Possible Coronary Sequelae of Kawasaki Disease in an Elderly Man

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Summary

Kawasaki disease (KD) is an acute self-limited syndrome that predominantly affects children. Coronary sequelae have been identified to be responsible for a small, but significant percentage of young adults who present with myocardial ischemia. In this study, we present a case of an elderly patient with possible coronary sequelae of KD. A 76-year-old man was referred to our outpatient department for silent myocardial ischemia. Axial images of coronary computed tomography showed multiple lumens in the proximal left anterior descending (LAD) artery. Coronary angiography demonstrated braid-like appearance in the proximal and distal segment of the LAD. Coronary intervention was successfully performed for the proximal LAD lesion using directional atherecetomy (DCA) catheter. Microscopic examination of the DCA specimens showed the following histological features: tissues in densely hyalinized fibrosis with occasional microcalcification, or those containing a number of smooth muscle cells (SMCs) with myxoid extracellular matrix. There was paucity of cholesterin crystals and aggregation of foamy cells. In addition, scarcely any inflammatory cell filtration was identified. In the section of SMC-containing samples, formation of multiple re-canalized vessels embracing endothelial cells was confirmed. These histopathologic findings indicated that the present coronary artery lesion has a high possibility of very late cardiovascular sequelae caused by arteritis due to KD, rather than arteriosclerosis. This is the oldest adult case with coronary artery disease possibly resulting from KD sequelae. This case highlights that KD sequelae must be considered as a cause of coronary artery lesion even in older patients.

Key words: Coronary artery disease, Arteritis, Multimodality imaging, Histopathology

Kawasaki disease (KD) is described as an arteritis of medium-sized arteries associated with the mucocutaneous lymph node syndrome. KD is an acute self-limited syndrome that predominantly affects children < 5 years of age. Coronary sequelae resulting from KD are responsible for a small, but important percentage of young adults who present with myocardial ischemia. Currently, coronary artery disease in young adults as a result of undiagnosed KD in childhood is increasingly recognized by cardiologists. The prevalence of coronary sequelae of untreated or missed KD vasculitis in early adulthood up to 40s has been reported. In this study, we present a case of an elderly patient with possible coronary sequelae of KD.

Case Report

A 76-year-old man was referred to our cardiovascular outpatient department for silent myocardial ischemia indicated by an abnormal electrocardiogram (ECG) during the preoperative examination for cholelithiasis. He was asymptomatic in his daily life and had not experienced pro-longed fever over the past few decades. Physical examination revealed a blood pressure of 112/70 mmHg and heart rate of 73 bpm. The cardiovascular examination was unremarkable. His ECG showed a normal sinus rhythm with poor R wave progression in leads V1-V4. The most recent ECG (7 years prior) was in the normal range. A transthoracic echocardiogram demonstrated hypokinesis of the left ventricular wall motion in the anterior septum, anterior wall, and apex.

He had been a smoker for more than 50 years. His medical history was unremarkable apart from diabetes mellitus that was optimally controlled with oral anti-hyperglycemics. He had never been admitted to the hospital for a febrile illness during childhood, to the best of his recollection.

Due to his older age and the traditional risk factors such as smoking history and diabetes, atherosclerotic coronary artery disease was assumed. Active systemic vasculitis was ruled out, given that neither systemic inflammatory signs nor conomorbid organ failure was found. Erythrocyte sedimentation rate and C-reactive protein were observed to be in the normal range. Retrospective
serological assays for immunoglobulins test, hepatotropic viruses, antinuclear antibody, or antineutrophil cytoplasmic antibody (ANCA) were negative. There was no finding of simultaneous presence of major vascular lesions such as aortic and peripheral arterial disease.

Coronary computed tomography (CT) showed a filling defect in the proximal left anterior descending (LAD) coronary artery (Figure 1A). Neither perivascular soft tissue surrounding the coronary lesion nor aneurysmal formation was noted. Axial CT images visualized multiple lumens in the proximal LAD lesion (Figure 1A'). Stress single-photon emission CT demonstrated anterior, septal, and apical reversible perfusion defects. Although he was asymptomatic, the patient was admitted to the cardiology department to further examine the silent myocardial ischemia. He then underwent coronary angiography, which showed a braid-like appearance in the proximal and distal segment of the LAD (Figure 1B). We scheduled coronary intervention for the proximal LAD lesion.

