Silent Very Late Thrombotic Occlusion of Sirolimus-Eluting Stent Confirmed by Directional Coronary Atherectomy

Takashi Nakayama, MD; Yoshio Kobayashi, MD; Hiroyuki Takano, MD; Nakabumi Kuroda, MD; Kenzo Hiroshima, MD*; Issei Komuro, MD

Stent thrombosis is defined as thrombotic occlusion of a stent resulting in acute coronary syndrome (ACS). However, all thrombotic occlusions of stents might not result in ACS. The present case report describes silent, very late thrombotic occlusion of a drug-eluting stent that was confirmed from specimens removed by directional coronary atherectomy.

Key Words: Angioplasty; Coronary artery disease; Restenosis; Stent; Stent thrombosis

Late stent thrombosis after drug-eluting stent (DES) placement has emerged as a major concern![1–4] Stent thrombosis is defined as thrombotic occlusion of a stent resulting in acute coronary syndrome (ACS)[5–7] but all thrombotic occlusions of stents might not result in ACS. The present case report describes silent, very late thrombotic occlusion of DES that was confirmed from specimens removed by directional coronary atherectomy (DCA)[8,9]

Case Report

A 61-year-old man with a history of hypertension was admitted because of exertional angina. Coronary angiography revealed 90% stenosis in the proximal left anterior descending coronary artery (LAD) and collaterals from the right coronary artery (**Fig 1A**), so the patient was referred for coronary angioplasty. An 18-mm sirolimus-eluting stent (SES, Cypher™, Cordis, Miami, FL, USA), premounted on a 3.5-mm balloon catheter, was deployed at 16 atm. The final angiogram (**Fig 1B**) and intravascular ultrasound (IVUS) (**Fig 2A**) showed a good result. He received ticlopidine (100 mg twice daily) plus aspirin (100 mg/day) for 3 months and thereafter was on aspirin monotherapy. Seven months later follow-up angiography demonstrated no in-stent restenosis (**Fig 1C**). Follow-up IVUS that was performed as part of clinical research demonstrated minimum intimal hyperplasia without incomplete apposition (**Fig 2B**).

Because of exertional angina persisting for several months, he was referred for coronary angiography 23 months after SES implantation. There were no electrocardiographic abnormalities to indicate ACS (**Fig 3**) or elevated levels of biomarkers for myocardial necrosis. Coronary angiography demonstrated total occlusion of the SES (**Fig 1D**) and complete filling of the LAD distal to the SES from the right coronary artery (**Fig 1E**). The patient was referred for coronary angioplasty. A 0.014-inch Conquest Pro guidewire (Asahi Intecc, Seto, Japan) supported with a tornus catheter (Asahi Intecc) was crossed through the total occlusion. Predilatation using a 2.0-mm Lacrosse balloon catheter (Goodman, Nagoya, Japan) inflated at 6 atm was performed. The guidewire was then changed to a flexi-wire (Guidant, Santa Clara, CA, USA). IVUS was performed and demonstrated a heterogeneous mass in the stent (**Fig 2C**). With the informed consent of the patient, DCA using a Flexicut directional atherectomy device (Guidant) was performed with the intention of obtaining tissue in the stent to clarify the mechanism of delayed total occlusion (**Fig 1F**)[8,9]; informed consent for a case report was obtained later. A total of 7 cuts were performed, inflating the balloon up to 50 psi. A 28-mm SES premounted on a 3.0-mm balloon catheter was then deployed at 18 atm. The final angiogram showed a good result (**Fig 1G**). Pathological examination of the DCA specimens demonstrated organized thrombus rather than neointima (**Fig 4**).

Discussion

DES has dramatically reduced the incidence of in-stent restenosis[6,7] but a new problem of late stent thrombosis has appeared![1–4] Previous clinical studies used relatively restrictive and non-uniform definitions of stent thrombosis[6,7] These definitions uniformly regarded evidence of any myocardial infarction with angiographic confirmation of in-stent thrombus or unexplained death within 30 days after the procedure as stent thrombosis, but varied when myocardial infarction was present without angiographic confirmation of target-vessel involvement. Thus, standardized definitions of stent thrombosis were required and were recently proposed by the newly formed Academic Research Consortium (ARC)[5] Their definition of definite stent thrombosis requires the presence of ACS with angiographic or autopsy evidence of thrombus or occlusion. Probable stent thrombosis includes unexplained death within 30 days after the procedure or acute myocardial infarction involving the target-vessel territory without angiographic confirmation.

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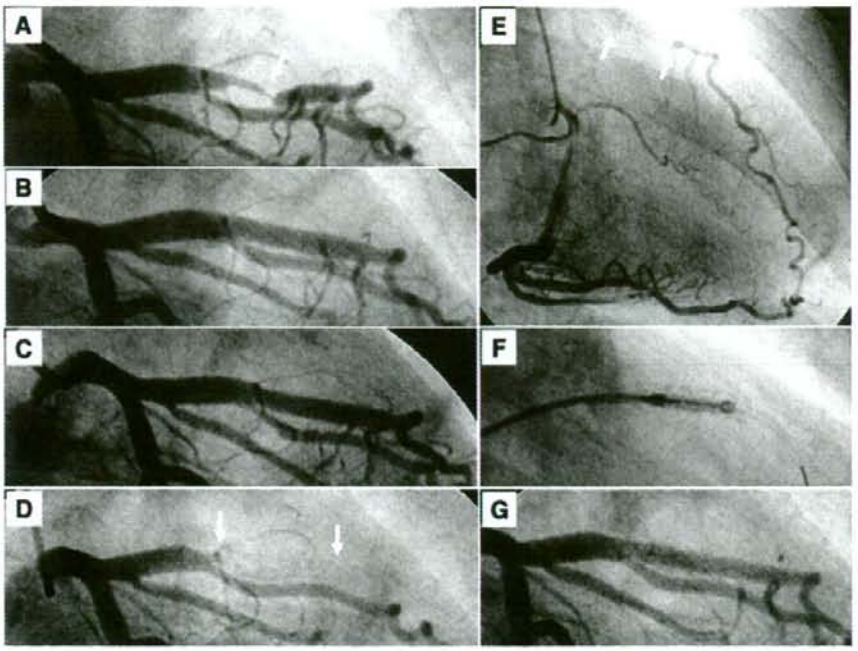

