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Multiple cardiovascular stenoses in a 66-year-old woman with neurofibromatosis type 1: virtual-histology intravascular ultrasound findings

Daisuke Kitano[1,2]*, Kazuo Harasawa[1], Tadahiro Saruya[1], and Toshihiko Tochihara[1]

[1]Department of Cardiology, Ukima Central Hospital, Tokyo, Japan; and [2]Divison of Cardiology, Department of Medicine, Nihon University School of Medicine, 30-1 Oyaguchi-kamicho, Itabashi-ku, Tokyo 173-8610, Japan

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Case summary

A 66-year-old Japanese woman with neurofibromatosis type 1 (NF1), also known as von Recklinghausen disease, visited our hospital with worsened dyspnoea and diagnosed congestive heart failure. She presented a differential blood pressure in the forearm arteries, vascular bruits in the right cervical region and periumbilical region, and left ventricular dysfunction on the echocardiogram. Both coronary and

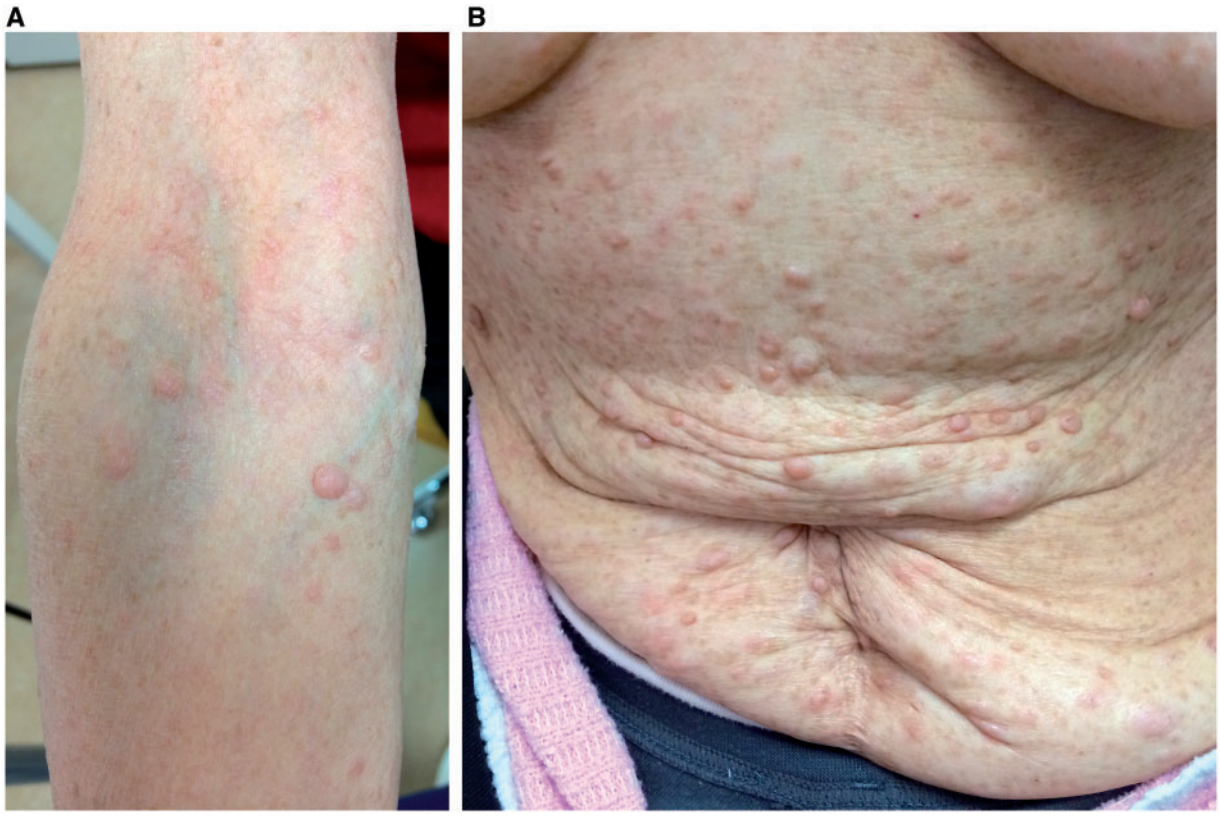

Figure 1 Multiple cutaneous neurofibromas (*A*) and café-au-lait spots and cutaneous neurofibromas (*B*) cover the patient's body.

* Corresponding author. Tel: +81 3 3972 8111, Email: kitano.daisuke@nihon-u.ac.jp. This case report was reviewed by Thomas Johnson, Maria Antonieta Albanez A de Medeiros Lopes, Riccardo Liga, and Gianluigi Savarese.

aortic angiography revealed multiple stenoses in the coronary arteries, cerebral artery, subclavian artery, abdominal aorta, and iliac arteries. In addition, virtual-histology intravascular ultrasound (IVUS) revealed the plaques mainly comprising fibrotic plaque. We performed revascularization to the arteries deploying stents. The patient's cardiac dysfunction improved, and the difference in the forearm arterial blood pressure disappeared.

