A Case of Takayasu Arteritis with Repeated Coronary Artery Restenosis after Drug-Eluting Stent Implantation Successfully Treated with a Combination of Steroids

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Abstract

A 52-year-old woman with Takayasu arteritis developed acute coronary syndrome and received percutaneous coronary intervention (PCI). The patient experienced restenosis three times even with drug-eluting stent (DES) implantation. We started steroid administration after the fourth PCI to reduce inflammation due to autoimmunity. With DES and a steroid combination, the patient remained free of chest pain, and a follow-up angiography demonstrated good patency of the stent site. Since in-stent restenosis may result from a complicated combination of neointimal proliferation and autoimmune mechanisms, physicians should consider a combination of DES and a steroid for the treatment of coronary artery disease in Takayasu arteritis.

Key words: Takayasu arteritis, coronary artery disease, restenosis, steroid


Introduction

Takayasu arteritis is a chronic vasculitis due to unknown etiology, which initially affects the aorta and its primary branches. Coronary lesions complicate Takayasu arteritis in about 10% of patients receiving a clinical diagnosis (1). There have been several reports regarding the usefulness of a drug-eluting stent (DES) for the treatment of repeated in-stent restenosis after implantation of a bare metal stent (BMS); (2-5) however, the therapeutic strategy for this kind of patient is still unclear.

We report here a case of Takayasu arteritis that developed repeated restenosis after percutaneous coronary intervention (PCI), even with a DES implantation. We could finally prevent in-stent restenosis by adding oral steroid therapy. Our experience provides valuable insight for the treatment of coronary arterial diseases in patients with Takayasu arteritis.

Case Report

A 52-year-old woman was admitted to our hospital because of sudden-onset chest pain and was diagnosed with acute coronary syndrome. At the age of 19 years, she had been diagnosed with Takayasu arteritis and started treatment with oral administration of steroid. After several years of maintenance therapy with low-dose steroid, the arteritis was considered to be inactive and the steroid administration was discontinued. She was a previous smoker and reached menopause at 50 years old, but she had no history of hypertension, dyslipidemia or diabetes. Physical examination on admission revealed bruit at both sides of the neck and a difference in blood pressure between the upper limbs, suggesting that the patient had stenoses in aortic branches. Indeed, whole body computed tomography (CT) imaging demonstrated significantly calcified aorta and occluded subclavian arteries, which was consistent with Takayasu arteritis (Fig. 1). Emergency coronary angiography showed a severe stenosis of the proximal left anterior descending (LAD) coronary artery (Fig. 2A), and PCI with a sirolimus-eluting stent (Cypher 3.5×18 mm, Cordis Corporation, Bridgewater, NJ, USA) was successfully performed on the proximal LAD. Figure 2B shows the good final angiographic results. At this point, C-reactive protein (CRP) level was mildly in-
creased (1.02 mg/dL); however, since this middle-aged female case showed severe LAD stenosis without coronary ostial involvement, we considered that the coronary lesion was mainly due to atherosclerosis.

Five months later, the patient complained of frequent chest pain and was re-admitted to our hospital. Angiography demonstrated severe in-stent restenosis of the LAD artery (Fig. 3A), and the intravascular ultrasound (IVUS) showed the significant lumen loss due to neointimal hyperplasia (Fig. 3C). CRP level was 0.58 mg/dL at this point. We performed the second PCI with a DES (Cypher 3.5×23 mm) and successfully dilated the coronary artery (Fig. 3B). However, the patient repeatedly suffered a relapse of chest pain and was required the third and the fourth PCI in 6 months. The stenosis occurred only in the stent site, the significant plaque progression or vessel narrowing was not observed in the other coronary arteries during first to fourth PCI.

At the time of the fourth PCI, the CRP showed a modest increase (0.47 mg/dL); the erythrocyte sedimentation rate (ESR) was also elevated (82 mm/h). We considered that inflammation due to Takayasu arteritis might still be active; thus, we decided to start with steroid therapy (prednisolone; 10 mg/day/body) after the fourth PCI. The follow-up angiography at eleven months after the fourth PCI demonstrated good patency of the stent site (Fig. 4). The continuous administration of low dose steroid maintained CRP at negative levels (<0.06 mg/dL) and ESR at low levels (<20 mm/h), and the patient has experienced no recurrence of chest pain for four years.

**Figure 1.** Maximum intensity projection (MIP) image of whole body enhanced CT showed significantly calcified aorta and occluded subclavian arteries (white arrows), which was consistent with Takayasu arteritis.

**Figure 2.** The coronary angiography demonstrated severe stenosis of the proximal left anterior descending (LAD) artery (A); the first PCI was performed with a sirolimus-eluting stent and achieved successful dilation (B).
Discussion

We encountered a patient who developed acute coronary syndrome due to a significant narrowing occurring at her proximal LAD without coronary ostial stenosis. The present case showed repeated restenosis after PCI even with DES (sirolimus-eluting stent) implantation. For several years after the beginning of steroid administration, the patient has not complained of chest pain, although she frequently complained of chest pain before steroids were administered. This case indicates that steroid therapy could prevent in-stent restenosis of coronary lesions in patients with Takayasu arteritis.