Fig 1. Coronary angiography showing 90% stenosis (arrow) of the proximal left anterior descending coronary artery (LAD) (**A**). After sirolimus-eluting stent (SES) implantation, angiography demonstrates a good result (**B**). Seven months later, follow-up angiography shows no in-stent restenosis (**C**). Coronary angiography demonstrates total occlusion of the SES (**D**) and complete filling of the LAD distal to the SES from the right coronary artery (**E**). Arrows (**D**,**E**) indicate the proximal and distal edges of the SES. Directional coronary atherectomy is performed (**F**) and the final angiogram shows a good result (**G**).

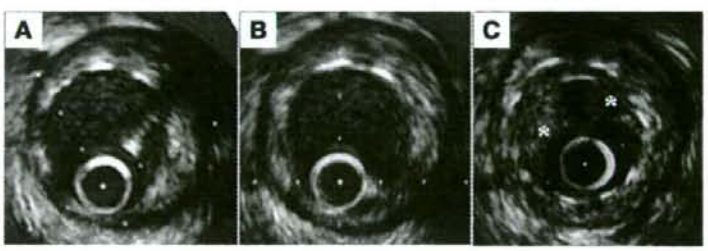

Fig 2. (**A**) Intravascular ultrasound (IVUS) after sirolimus-eluting stent implantation (stent cross-sectional area 7.6 mm^2). (**B**) Follow-up IVUS (stent cross-sectional area 7.7 mm^2). Note minimum intimal hyperplasia without incomplete apposition. (**C**) IVUS after predilatation for total occlusion (lumen cross-sectional area 2.6 mm^2 and stent cross-sectional area 7.7 mm^2). *Note heterogeneous mass in the stent.

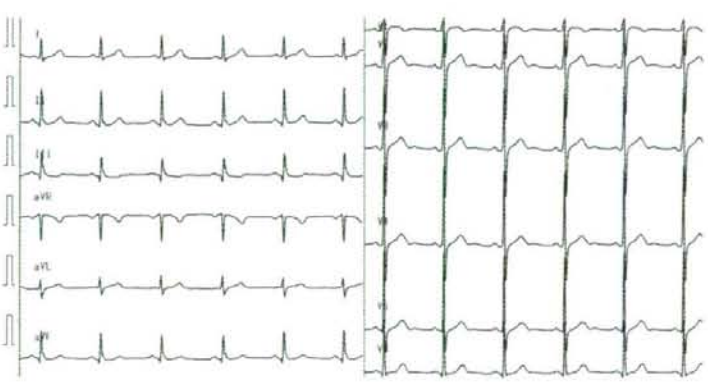

Fig 3. Electrocardiogram at 23 months after sirolimus-eluting stent implantation.

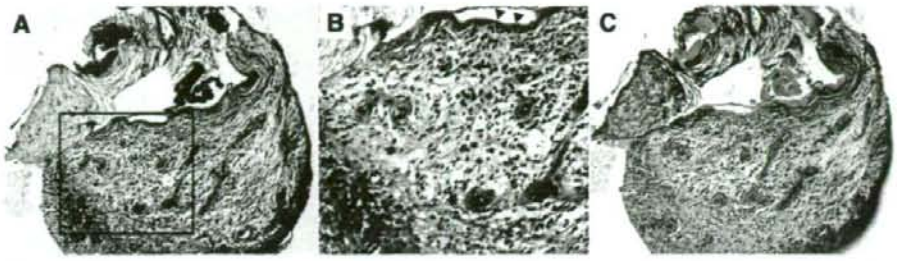

Fig 4. Hematoxylin and eosin (HE)-stained (**A**, **B**) and elastica van Gieson-stained (**C**) sections of a directional coronary atherectomy (DCA) specimen. (**B**) is a magnified view of the inset in (**A**). HE demonstrates fibrin (arrowheads), lymphocytes, fibroblast, hemosiderin-laden macrophages (black arrow) and neovascularization (white arrow). There are no smooth muscle cells and scant collagen fibers (red in **C**), which indicate that the DCA specimen is organized thrombus rather than neointima.

Possible stent thrombosis includes any unexplained death occurring at least 30 days after the procedure. Stent thrombosis was also classified as early (0–30 days), late (31–360 days) and very late (>360 days).

The reported incidence of late and very late stent thrombosis after DES implantation ranges between 0.2% and 0.7%[1–3] In the present case, very late thrombotic occlusion of SES occurred in a patient without ACS, which might be considered as delayed in-stent restenosis (late catch-up phenomenon)[10] unless DCA and pathological examination were performed. According to the definitions of stent thrombosis by either previous clinical studies or the ARC[5–7] the thrombotic occlusion of SES in the present case is not defined as stent thrombosis because the patient did not present with ACS. Thus, the incidence of thrombotic occlusion of DES may be higher than reported. There were well-developed collaterals in the present case, which might have prevented the patient from presenting with ACS. A previous study showed that, utilizing a sensor-tipped pressure guidewire, one-fifth of individuals without stenotic lesions had immediately recruitable collateral flow to the respective vascular area sufficient to prevent myocardial ischemia during a brief coronary occlusion[11] In the present case, before SES implantation, collateral vessels from the right coronary artery supplied the distal LAD, so there may have been rapid recruitment of well-developed collaterals[11,12] Gradual thrombus formation in SES, not resulting in sudden total occlusion, and recruitment of well-developed collaterals is another possibility for the patient not having presented with ACS. Silent thrombotic occlusion of a stent may occur in patients with no symptoms of myocardial ischemia (ie, some patients with diabetes mellitus or stent implantation in the infarct-related artery)[13] although the present case had exertional angina and did not have diabetes mellitus or a history of previous myocardial infarction.

