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Aggressive In-Stent Restenosis after Carotid Artery Stenting in a Patient with HIV Infection

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Dear Editor,

HIV-positive patients receiving antiretroviral therapy (ART) have a high risk of cerebrovascular disease.[1] We report a case of long-segment in-stent restenosis (ISR) at 12 months after carotid artery stenting in an HIV-positive patient.

A 54-year-old HIV-positive male smoker who reported a single episode of involuntary clonic movement involving his right arm and head lasting less than 30 seconds was referred to the neurology department for magnetic resonance angiography (MRA) of asymptomatic severe stenosis affecting the left proximal internal carotid artery (ICA). The patient exhibited mild dysarthria after a previous stroke. His HIV infection had been diagnosed after being admitted for acute cerebral infarction 14 years previously at another hospital, and was managed for the past 5 years with two nucleoside reverse transcriptase inhibitors (600-mg abacavir and 300-mg lamivudine daily) and a protease inhibitor (400-mg atazanavir daily). Fluid-attenuated inversion recovery images showed localized tissue loss in the precentral gyrus. MRA revealed multiple luminal irregularities in extracranial and intracranial arteries excluding the left proximal ICA, without significant stenosis. Recent laboratory tests indicated a low-density lipoprotein level of 113 mg/dL and did not detect HIV-1 RNA.

Digital subtraction angiography (DSA) confirmed 72% stenosis of the left proximal ICA (Fig. 1A). Carotid artery stenting of the lesion was performed using a 7.0×40 mm carotid WALLSTENT device (Boston Scientific, Marlborough, MA, USA) (Fig. 1B). ART, dual antiplatelet (aspirin and clopidogrel), and atorvastatin therapies were administered after the procedure, but the patient did not stop smoking.

During the 1-year follow-up, the CD4+ T-cell counts remained at >500 cells/μL, and the CD4+/CD8+ ratio ranged between 1.1 and 1.4. Consistently, HIV-1 RNA was less than 40 copies/mL. Low-density lipoprotein cholesterol remained below 70 mg/dL. High-sensitivity C-reactive protein was measured at 7.6 mg/dL once, but it was less than 3 mg/dL in three subsequent tests (Supplementary Table 1 in the online-only Data Supplement). However, severe concentric ISR greater than 50% along the stent was confirmed by DSA at the regular 1-year follow-up (Fig. 1C). The patient remained asymptomatic and refused retreatment. Thereafter, lesion progression was not observed in two additional computed tomography angiographs obtained during the following 18 months (Fig. 1D).

This case exhibited a diffuse intrastent type of ISR, which is generally rare compared with the focal type, but is frequently detected in HIV-positive patients.[2-4] The presence of HIV is considered a vascular risk that accelerates atherosclerosis and arterial inflammation in all anatomical regions.[5] Smoking might also have influenced the ISR in the present patient. However, the viral load, inflammatory markers, and lipid profile were well controlled. No progression of atherosclerotic lesions in other vessels was observed. These findings suggest that HIV or ART can impact on ISR.

ISR is generally characterized by the proliferation of smooth-muscle cells (SMCs) and the

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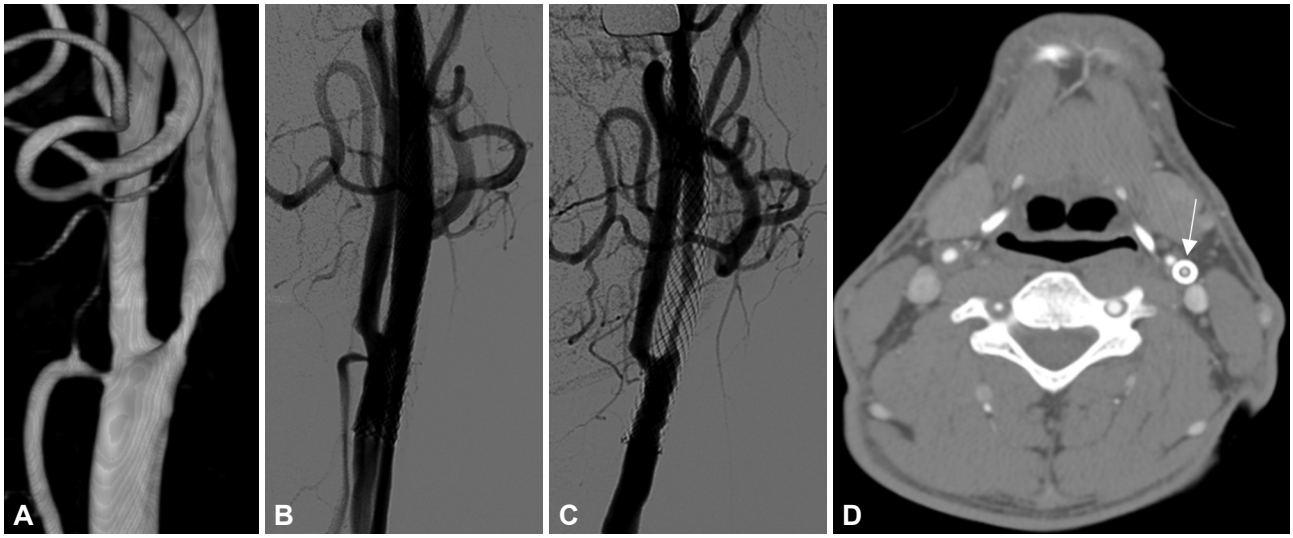

Fig. 1. Chronologic sequence of left proximal ICA stenosis. A: Three-dimensional rotational DSA revealed 72% stenosis in the left proximal ICA. B: A carotid artery stent was successfully deployed. C: Follow-up DSA after 1 year revealed severe diffuse intrastent in-stent restenosis. D: Arrow indicates the location of in-stent concentric narrowing at follow-up carotid computed tomography angiography performed 2 years after ICA stenting. DSA: digital subtraction angiography, ICA: internal carotid artery.

accumulation of extracellular matrix. Concentric proliferation of SMCs has frequently been confirmed in young patients who succumb to HIV infection.[6] Also, in vivo and in vitro studies have shown direct infection of human SMCs with HIV, and concentric SMC proliferation.[7] The concentric ISR in the present case may have been induced by the proliferation of HIV-infected SMCs.

It is suspected that ART medications can also affect ISR. Animal experiments investigating the carotid artery following balloon injury have shown that the ART (lamivudine, lopinavir, ritonavir, and zidovudine) treatment regimen can alter the response of vascular SMCs and that injury-induced restenosis is associated with fewer inflammatory changes than is atherosclerosis.[8] Prior to the use of drug-eluting stents (DESs), restenosis developed in 52% of HIV-positive patients who underwent percutaneous coronary intervention.[9] Despite the use of a DES, angiographic restenosis was still observed during 8-month follow-ups among 24% of HIV-positive patients taking ART, which is higher than the rate of 13.4% in the general population.[10] These findings indicating that it is worthwhile to investigate the effect of ART on ISR.

This study was limited by carotid ultrasonography not being used to provide any pathologic clue. Further studies investigating the effects of HIV and ART on carotid ISR are needed given the increasing number of HIV-positive patients requiring carotid artery revascularization.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2021.17.1.134.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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