Granulation Tissue With Eosinophil Infiltration in the Restenotic Lesion After Coronary Stent Implantation
—— A Case Report ——

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Although stents reduce the rate of vessel restenosis, in-stent restenosis is a recognized clinical problem and it appears that patients positive for allergic patch-test reactions to the stent components nickel and molybdenum have increased rates of it. A patient with angina pectoris had repeated episodes of restenosis after stent implantation and histological examination demonstrated granulation tissue with eosinophil infiltration in the restenotic lesion of the coronary artery. The patient was positive for an allergic reaction to the stent components. (Circ J 2004; 68: 722–723)

Key Words: Allergy; Coronary artery; Eosinophil; In-stent restenosis

A 57-year old Japanese female had chest pain and was admitted to hospital in October, 2000. Coronary angiography showed a total occlusion in segment 6 and 90% stenosis in segment 9 of the left coronary artery. A coronary 316L stainless-steel stent was successfully inserted in segment 6, and plain old balloon angioplasty (POBA) was performed for the stenosis of segment 9. After stenting, aspirin 100mg/day and cilostazol 100mg/day were prescribed. At 3 months after the coronary intervention, she had in-stent restenosis and the Cutting Balloon™ was used to dilate it, and subsequently the anti-allergic drug, tranilast 300mg/day, was added to her medication. However, in-stent restenosis recurred 3 times after the first incident and she underwent repeat coronary intervention with Cutting Balloon™ for the second and third restenoses. Finally, directional coronary atherectomy was used after the fourth occurrence of in-stent restenosis.

Histologically, the atherectomized tissue comprised granulation tissue with cell infiltration, including eosinophils, and neointimal hyperplasia with the proliferation of smooth muscle cells and accumulation of extracellular matrix protein (Fig 1). We suspected that allergy to the stent metal was the cause of the restenoses and the patient underwent a Patch test using the Finn chamber and a 316L stainless-steel plate. The test was carried out and analyzed according to the recommendation of the International Contact Dermatitis Research Group. The test was read by dermatologists after 48h of contact with the plate and the patient was positive for an allergic reaction to the stent material, including nickel and molybdenum (Fig 2).
In-Stent Restenosis With Eosinophilic Granulation

Discussion

Intracoronary stent placement is increasingly being used for the treatment of atherosclerotic coronary artery disease because the rate of restenosis is more reduced than with POBA. However, in-stent restenosis still remains a recognized clinical problem. The histopathology of human coronary in-stent and post POBA restenoses are quite different. In-stent restenosis results from an excessive fibroproliferative and inflammatory response to medial injury, as well as lipid core penetration by the struts of the stent in the coronary arterial wall. Kornowski et al reported that the inflammatory reaction consisted of groups of pale histiocytes adjacent to the strut of the stent, with occasional multinucleated foreign body giant cells, and that eosinophils and plasma cells were not prominent.

The present case had prominent eosinophils in the granulation tissue atherectomized from the restenotic lesion in the stent-implanted coronary artery. In a patient without metal allergy, proliferation of smooth muscle cells and accumulation of extracellular matrix protein predominated, but cell proliferation was not prominent in the atherectomized tissue of the in-stent restenosis of the present patient (Fig 3).

The precise mechanism of in-stent restenosis is not yet understood. Oshima et al reported that monocyte chemoattractant protein-1 (MCP-1) production at stented coronary arterial sites was associated with an increased risk for restenosis after stent implantation. Chemokines, including MCP-1, activate cells and thus indirectly activate the inflammatory mediator release by eosinophils. Therefore, MCP-1 may play an important role in eosinophil-related in-stent restenosis. A relationship between the DD genotype of angiotensin-converting enzyme (ACE) polymorphism and coronary stent restenosis has also been reported in Japanese patients and quinapril prevented restenosis after coronary stenting in patients with the ACE D allele. However, there has not been a report of a relationship between the genotype of ACE polymorphism and metal allergy.

Köster et al reported that patients positive for allergic patch-test reactions to the stent components nickel and molybdenum appear to have increased rates of in-stent restenosis. We confirmed histologically for the first time that allergy to the stent metal induces restenosis of the coronary artery after stent implantation in a patient who has a positive allergic reaction to stent. Therefore, it is necessary to take metal allergy into consideration before coronary stenting because in the present case, in-stent restenosis occurred repeatedly once the stent was implanted and a standard anti-allergic drug, tranilast, could not prevent it.

The treatment and prevention of in-stent restenosis have been discussed. The recently developed sirolimus-eluting stent has shown good results for preventing restenosis, when compared with a standard stent, and may also suppress the restenosis associated with stent metal allergy.

References