Conclusions

This case report shows very late thrombotic occlusion of DES in a patient without ACS, which was confirmed by specimens extracted by DCA. The incidence of very late thrombotic occlusion of DES might be higher than reported.

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Letter to the Editor

Buerger's disease-like vasculitis associated with Kimura's disease

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Abstract

A 46-year-old man was first diagnosed as Buerger's disease according to his clinical and radiological features because he had no evidence of parasitic, allergic and connective tissue disease. Soft subcutaneous nodules suspected of lymphadenopathy on the bilateral inguinal regions were recognized after admission. Positron emission tomography scan showed the increased uptake of ^{18}F-fluoro-2-deoxyglucose in the bilateral inguinal regions. We finally diagnosed him as Kimura's disease based on pathologic findings and laboratory data, and started steroid therapy. The uptake of ^{18}F-fluoro-2-deoxyglucose disappeared and his leg pain was improved after the treatment. This is the first case report presenting a patient of Kimura's disease with Buerger's disease-like vasculitis who was demonstrated by positron emission tomography.

Keywords: Buerger's disease; Eosinophilia; Kimura's disease; Positron emission tomography; Prednisolone

1. Introduction

Buerger's disease (BD) is a nonatherosclerotic inflammatory disorder of unknown etiology that affects small and medium-sized vessels of the extremities. The diagnosis of BD requires the elimination of many other diseases because of the absence of specific diagnostic criteria. Kimura's disease (KD) is a rare chronic inflammatory disorder presenting subcutaneous masses predominantly in the head and neck region, and peripheral eosinophilia. Positron emission tomography (PET) scan is a powerful imaging technique in the diagnosis and follow-up of many diseases including cancer, infection and inflammation. We report a case of KD with BD-like vasculitis who was demonstrated by ^{18}F-fluoro-2-deoxyglucose (FDG)-PET.

2. Case report

A 46-year-old man was admitted with a 1-month history of sharp rest pain in right calf. He had ischemic ulceration between the third and fourth toes of his right foot (Figs. 1A and 2A). He has smoked 10 cigarettes or less per day for 25 years. The digital subtraction angiogram of the extremities showed multiple occlusions of the distal arteries including right anterior tibial artery, right posterior tibial artery, right peroneal artery, left anterior tibial artery and left peroneal artery (Fig. 3). He was first diagnosed as BD according to his clinical and radiological features because he had no evidence of parasitic, allergic and connective tissue disease. Soft subcutaneous nodules suspected of lymphadenopathy on the bilateral inguinal regions were recognized after admission. No other lymph node was palpable. PET using FDG performed after overnight fasting and heparin sodium injection (2000 IU) revealed increased uptake of FDG in the bilateral inguinal regions (Fig. 4A). Since these lesions were considered as lymphoproliferative disorder, an excision biopsy of left inguinal nodule was performed. The pathology of the specimen revealed hyperplasia of lymphoid follicles

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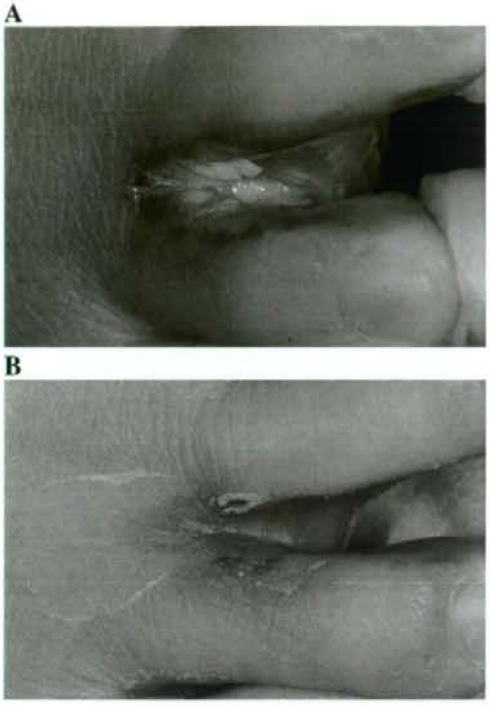

Fig. 1. Ischemic ulceration between the third and fourth toes of right foot (A) on admission and (B) after steroid therapy.

with germinal centers and massive infiltration of eosinophils without malignancy, which are typical findings of KD (Fig. 5A and B). Laboratory tests showed peripheral eosinophilia (WBC 20800, 56% eosinophils) and elevated serum immunoglobulin E level of 1921 U/mL. Screening for rheumatoid factor, anti-nuclear antibodies and ANCA were all negative. Protein C and protein S were within normal ranges. We finally diagnosed him as KD based on pathologic findings and laboratory data, and started the treatment with prednisolone 40 mg/day. After the treatment, eosinophilia, the ulcer and rest pain of right foot improved quickly (Figs. 1B and 2B). The FDG uptake in the bilateral inguinal regions disappeared after 4 weeks by the treatment with prednisolone (Fig. 4B).