Due to the atypical CT and angiographic features for atherosclerotic coronary lesions, we used a directional coronary atherectomy (DCA) catheter to examine the coronary artery plaque characteristics. Intravascular ultrasound (IVUS) demonstrated multiple channels in both segments of the LAD (Figure 1C' and C''). Diligent plaque debulking provided optimal luminal gain in the proximal LAD lesion (Figure 2). Microscopic examination of the DCA specimens was conducted. Arterial tissues obtained from the proximal LAD segment consisted of the intima with the following histological features: tissues with densely hyalinized fibrosis with occasional microcalcification (Figure 3A) or those containing a number of SMCs with myxoid extracellular matrix (Figure 3B). There was a paucity of cholesterol crystals and aggregation of foamy cells. In addition, minimal inflammatory cell infiltration was identified. In some samples, the formation of multiple re-canalized vessels embracing endothelial cells was confirmed (Figure 3B-D). The pathological study indicated characteristics of coronary arteritic sequelae. There are multiple forms of medium-sized arteritis to be differentiated including Takayasu arteritis, giant cell arteritis, polyarteritis nodosa (PAN), ANCA-associated vasculitis, and IgG4-related disease. Nevertheless, these can be excluded because of lacking pathognomonic symptoms, physical signs, and serological and histopathological findings. We conjectured that the present coronary artery lesions were likely caused by KD after considering the multimodality imaging and histopathological observations.

After the coronary revascularization, the patient’s condition improved without any recurrent ischemic events during follow-up.

**Discussion**

Although this patient was unusually old, we speculated that the present coronary artery lesion had a high

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**Figure 1.** CT, angiography, and IVUS images of the LAD lesions. **A:** Curved planar reconstruction of the LAD coronary artery by CT angiography. A': Axial CT image of the proximal LAD. Multiple lumens are visualized. **B:** Left coronary angiography (RAO30°/CR30°). Braid-like appearance of the proximal (B') and distal LAD (B''). C (C' and C''): The IVUS images corresponding to B (B' and B''), respectively. IVUS demonstrates multiple channels in both segments of the LAD (asterisks). CFX, circumflex; CT, computed tomography; DB, diagonal branch; IVUS, intravascular ultrasound; LAD, left anterior descending.
possibility of very late cardiovascular sequelae caused by arteritis due to KD, rather than arteriosclerosis, based on the multimodality imaging and histopathological findings. The angiographic lesion morphology of braid-like appearance \(^{5,6}\) was generalized by multiple lumens and referred to as a “lotus root” structure, as illustrated by IVUS. \(^7\) It is interesting to note that the target lesion was immune from atherosclerotic development despite his age and the cardiovascular risk factors. As the histological examination showed, the tissue samples were comprised of densely hyalinized fibrosis which corresponded to organized thrombi. Scattered lumens are consistent with re-canalized vessels characterized by the expression of the endothelial layers. Re-canalized vessels can be observed in atherothrombotic lesions, but these are structurally uncertain in most settings compared with those observed in arteritic plaques. Given that there was no histological evidence of atheromatous plaques in the arterial tissue samples, the re-canalized vessels were probably induced as a sequelae of arteritis. Orenstein and colleagues conducted a histological analysis of coronary arteries obtained from 41 patients with KD, wherein they found no histological fea-

Figure 2. Pre- (A) and post-procedural (B) coronary angiography and corresponding IVUS images (A’ and B’) of the LAD proximal target lesion. IVUS, intravascular ultrasound; LAD, left anterior descending.

Figure 3. Microscopic findings. A: Section of the LAD coronary artery demonstrating intima with densely hyalinized fibrosis with occasional microcalcification (white arrows; hematoxylin and eosin stain [H&E]). B: Another section of the LAD demonstrating the formation of a re-canalized vessel (black arrow, H&E). C: Corresponding section with immunohistochemical study showing the re-canalized vessel embracing anti-CD31 antibody-positive endothelial cells (black arrow). D: Another section of the LAD visualizing α-smooth muscle actin-positive vascular smooth muscle cells surrounding the re-canalized vessel (black arrow). LAD, left anterior descending.
tures of atherosclerosis even in patients who died later in life. There are multiple forms of arteritis to be differentiated from KD. Among the several types of arteritis, PAN is a major differential diagnosis since it affects medium-sized vessels as is the case with KD. Nevertheless, PAN can be excluded because of lacking polyneuropathy signs and his self-limiting disease trajectory for cardiac involvement. The remaining large and medium vessel vasculitides have a very low likelihood of the etiology based on our differential diagnosis. The present coronary lesions did not show any aneurysm formation which is atypical for KD; however, aneurysm regression has been consistently reported to occur in KD patients. A long-term follow-up study demonstrated the development of localized stenosis > 10 years after aneurysm regression. Furthermore, a pathological observation showed that patients who had a history of KD and died of traffic accidents or malignancies had no symptoms of ischemic heart disease while alive and no coronary artery aneurysm was found at autopsy, but lesions of coronary arteritis were noted.

