: 535-6.