3. Discussion

BD is a nonatherosclerotic inflammatory disorder of unknown etiology that affects small and medium-sized vessels of the extremities and has a strong association with smoking [1]. Typically, affected persons are young men and the symptoms appear before the age of 40 years old. Cessation of cigarette smoking is the only known effective therapy. The diagnosis of BD requires ruling out other diseases because of the absence of specific diagnostic criteria. KD is a rare chronic inflammatory disorder presenting subcutaneous masses predominantly in the head and neck region, peripheral eosinophilia and elevated serum immunoglobulin E level [2]. Histologically, lymphoid follicles formed from lymphocytes,

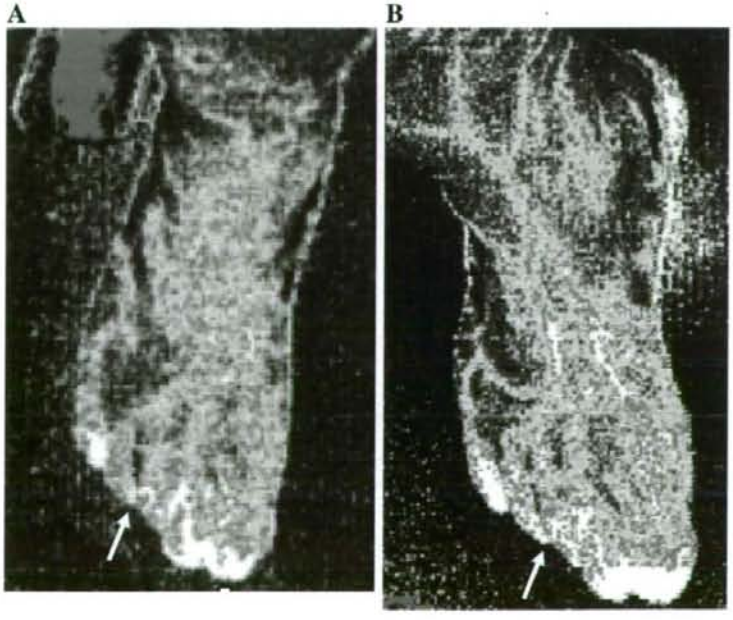

Fig. 2. Laser Doppler imaging of right foot (A) on admission and (B) after steroid therapy. Color-coded images represent blood flow distribution. The highest perfusion is displayed as white. The steroid therapy improved the peripheral blood supply (arrows).

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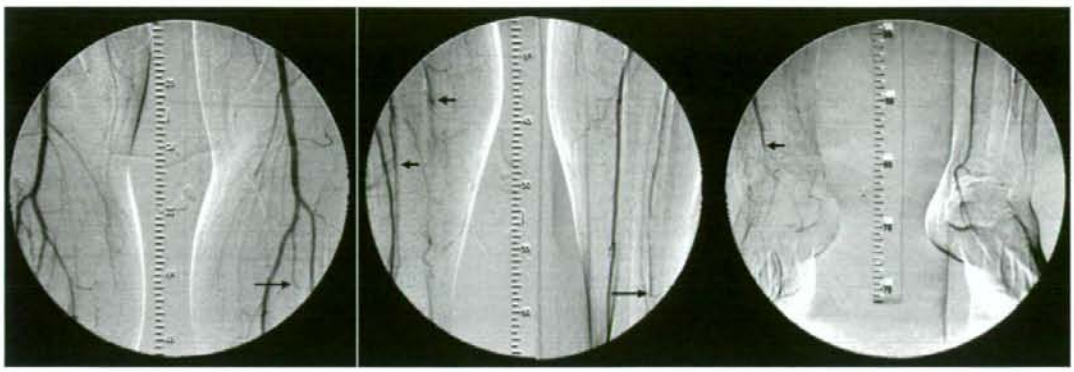

Fig. 3. Multiple occlusions of the crural arteries including right anterior tibial artery, right posterior tibial artery, right peroneal artery (arrowheads), left anterior tibial artery and left peroneal artery (arrows).

plasma cells and abundant eosinophils are characteristic. KD occurs endemically in Asian males. Renal abnormalities are associated with KD [3], but there is only one case on KD patient with BD [4]. PET scan is a powerful imaging technique in the diagnosis and follow-up of many diseases including cancer, infection and inflammation. Recently, the generalized lymphadenopathy was demonstrated in a patient with KD by FDG-PET [5]. In the present case, FDG-PET showed the increased uptake of FDG in the bilateral inguinal regions, which disappeared after steroid therapy. Concomitantly, the pain and ulceration of his right leg were improved. To our knowledge, there is no report presenting a patient of KD with BD-like vasculitis who was demonstrated by FDG-PET. Although the pathogenesis of BD is still unknown, steroid therapy is effective to stabilize inflammation in the patients with BD-like vasculitis. Therefore, it is important to

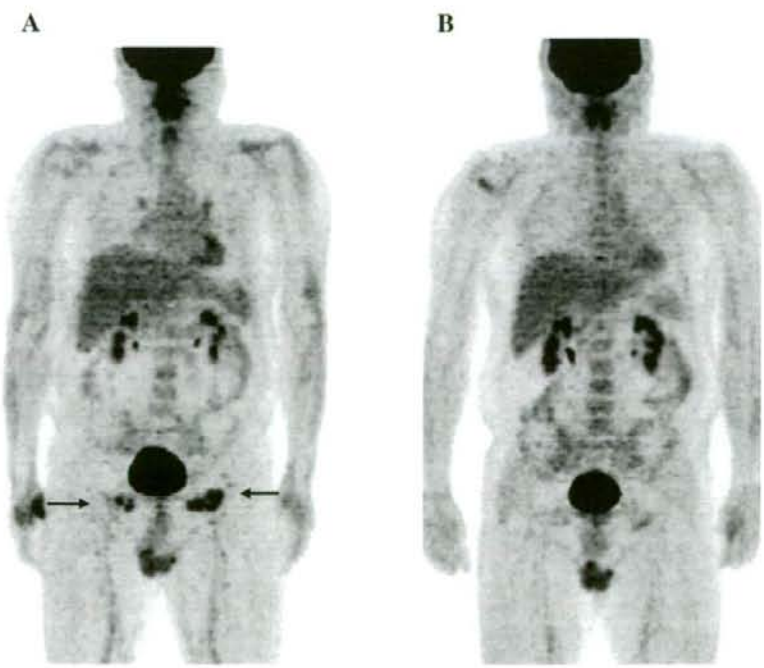

Fig. 4. FDG uptake (A) on admission and (B) after steroid therapy. The FDG uptake in the bilateral inguinal regions (arrows) disappeared 4 weeks after the steroid therapy.