Takayasu arteritis is a large vessel vasculitis that involves the aorta and its main branches, the pulmonary arteries and the coronary arterial tree. It has a worldwide distribution, with the greatest prevalence in Asians. In Japan, there are approximately 5,000 patients, and it has been estimated that 150 new cases occur each year. It affects young females...
nine times more frequently than males, with the usual age of onset between 10 and 20 years (1). The etiology of Takayasu arteritis is still unknown, but infectious agents, genetic factors, and autoimmunity are thought to play major roles. From a pathogenic point of view, T-cell-dependent immunity, chemokine- and cytokine-dependent immunity and, less clearly, B-cell-dependent immunity are the main pathogenic mechanisms leading to arterial wall injury (6). Early diagnosis of Takayasu arteritis by MRA, CT and other techniques facilitates early treatment and thereby improves the prognosis so that in recent years patients are enjoying longer lives than before. Complications of atherosclerosis appear earlier than in patients without Takayasu arteritis, and pose new threats for patients. Several studies have demonstrated that these vascular inflammatory changes progress from the adventitial side to the intimal side of the vessel, and finally manifest in the intima (7).

Angina pectoris because of coronary involvement is not a common feature, having been reported in about 10% of cases of Takayasu arteritis. Among coronary stenosis cases, ostial lesions of the left main coronary artery and/or right coronary artery are the most common, at 87.5% incidence (8). In those diseased vessels, luminal narrowing is caused by the extension of the inflammatory processes of intimal proliferation and contraction of the fibrotic media and adventitia from the ascending aorta. However, a significant narrowing occurs in some coronary arteries without coronary ostial stenosis, so-called “skipped lesions”. This postmenopausal woman had few coronary risk factors, but developed a severe LAD lesion without coronary ostial stenosis. A previous study suggested the possibility that atherosclerotic change was accelerated in Takayasu arteritis (9). Thus, atherosclerosis might be involved at least in part in the pathogenesis of coronary stenosis in the present case. Although we could not perform at the time of first PCI, IVUS or coronary computed-tomography (CT) angiography findings might be useful to understand the characteristics of plaque property of the coronary lesion.

As discussed by Furukawa and colleagues, the predominant pathological feature of diseased vessels in Takayasu arteritis is infiltration of various kinds of immunocytes (2). Because stenosis in Takayasu arteritis is caused by inflammation of the blood vessels by the autoimmune reaction, DES as an immunosuppressive agent was expected to reduce the incidence of in-stent restenosis. In fact, there have been a few reports discussing whether or not DES placement is effective against coronary artery in-stent restenosis in BMS caused by arteritis (2-5).

Sirolimus was originally discovered as an antibiotic and then developed as an immunosuppressive agent. It inhibits cell-cycle progression at the late G1 stage and suppresses activated T-cell proliferation. In addition to its inhibitory effects on T cells, sirolimus markedly suppresses the allo-stimulatory activity of antigen-presenting dendritic cells. These immunosuppressive properties of sirolimus may have a beneficial synergistic effect with its anti-proliferative action on vascular smooth muscle cells in the prevention of restenosis after coronary stenting in Takayasu arteritis (2). Therefore, given the recent progress in vascular biology clearly demonstrating the significant roles of cytokines produced by endothelial cells, smooth muscle cells, macrophages, and even lymphocytes in the progression of atherosclerosis (10), sirolimus alone may not be sufficient to prevent in-stent restenosis of Takayasu arteritis. In fact, Katawama et al reported a case of Takayasu arteritis with repeated in-stent restenosis after implantation of DES without a steroid, in which coronary artery bypass grafting was performed (11). Steroids have anti-inflammatory effects such as preventing the arachidonate metabolism and production of cytokines and inhibiting proliferation of lymphocytes especially immature T cells, which may be a concern in Takayasu arteritis-related atherosclerosis. However, steroids may not prevent the production of proliferative factors such as platelet-derived growth factor (PDGF), transforming growth factor (TGF)-β, and fibroblast growth factor (FGF). There are several reports regarding the prevention of in-stent restenosis in which DES was applied for repeated in-stent restenosis after implantation of a bare metal stent; these cases were administered a steroid before the PCI (2, 3). Enhanced arterial inflammation might play an important role in restenosis after coronary stenting, as well as in the initial onset of angina and its worsening (2). Therefore, steroid mono-therapy could not prevent intimal proliferation, which is one of the main causes of coronary narrowing resulting from arteritis. Although the present case had restenosis repeatedly after PCI even with a DES implantation, in-stent restenosis was deterred by the addition of steroid administration. From this result, we considered that DES alone may not be sufficient to prevent in-stent restenosis after PCI in Takayasu arteritis and that the combination of DES and a steroid might prevent in-stent restenosis in such cases.

In conclusion, in-stent restenosis of the coronary artery in Takayasu arteritis may result from a complicated combination of neointimal proliferation, autoimmune mechanisms especially affecting immature T cells, and atherosclerosis. Physicians should consider using a combination therapy of DES and steroid for the treatment of coronary artery disease requiring PCI in Takayasu arteritis. In the future, it will be necessary to undertake a prospective study to evaluate the usefulness of combination therapy with DES and a steroid.

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

References

3. Kang WC, Han SH, Ahn TH, Shin EK. Successful management of