The prevalence of coronary sequelae of untreated or missed KD in early adulthood up to the age of 40 has been reported. This patient was quite a rare case of KD, considering his age (76 years) and uncertain clinical history in childhood. A clinical survey in Japan has identified 130 patients up to 63 years old with angiographically proven coronary artery disease that could reasonably be attributed to antecedent KD. In addition, a large majority of patients with coronary lesions had no clear history of KD in childhood. Diagnosis of KD is thoroughly based upon evidence of systemic inflammation in association with signs of mucocutaneous inflammation, not on the pathological appearance. Therefore, we have to accept the criticism that our clinical view remains speculative to no small extent. However, given that the acute phase of KD is self-limited and the syndrome had not been internationally recognized before his childhood, the idea that this patient contracted KD subclinically in his childhood could not be excluded. To the best of our knowledge, this is the oldest adult case with coronary artery disease possibly resulting from KD sequelae. Cardiologists specializing in adult patients should acknowledge the importance of considering antecedent KD coronary lesions even in middle-aged and older patients.

Conclusion

This report demonstrated a rare case of an elderly man with possible coronary sequelae of KD, as indicated by multimodality imaging and in vivo histopathological evaluation. We believe that etiologic assessment may be important in coronary artery disease even in older patients.

Disclosure

Conflicts of interest: None.

References

1. Daniels LB, Tijjadi MS, Walford HH, et al. Prevalence of Kawasaki disease in young adults with suspected myocardial ischemia. Circulation 2012; 125: 2447-53.
2. Kato H, Inoue O, Kawasaki T, Fujiwara H, Watanabe T, Toshima H. Adult coronary artery disease probably due to childhood Kawasaki disease. Lancet 1992; 340: 1127-9.
3. Burns JC, Shike H, Gordon JB, Malhotra A, Schoenwetter M, Kawasaki T. Sequelae of Kawasaki disease in adolescents and young adults. J Am Coll Cardiol 1996; 28: 253-7.
4. Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013; 65: 1-11.
5. Suzuki A, Kamiya T, Ono Y, Kinoshita Y, Kawamura S, Kinura K. Clinical significance of morphologic classification of coronary arterial segmental stenosis due to Kawasaki disease. Am J Cardiol 1993; 71: 1169-73.
6. Kim YJ, Lee HJ, Hur J, et al. Braid-like appearance of the coronary artery in Kawasaki disease: typical computed tomography and angiography findings. Eur Heart J 2008; 29: 2791.
7. Terashima M, Awano K, Honda Y, et al. Images in cardiovascular medicine. “Arteries within the artery” after Kawasaki disease: a lotus root appearance by intravascular ultrasound. Circulation 2002; 106: 887.
8. Orenstein JM, Shulman ST, Fox LM, et al. Three linked vasculopathic processes characterize Kawasaki disease: a light and transmission electron microscopic study. PLoS One 2012; 7: e38998.
9. Takahashi K, Oharaseki T, Yokouchi Y. Histopathological aspects of cardiovascular lesions in Kawasaki disease. Int J Rheum Dis 2018; 21: 31-5.
10. Kato H, Koike S, Yamamoto M, Ito Y, Yano E. Coronary aneurysms in infants and young children with acute febrile mucocutaneous lymph node syndrome. J Pediatr 1975; 86: 892-8.
11. Suzuki A, Yamagishi M, Kimura K, et al. Functional behavior and morphology of the coronary artery wall in patients with Kawasaki disease assessed by intravascular ultrasound. J Am Coll Cardiol 1996; 27: 291-6.
12. Naoe S, Takahashi K, Masuda H, Tanaka N. Coronary findings post Kawasaki disease in children who died of other causes. Prog Clin Biol Res 1987; 250: 341-6.
13. Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H. A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. Pediatrics 1974; 54: 271-6.