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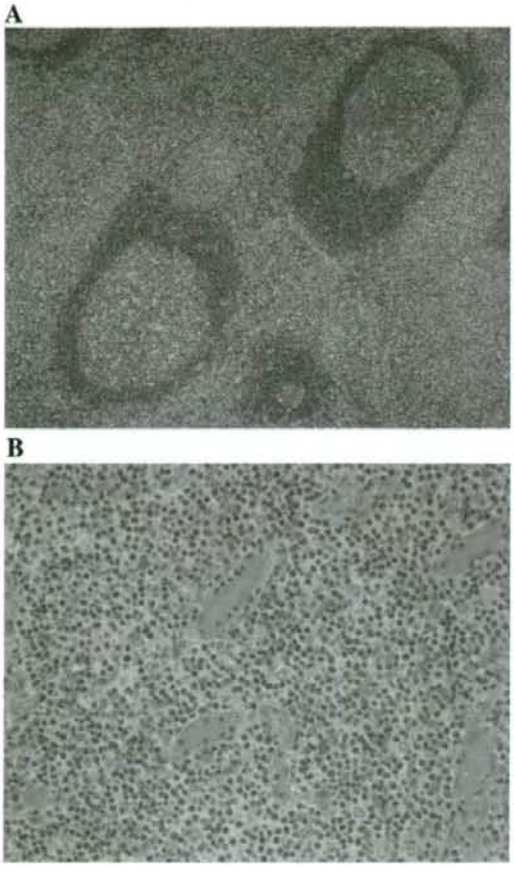

Fig. 5. Photomicrograph of the left inguinal nodule showed hyperplasia of lymphoid follicles with germinal centers and massive infiltration of eosinophils (hematoxylin and eosin staining). A, lower magnification, × 40. B, higher magnification, × 200.

examine the patients with vasculitis by FDG-PET whether they have lymphadenopathy or tumor-like lesion.

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Letter to the Editor

Abdominal aortic pseudoaneurysm caused by prolonged methicillin-resistant *Staphylococcus aureus* sepsis

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Abstract

The mechanism of pseudoaneurysm formation caused by prolonged sepsis is thought to be related to the vascular endothelium being directly invaded and broken by bacteria. Moreover, matrix metalloproteinases (MMPs) which are up-regulated by chronic inflammation have been reported to be implicated in the pathogenesis of aneurysm development through increased proteolysis of extracellular matrix proteins. An effective treatment for infected pseudoaneurysm remains unsettled. Surgery is generally performed, however, because the patients in most of these cases are in very poor physical condition, the operation is associated with high morbidity and mortality. A more successful alternative is endovascular treatment. Recent reports indicate low morbidity and mortality rates with this treatment. If the patient in this case had been in better condition, we could have selected endovascular stent-grafting for her treatment.

Keywords: Pseudoaneurysm; Multi-slice CT; Matrix metalloproteinases

1. Case report

In October 2006, a 77-year-old woman underwent pancreatoduodenectomy for a malignant pancreatic tumor. On the 8th postoperative day, her temperature was 39.3 °C. At that time, laboratory tests showed a white cell count of $1.82 \times 10^4/\mu l$ and a C-reactive protein (CRP) of 5.6 mg/dl. The central venous catheter tip and blood cultures were positive for methicillin-resistant *Staphylococcus aureus* (MRSA). In view of antibiotic sensitivity test results, arbekacin (ABK) was the most sensitive to MRSA and the treatment with ABK was started. On the 13th postoperative day, she suddenly complained of right inguinal pain and lumbar pain. Abdominal and pelvic X-ray revealed no abnormal findings. A 64-slice computed tomography (CT) resulted in the same (Fig. 1A and B). However, the patient continued to complain of the lumbar pain. A second series of blood cultures made after 15 days of the treatment with ABK were still positive for MRSA. Therefore, ABK treatment was changed into vancomycin (VCM). On the 31st postoperative day, the 64-slice CT for the second time showed that a 2.1-cm false aneurysm of abdominal aortaproximal to the divergence of common iliac artery (Fig. 1C and D). We consulted cardiac surgeons about indication of the surgery, however, surgery was ruled out owing to her greatly weaken condition. Although medication was continued, patient's hypotension and MRSA sepsis were not controlled. On the 72nd postoperative day, she died of progressive renal failure.

2. Discussion

Pseudoaneurysm is usually known to be caused by trauma [1] and surgical treatment [2] but rarely MRSA infection.

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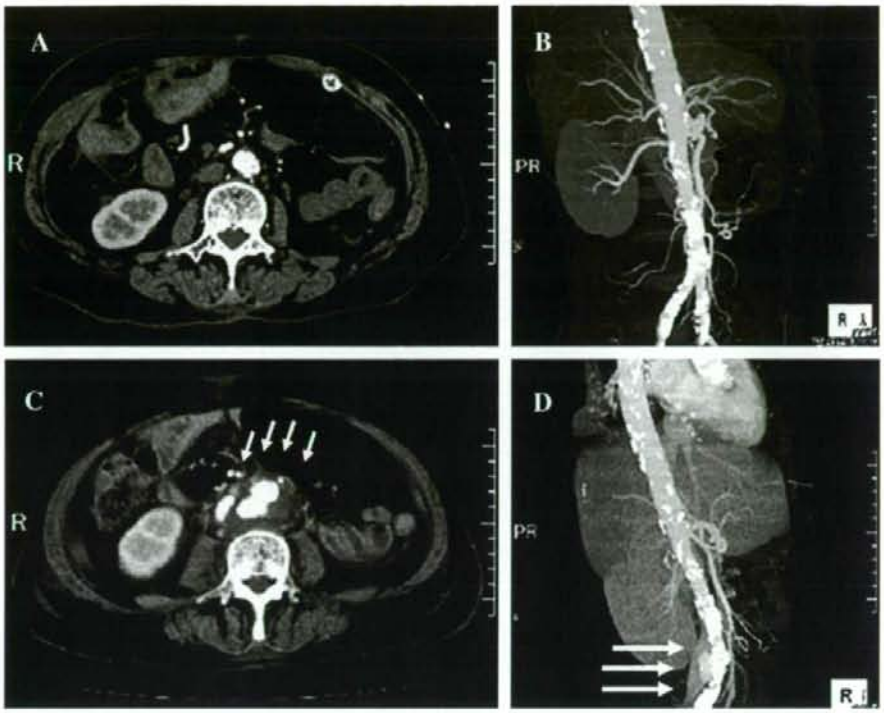

