Takayasu Arteritis Presenting with Cholesterol Emboli

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ABSTRACT

Introduction: Takayasu arteritis is chronic vasculitis involving large vessels. Accelerated atherosclerosis has been documented in patients with Takayasu arteritis.

Case presentation: We have described a 53 year-old Thai woman who presented with 2-weeks history of painful erythematous to purplish patches on both soles. She has had hypertension since she was 29 years old and she has diabetes mellitus, dyslipidemia and cerebrovascular disease. Physical examination revealed decreased pulsation of her left brachial artery, difference in systemic blood pressure between both arms and bruit over subclavian arteries and the abdominal aorta. Dermatologic examination demonstrated multiple discrete ill-defined painful non-blanchable erythematous to violaceous macules and patches on her toes and soles. Some lesions were reticulated blanchable erythematous patches. Ulcer, digital cyanosis and gangrene were found on the tips of her toes. Magnetic resonance angiographic finding of her aorta and its branch was compatible with Takayasu arteritis. Skin biopsy was obtained from the livedo reticularis area of her left foot. The section revealed occlusion of arterioles by cholesterol crystal emboli.

Conclusion: Accelerated atherosclerosis has been reported in patients with Takayasu arteritis. Cholesterol emboli can be a rare presentation from atherosclerosis. Prevention and early recognition for atherosclerotic plaque should be performed in patients with Takayasu arteritis. Moreover, the effective control of traditional atherosclerotic risk factors is needed, in addition to the effective suppression of disease activity, for the management of Takayasu arteritis.

Keywords: Takayasu arteritis, atherosclerosis, cholesterol emboli

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CASE REPORT

A 53 year-old Thai woman presented with 2- weeks history of painful erythematous to purplish patches on both soles. She has had hypertension since she was 29 years old. She denied history of claudication. She received atenolol 50 mg/day and losartan 50 mg/day for hypertension treatment. Her blood pressure was well controlled. She has had diabetes mellitus and dyslipidemia for seven years. Her diabetes mellitus has been controlled by diet modification and she achieved her goal of glycemic level. She received simvastatin 20 mg/day for dyslipidemia treatment. Her recent fasting blood sugar and cholesterol levels were 93 mg/dl and 196 mg/dl, respectively. The patient denied cigarette smoking or alcoholic consumption.

One year ago, she presented with right hemiparesis. Computed tomography demonstrated left middle cerebral artery infarction. Her electrocardiography showed paroxysmal atrial fibrillation. No emboli were found on echocardiography. Carotid doppler ultrasound revealed no significant stenosis of carotid arteries. She received warfarin, adjusted following her INR level.

One month ago, she presented with bruises on her legs. Her INR level was 4.37. The physician decreased her dosage of warfarin and appointed her for one-month follow up.

Two weeks before her appointment, the patient developed painful erythematous to violaceous patches on her toes and soles. She denied fever and weight loss. No invasive cardiovascular procedure was done before the rash developed.

Physical examination revealed blood pressure of her right arm, left arm, right leg and left leg were 155/59,

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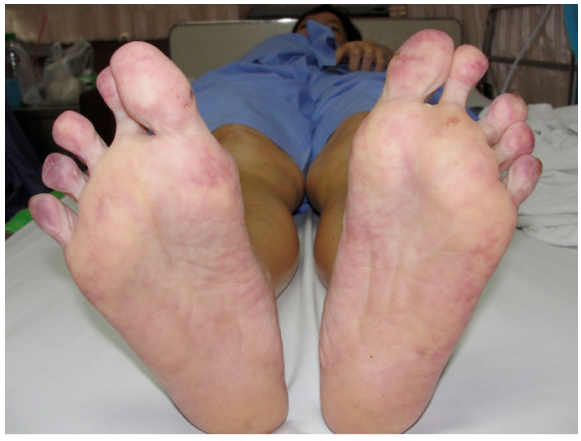

Fig 1. Ill-defined non blanchable erythematous to violaceous macules and patches on toes and soles. Some lesions were reticulated blanchable erythematous patch. Digital cyanosis and gangrene presented on tip of toes.