Case description

In a 66-year-old Japanese woman, NF1 was diagnosed at the age of 55 years. She had a family history of von Recklinghausen disease, including her grandfather, father, daughter, and son; her father died unexpectedly, and her mother suffered a myocardial infarction and underwent primary percutaneous coronary intervention. The patient's only complaints were café-au-lait spots and cutaneous tumours (*Figure 1*). She presented no coronary risk factors other than the hyperlipidaemia: low-density lipoprotein cholesterol level, 158 mg/dL on 10 mg of pravastatin.

The patient presented to our hospital with dyspnoea and orthopnoea that had worsened over 2 months. Upon congestive heart failure diagnosis, she was admitted to our hospital. The physical examination upon admission revealed a difference in the forearm arterial blood pressure with cold feeling: right arm, 118/70 mmHg; left arm, 158/90 mmHg, and vascular bruits in the right cervical and periumbilical regions. While electrocardiography revealed ST depression in leads I, aVL, and V4–V6, echocardiography revealed global hypokinesis in the left ventricle and left ventricular ejection fraction (LVEF) reduction to 48%. Based on these findings, she was treated with angiotensin-converting enzyme inhibitor and diuretic agent, and her heart function was rapidly compensated up to 58% LVEF. Furthermore, computed tomography angiography revealed stenoses in the abdominal aorta (*Figure 2B*) and both common iliac arteries (*Figure 2C*). Magnetic resonance angiography revealed a right middle cerebral artery stenosis (*Figure 2A*). In addition, percutaneous coronary and brachiocephalic artery angiography revealed severe stenoses in the coronary arteries and the right subclavian artery: 99% stenosis of the ostium and 90% stenosis of the middle portion in the left circumflex coronary artery (LCx), 90% stenosis of the middle portion in the right coronary artery (RCA), and 99% stenosis of the proximal segment in the right subclavian artery (*Figure 3A–D*, and Supplementary material online, *Videos S1–S4*). We implanted drug-eluting stents into the LCx and RCA, and a bare metal stent into the subclavian artery. While revascularization improved the patient's cardiac function: 73% LVEF, the difference in the forearm arterial blood pressures and cold feeling of the right arm disappeared: right arm, 130/51 mmHg; left arm, 133/54 mmHg.

In 1944, Reubi[1] was the first to report vascular abnormalities associated with NF1. Although vascular abnormalities, such as stenosis or aneurysm, were incidentally found in multiple vessels at younger age, coronary artery diseases, especially NF1-related multiple artery stenoses, were sporadic.[2] To date, the pathophysiology and mechanism of vascular changes in patients with NF1 remain poorly understood. Green *et al.*[3] suggested that fibromuscular dysplasia with prominent thickening of the intima resulted from smooth muscle cell proliferation. Lie[4] reviewed the histopathological pattern of NF1-related vasculopathy and demonstrated that intimal vascular smooth muscle cell proliferation and neoangiogenesis in coronary artery might cause arterial stenosis. While virtual-histology with IVUS characterized that coronary plaques were primarily fibrotic and lipid-poor plaques (*Figure 3E–G*), a grey-scale IVUS image of the subclavian artery revealed concentric fibrous plaque (>*Figure 3H*)—all consistent with the autopsy findings of Hamilton *et al.*[5] Hence, we believe that plaques in our patient were related to NF1 plaques rather than atherosclerotic plaques. To our best knowledge, this is the first report of multiple stenoses, revascularization with stent implantation, and virtual-histology findings in patients with NF1.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