Fig. 1. Multi-slice CT changes shown in abdominal aortic pseudoaneurysm. A 64-slice CT revealed no abnormal findings (A, B). On the 31st postoperative day, the 64-slice CT for the second time showed that a 2.1-cm false aneurysm of abdominal aorta proximal to the divergence of common iliac artery (arrows) (C, D).

This case was thought to have been caused by prolonged MRSA sepsis based on the comparison between CT findings for the first time (Fig. 1A and B) with for second time (Fig. 1C and D). Additionally, it was hardly possible that abdominal aorta had been injured by the surgical procedure in view of its site.

If we suspect pseudoaneurysm with infection, multi-slice CT may be a useful tool in detecting unexpected lesion in a non-invasive manner [3,4]. In fact, CT angiography was very helpful in detecting the pseudoaneurysm and we should further use multi-slice CT.

The mechanism of pseudoaneurysm formation caused by prolonged sepsis is thought to be related to the vascular endothelium being directly invaded and broken by bacteria. Moreover, matrix metalloproteinases (MMPs) which are up-regulated by chronic inflammation have been reported to be implicated in the pathogenesis of aneurysm development through increased proteolysis of extracellular matrix proteins [5].

An effective treatment for infected pseudoaneurysm remains unsettled. Surgery is generally performed, however, because the patients in most of these cases are in very poor physical condition, the operation is associated with high morbidity and mortality [6]. A more successful alternative is endovascular treatment. Recent reports indicate low morbidity and mortality rates with this treatment [6]. If the patient in this case had been in better condition, we could have selected endovascular stent-grafting for her treatment.

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Letter to the Editor

Active myocarditis in a patient with chronic active Epstein–Barr virus infection

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Abstract

Chronic active Epstein–Barr virus (CAEBV) infection is characterized by chronic or recurrent infectious mononucleosis-like symptoms and the prognosis of CAEBV infection is quite poor. The incidence of myocarditis as a complication of EBV infection is not so high and it is unusual that heart failure appears as the initial symptom. However, it is very important to detect and treat chronic active myocarditis in the early phase of CAEBV infection because chronic active myocarditis disorganizes and decreases cardiomyocytes, resulting in the progression to heart failure. We report a case of a 45-year-old man with CAEBV infection for 5 years. Echocardiography revealed moderate left ventricular systolic dysfunction with mild pericardial effusion. Endomyocardial biopsies demonstrated massive lymphocytic infiltration with adjacent myocytolysis and necrosis of cardiomyocytes suggesting active myocarditis. Immunohistological analysis of biopsies revealed that the infiltrating cells were mainly T lymphocytes. And some of the infiltrating cells showed a positive signal for the EBV-encoded small nuclear RNA by *in situ* hybridization. Positron emission tomography using ^{18}F-fluoro-2-deoxyglucose (^{18}F-FDG) performed revealed increased uptake of ^{18}F-FDG of whole left ventricular wall with mild heterogeneity.

Keywords: Biopsy; Epstein–Barr virus; Myocarditis; PET

1. Introduction

Epstein–Barr virus (EBV), a ubiquitous virus classified as a γ-herpesvirus, causes infectious mononucleosis and post-transplant lymphoproliferative disorder. Chronic active EBV (CAEBV) infection is characterized by chronic or recurrent infectious mononucleosis-like symptoms and by an abnormal pattern of anti-EBV antibodies with high titers to virus capsid antigen (VCA) and early antigen (EA), and low titers to Epstein–Barr nuclear antigen (EBNA) [1]. The prognosis of CAEBV infection is quite poor and the major causes of death are liver failure and haemophagocytic syndrome.

2. Case report

A 45-year-old man has had fever of unknown origin and general malaise for 5 years from 2000. He was diagnosed as having CAEBV infection because of his symptoms and the abnormal patterns of anti-EBV antibodies in 2003 and followed up without any medication. He developed fever, dyspnea on exertion, general malaise, and hepatosplenomegaly in April 2005. Antibody titer tests against EBV revealed EBVVCA-IgG ×10,240, EBVEA-IgG ×640, and EBNA ×10. As his symptoms persisted despite treatment with prednisolone, he was admitted to our hospital in September 2005 for evaluation of heart failure and further treatments with chemotherapy. The ECG on admission displayed atrial fibrillation and sporadic ventricular premature contractions. Echocardiography revealed moderate left ventricular (LV)