104/57, 139/64 and 131/60 mmHg, respectively. Her heart rate was 68 beats per minute and regular. Left brachial and radial arterial pulses were reduced when compared with the right side. Arterial pulses of lower extremities were normal. Bruit was noted over both carotid areas and both sides of her abdomen. Cardiovascular system revealed a systolic ejection murmur grade III along her left parasternal border. Hollenhorst plaque was not found from ophthalmologic examination.

Dermatologic examination demonstrated multiple discrete ill-defined non branchable erythematous to violaceous macules and patches on her toes and soles. Some lesions were reticulated blanchable erythematous patches. Digital cyanosis and gangrene presented on the tips of her toes. (Fig 1) The remainder of the physical examination was unremarkable.

Laboratory tests demonstrated normochromic normocytic anemia from chronic disease, normal white blood cells and platelet count. Her INR was 3.04, her erythrocyte sedimentation rate was 81 mm/hr, her serum creatinine was 3.0, and her urine analysis was normal. Investigation of the acute renal failure cause demonstrated prerenal acute renal failure. Ultrasound doppler was done and found significant stenosis of both renal arteries. Her liver function test was normal.

Magnetic resonance angiography demonstrated irregularity of her aortic wall with significant stenosis of the proximal part of both subclavian arteries, ostium of celiac artery, superior mesenteric artery and both renal arteries. Thickening with myxomatous change of mitral valve with moderate mitral regurgitation was found. These findings were compatible with Takayasu arteritis.

Skin biopsy was obtained from the livedo reticularis area of her left foot. The section revealed biconvex needle-shaped clefts in the lumen of arterioles. The clefts were created by dissolution of cholesterol crystals during the fixation process. (Fig 2) There were 2-3 cholesterol crystals in the small vessels of each five slide step sections from 14 slide serial step sections. Thus, multiple level step sections of H&E should be performed in case of suspicion of cholesterol crystal emboli.

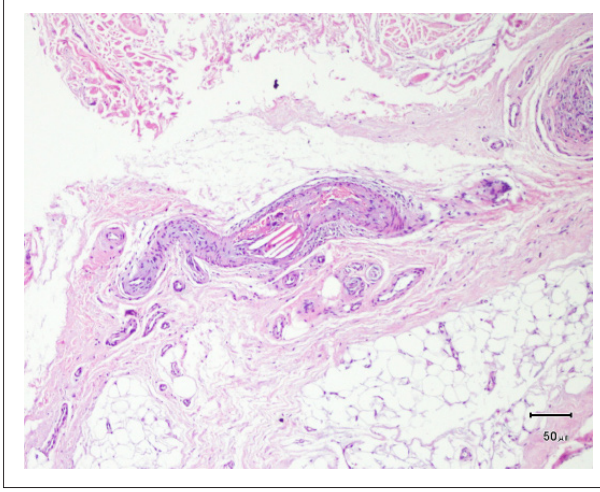

Fig 2. Cholesterol emboli. Needle-shaped clefts are detected in the lumen of arterioles associated with thrombus and fibrin (H&E x100).

DISCUSSION

Takayasu arteritis is a chronic vasculitis which primarily affects the aorta and its primary branches. It was diagnosed following the American College of Rheumatology (ACR) classification criteria. Evidence of vascular involvement and insufficiency becomes clinically apparent due to dilation, narrowing, or occlusion of the proximal or distal branches of the aorta.[1]