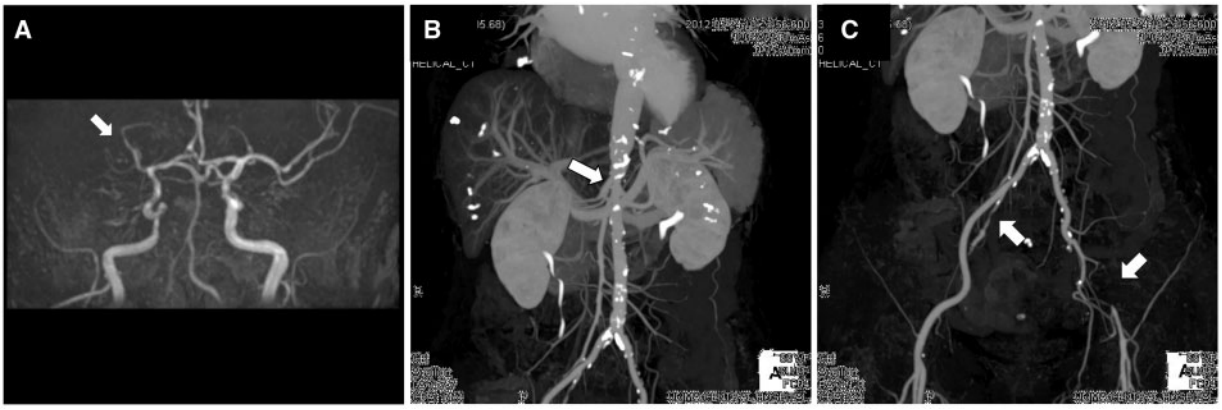

Figure 2 Magnetic resonance angiography shows stenosis of the right middle cerebral artery (*A*). Multiplanar reconstructed computed tomography angiography images indicate stenosis in the abdominal aorta at the proximal renal artery bifurcation (*B*) in addition to bilateral common iliac artery stenoses (*C*).

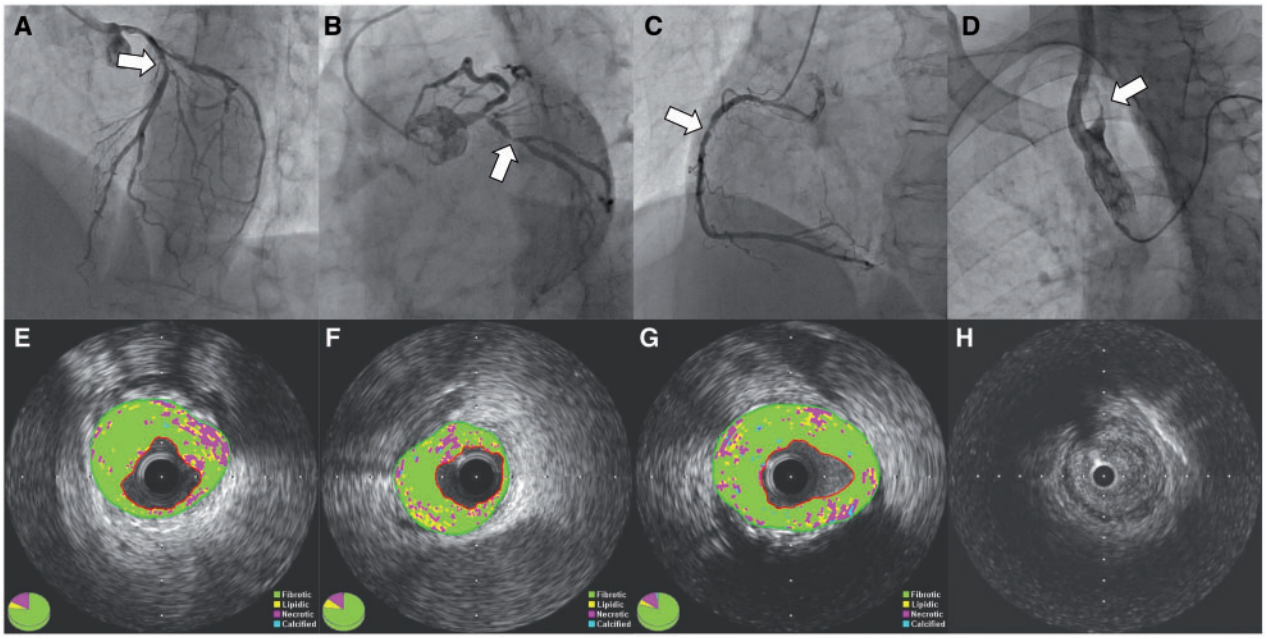

Figure 3 (*A*) Left anterior oblique cranial view of the left coronary artery shows 75% stenosis in the middle portion of the left anterior descending coronary artery and the diagonal braches. (*B*) Left anterior oblique caudal view of the left coronary artery shows 99% stenosis in the ostium and 90% stenosis in the middle portion of the left circumflex coronary artery. (*C*) Left anterior oblique view of the right coronary artery angiogram shows 90% stenosis in the middle portion of the right coronary artery. (*D*) Brachiocephalic artery angiogram shows 99% stenosis in the proximal segment of the right subclavian artery. (*E–G*) Characterization of the coronary artery tissues of each cross-sectional segment indicated with the arrows at the top (left anterior descending coronary artery, left circumflex coronary artery, and right coronary artery, respectively) by means of iMap intravascular ultrasound (iMap, 40 MHz, mechanical-type transducer, 3.2 F Atlantis; Boston Scientific Corp., Marlborough, MA, USA; QIvus analytical software, Medis Medical Imaging Systems bv, Leiden, the Netherlands). Green, fibrotic plaque; yellow, lipidic plaque; pink, necrotic plaque; blue, calcified plaque. (*H*) A cross-sectional grey-scale intravascular ultrasound image of the stenosis segment in the right subclavian artery (arrow on the top, *D*). In this case, plaques were fibrotic-dominant plaques.

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Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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