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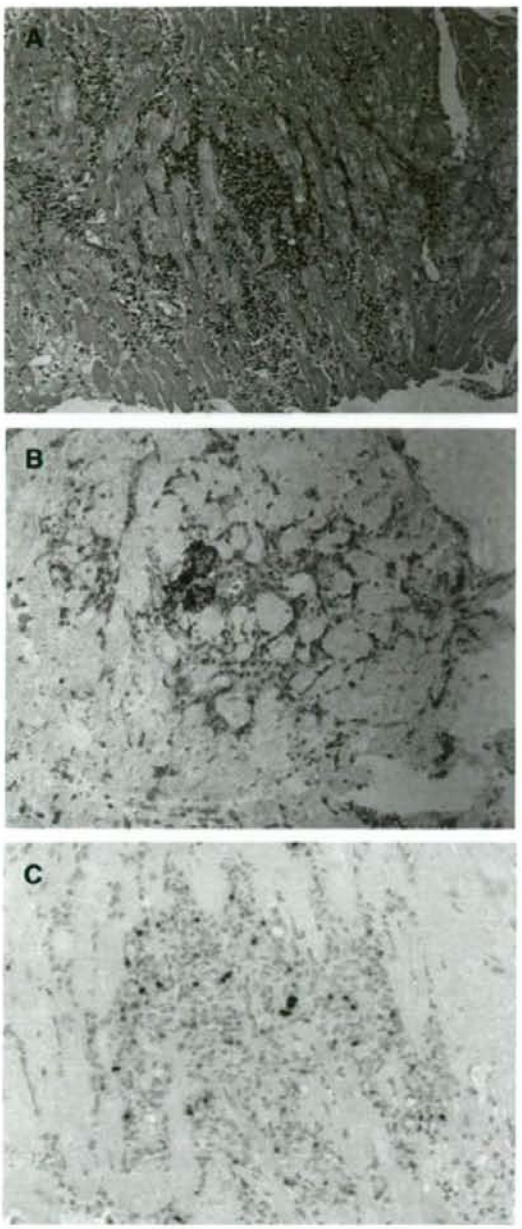

Fig. 1. Histological results of endomyocardial biopsies. A, Histology (hematoxylin and eosin staining) demonstrated active myocarditis with focal lymphocytic infiltration with adjacent myocytolysis (×100). B, Immunohistological staining of CD45RO/UCHL-1^{+} T cells with focal infiltration pattern (×100). C, *In situ* hybridization study for Epstein–Barr virus-encoded small RNA in T cells (×200).

systolic dysfunction with mild pericardial effusion. Endomyocardial biopsies obtained from the LV demonstrated massive lymphocytic infiltration with adjacent myocytolysis and necrosis of cardiomyocytes suggesting active myocarditis (Fig. 1A). Immunohistological analysis of biopsies revealed that the infiltrating cells were mainly T lymphocytes (Fig. 1B). And some of the infiltrating cells showed a positive signal for the EBV-encoded small nuclear RNA by *in situ* hybridization (Fig. 1C). Positron emission tomography (PET) using ^{18}F-fluoro-2-deoxyglucose (^{18}F-FDG) performed after overnight fasting and heparin sodium injection (2000 IU) revealed increased uptake of ^{18}F-FDG of whole LV wall with mild heterogeneity (maximum at lateral wall) (Fig. 2). Since his liver dysfunction got worse in spite of prednisolone, immunochemotherapy with prednisolone, cyclosporin A, and etoposide was started. Although his physical condition and liver dysfunction were temporarily ameliorated, multiple organ failure and disseminated intravascular coagulation were accompanied later and he died 3 months after the admission.

3. Discussion

The patient was thought to have been suffering from CAEBV infection for 5 years. He did not have heart failure at first and the examination for cardiac function was not performed. The incidence of myocarditis as a complication of EBV infection is not so high and it is unusual that heart failure appears as the initial symptom [2,3]. However, chronic active myocarditis disorganizes and decreases cardiomyocytes, resulting in the progression to heart failure. It is very important to detect and treat chronic active myocarditis in the early phase of CAEBV infection. Endomyocardial biopsies are useful but invasive. ^{18}F-FDG PET images can detect myocardial inflammation such as sarcoidosis and myocarditis when obtained at fasting state [4]. Although recent studies demonstrated that contrast-enhanced cardiac magnetic resonance is useful to detect acute myocarditis, late enhancement is mainly related to myocardial necrosis and interstitial edema characterizing the acute phase of inflammatory process [5]. In contrast, non-physiological myocardial uptake of ^{18}F-FDG under the fasting condition may indicate the activity of myocardial inflammation. In the present case, the results of the biopsy specimens and ^{18}F-FDG PET images of the patient revealed myocardial inflammation suggesting the existence of myocarditis. To our knowledge, this is the first report indicating the usefulness of endomyocardial biopsy and ^{18}F-FDG PET in the identification of myocarditis with CAEBV infection.

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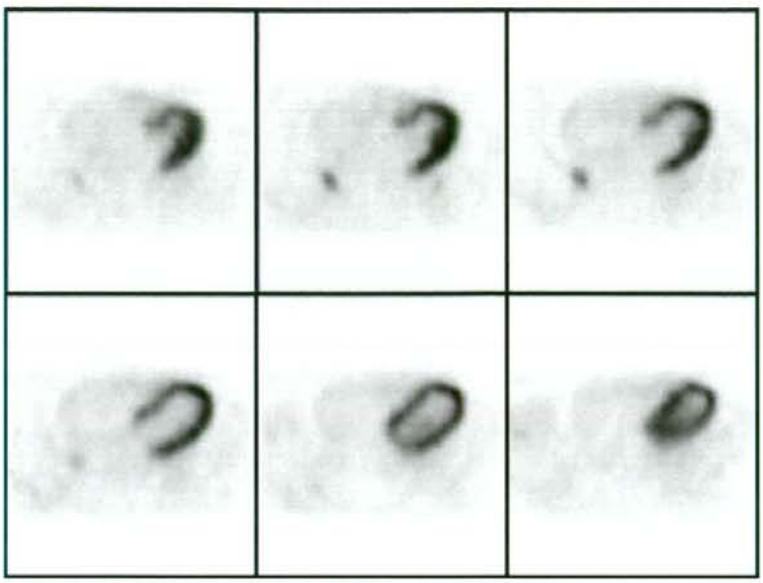

Fig. 2. Transaxial view of cardiac ^{18}F-FDG PET. Diffuse uptake of ^{18}F-FDG of the left ventricle with mild heterogeneity (maximum at lateral wall) was observed even after overnight fasting with heparin sodium injection.