Accelerated atherosclerosis has been documented in patients with Takayasu arteritis. Autopsy studies revealed atherosclerosis lesions in young patients with Takayasu arteritis.[2,3] More atherosclerosis plaques and higher mean intima-media thickness, by using B-mode ultrasonography, were observed among patients with Takayasu arteritis, than in the healthy controls. The secondary atherosclerosis is more common in areas where primary vessel wall disease is more prominent.[4] Arterial stiffness which is a premature sign of atherosclerosis is more pronounced in areas affected by the disease process in Takayasu patients, like the carotid arteries and the aorta, but stiffness is not increased in femoral arteries which are not typically affected by Takayasu arteritis.[5,6] Histologically, the skipped areas of Takayasu arteritis are replaced by atherosclerosis.[2] In addition, endothelin-1 levels that are usually increased in patients with endothelial dysfunction, which is considered the first step in atherosclerosis, were higher in patients than controls.[7] From literature review, there has been no study or case report about Takayasu arteritis presenting with cholesterol emboli. Our case was diagnosed as Takayasu arteritis following ACR criteria. Cholesterol emboli can be a rare presentation spontaneously originated from atherosclerosis related with Takayasu arteritis.

Increased atherosclerosis in patients with Takayasu arteritis may be multifactorial. It may be associated with local and systemic disease activity as well as traditional atherosclerosis risk factors. Local and systemic persistent

inflammation from the disease itself, arterial injury due to functional abnormalities or turbulent blood flow and shear stress in stenotic segments, may all play a part in the pathogenesis of the atherosclerosis observed in Takayasu arteritis. The traditional atherosclerotic risk factors such as hypertension, diabetes mellitus and hyperlipidaemia may be contributing factors. These risk factors may well develop secondary to Takayasu arteritis or may develop as the side effects of the disease itself.[4] There were studies that demonstrated that patients with Takayasu arteritis had a higher prevalence of hypertension, higher triglyceride and cholesterol levels and lower high-density lipoprotein cholesterol level than controls.[7,8] No difference in the lipids was observed between patients with and without clinical activity. Lipids were similar in patients under glucocorticoid therapy compared to those without this therapy.[8]

The effective control of traditional atherosclerotic risk factors is needed, in addition to the effective suppression of disease activity, for the management of Takayasu arteritis.[4] Prevention and early recognition for atherosclerotic plaque should be performed in patients with Takayasu arteritis.

REFERENCES

1. Weyand CM, Goronzy JJ. Medium- and large-vessel vasculitis. N Engl J Med. 2003 Jul 10;349(2):160-9.
2. Numano F. Vasa vasoritis, vasculitis and atherosclerosis. Int J Cardiol. 2000 Aug 31;75 (Suppl 1):S1-8.
3. Filer A, Nicholls D, Corston R, Carey P, Bacon P. Takayasu arteritis and atherosclerosis: illustrating the consequences of endothelial damage. J Rheumatol. 2001 Dec;28(12):2752-3.
4. Seyahi E, Ugurlu S, Cumali R, Balci H, Seyahi N, Yurdakul S, et al. Atherosclerosis in Takayasu arteritis. Ann Rheum Dis. 2006 Sep;65(9): 1202-7.
5. Ng WF, Fantin F, Ng C, Dockery F, Schiff R, Davies KA, et al. Takayasu's arteritis: a cause of prolonged arterial stiffness. Rheumatology (Oxford). 2006 Jun;45(6):741-5.
6. Raninen RO, Kupari MM, Hekali PE. Carotid and femoral artery stiffness in Takayasu's arteritis. An ultrasound study. Scand J Rheumatol. 2002; 31(2):85-8.
7. de Souza AW, Ataide Mariz H, Torres Reis Neto E, Diniz Arraes AE, da Silva NP, Sato EI. Risk factors for cardiovascular disease and endothelin-1 levels in Takayasu arteritis patients. Clin Rheumatol. 2009 Apr;28 (4):379-83.
8. de Carvalho JF, Bonfa E, Bezerra MC, Pereira RM. High frequency of lipoprotein risk levels for cardiovascular disease in Takayasu arteritis. Clin Rheumatol. 2009 Jul;28(7):801-5.