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Letter to the Editor

Takayasu arteritis evaluated by multi-slice computed tomography in an old man

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Abstract

In the case of patients with Takayasu arteritis (TA), they consult a doctor for the first time when they have a slight fever, shoulder pain, chest pain, back pain, or headache, or when they are pointed out to have high CRP or anemia by chance in medical check-up. In TA, they are usually young women. In our case, the very old patient had bilateral massive pleural effusion and aortic aneurysm with a 64-slice computed tomography (CT). TA commonly affects primarily large elastic arteries such as the aorta and its main branches. Steroid was very effective for suppression of inflammatory symptom being dose-dependent. His pleural effusion had been decreasing without reducing the size of aortic aneurysm. Multi-slice CT was a very useful tool to detect unexpected lesion in Takayasu arteritis in a non-invasive manner.

Keywords: Takayasu arteritis; Multi-slice CT; Matrix metalloproteinases

1. Case report

In August 2007, a 94-year-old man was admitted to the hospital with low appetite, left shoulder pain and slight fever rising. He had hypertension, but his eye ground findings were not particular. He didn't show extremities claudication, bruit, blood pressure asymmetries and pulse asymmetries. White blood cell counts, liver and renal function were normal. He had inflammatory anemia (Hb 8.8 g/dl, UIBC 81 μg/dl, TIBC 95 μg/dl) and high C-reactive protein (CRP) (9.4 mg/dl). His antinuclear antibody was positive (320 times) and his complement activity was low in blood serum. On the other hand, bacterial culture and other evidence for secondary vasculitis due to other inflammatory indicators (p-ANCA, c-ANCA) were negative. Ultrasonic echocardiography showed only mild left ventricular hypertrophy due to hypertension. It did not show aortic regurgitation and normal left ventricular wall motion. A 64-slice computed tomography (CT) showed bilateral massive pleural effusion and aortic aneurysm with mural thrombus (arrow in Fig. 1A) and wall thickening in aortic arch (arrowhead in Fig. 1B). But we had detected no stenosis on the three branches of aortic arch and no abdominal aortic aneurysm. We had thought that he had inflammatory aortic aneurysm (vasculitis syndrome) and we made a diagnosis of a part of aortic arch syndrome (Takayasu arteritis: TA) with diagnostic criteria by the Ministry of Health and Welfare in Japan. We administrated predonisolone (PSL) 20 mg/day which decreased the fever and CRP decreased from 14.1 to 1.1 for 20 days. His pleural effusion had been decreasing without reducing the size of aortic aneurysm and we controlled PSL 20 mg. Steroid was very effective for suppression of inflammatory symptom being dose-dependent.

2. Discussion

In case of patients with aortic arch syndrome, they consult a doctor for the first time when they have a slight fever,

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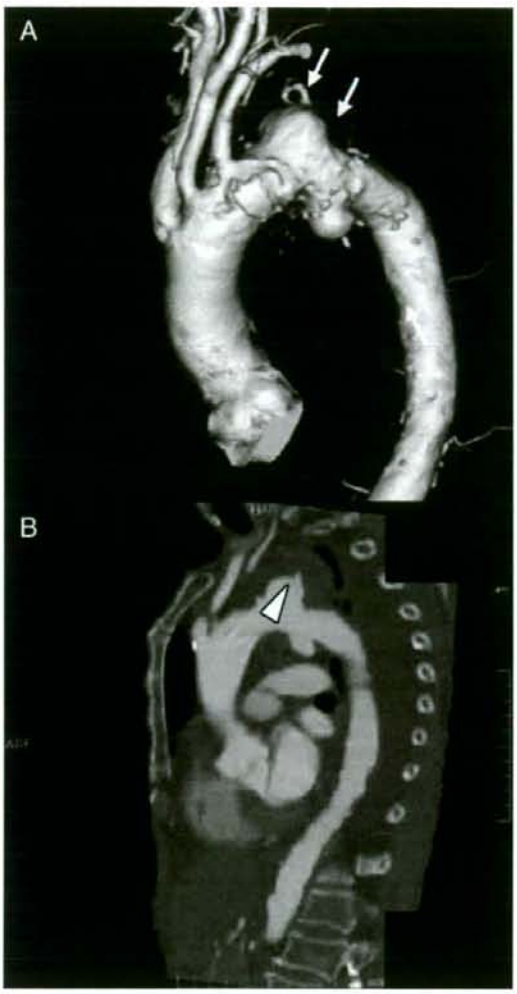

Fig. 1. (A) A 64-slice computed tomography (CT) showed massive aortic aneurysm (arrows), and (B) wall thickening in aortic arch (arrowhead).

shoulder pain, chest pain, back pain, or headache, or when they are pointed out to have high CRP or anemia by chance in medical check-up. In TA, women aged 20–30 years old are usually affected [1], and an old man in this case is very unique.

TA commonly affects primarily large elastic arteries such as the aorta and its main branches. We differentiated it from typical atherosclerosis, a disease much more likely to affect the lower extremity large vessels than the arms and the abdominal aorta than the aortic arch and root. Aneurysms are the most common and clinically most significant in the aortic root, where they can lead to valvular regurgitation. The earliest histological change appears to be a granulomatous inflammation in the adventia and outer layers of the affected arteries, followed by gradual progression to a panarteritis with inflammatory mononuclear cell infiltration. Inflammation and subsequent neointimal proliferation (intimal thickening) result in stenotic or occlusive lesions, whereas destruction of the elastica and muscularis may form dilatation or aneurysms [2]. In this process, proteases secreted from infiltrated cells are thought to play some role in the destruction of elastic fibers. Recently there was a report that matrix metalloproteinases (MMPs) are involved with inflammatory processes [3].

If they don't have appropriate therapy by steroid and inflammatory symptom is not well controlled, ischemic symptom, hypertension, and cardiac failure appear with progression of the disease. Multi-slice CT was a very useful tool to detect unexpected lesion in Takayasu arteritis in a non-invasive manner [4,5].

Because our patient was an old man, we did not expect that he had Takayasu arteritis. Since CT angiography was very helpful in detecting the aortic arch syndrome, we should further use multi-slice CT.

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