Indian J Pediatr (January 2016) 83(1):47–52
DOI 10.1007/s12098-015-1858-4

REVIEW ARTICLE

Recent Advances in Kawasaki Disease – Proceedings of the 3rd Kawasaki Disease Summit, Chandigarh, 2014

Surjit Singh[1] · **Dhrubajyoti Sharma**[1] · **Sagar Bhattad**[1] · **Saji Phillip**[2]

Received: 2 April 2015 / Accepted: 22 July 2015 / Published online: 30 August 2015

Abstract Kawasaki disease (KD) is the most common cause of acquired heart disease in children in Japan, North America and Europe. It is now being increasingly recognized from the developing countries as well. If not diagnosed and treated in time, KD can result in coronary artery abnormalities in approximately 15–25 % cases. The long-term consequences of these abnormalities may manifest in adults as myocardial ischemia and congestive heart failure. Intravenous immunoglobulin (IVIg) remains the drug of choice for treatment of KD, but several new agents like infliximab, cyclosporine, glucocorticoids and statins are now being increasingly used in these patients. While echocardiography has been the preferred imaging modality hitherto, CT coronary angiography has emerged as an exciting new supplementary option and provides an entirely new dimension to this disease. The incidence of KD has shown a progressive increase in several countries and it is likely that this disease would impact public health programmes in the near future even in the developing countries.

Keywords Kawasaki disease · Recent advances · India

✉ Surjit Singh
surjitsinghpgi@rediffmail.com

[1] Pediatric Allergy Immunology Unit, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research, Chandigarh 160012, India

[2] Kawasaki Disease Foundation of India, St. Gregorios Cardiovascular Centre, Parumala, Kerala, India

Introduction

Kawasaki disease (KD) is a medium vessel vasculitis seen in young children with preferential involvement of the coronary arteries [1]. It is now the most common cause of acquired heart disease in children in Japan, North America and Europe [1, 2]. Anecdotal reports suggest that it may soon replace rheumatic fever to become the commonest acquired pediatric heart disease in the developing countries as well [3]. Although the first case was diagnosed by Dr. Tomisaku Kawasaki more than 50 y ago [4], etiology of this disorder still remains an enigma.

Kawasaki disease is now being diagnosed and treated all over India but many cases, perhaps the majority, are still being missed [5–8]. There is a lot that needs to be done to increase the awareness of this condition amongst pediatricians and internists in our country. It is heartening to note that discussions on KD are now part of several specialty chapters of Indian Academy of Pediatrics. Another laudable initiative that has been taken in this regard is the organization of the biennial Indian Kawasaki Disease Summits. The first such summit was organized in 2010 at Parumala, Kerala and the second at Chennai in 2012. In October 2014, the Post Graduate Institute of Medical Education and Research, Chandigarh hosted the third KD Summit. This manuscript provides an overview of the deliberations that took place at this meeting. The faculty included Dr. Jane Burns (San Diego, USA), Dr. Marian Melish (Honolulu, USA), Dr. John Gordon (San Diego, USA), Dr. Ross Petty (Vancouver, Canada), Dr. Saji Phillip (Parumala, Kerala) Dr. Vikas Kohli (New Delhi), Dr. ManojKumar Rohit (Chandigarh) and Dr. Manphool Singhal (Chandigarh).

Epidemiology

The first case of KD was diagnosed in 1961 by Dr. Tomisaku Kawasaki in Tokyo, Japan. He described it as ‘mucocutaneous

lymph node syndrome'. He published the first 50 cases in the Japanese language journal, 'Arerugi' [9]. His contemporaries challenged the notion that it was a new disease and argued it to be a variant of scarlet fever [4]. Dr. Kawasaki, however, was convinced that he was dealing with something new. Soon thereafter, Dr. Marian Melish identified similar cases in the USA [4]. Dr. Tanaka was the first pathologist to demonstrate coronary aneurysms and thrombosis at autopsy in KD [4]. Over the coming years, it not only became evident that a new disease had indeed been recognized, but what was worrying was the number of cases that soon started getting diagnosed. Three major epidemics were noted in Japan - in 1979, 1982 and 1986 [10–15].

It has now become clear that the incidence of KD shows two distinct trends. While several countries in the Far East like Japan, Korea and Taiwan report incidence rates that are progressively increasing on a decadal basis, the incidence in North America, Australia and Europe has plateaued for reasons which are not clear. In Japan, the current incidence is 265/100,000 children below 5 y of age. This is the highest figure reported so far from anywhere in the world. Korea and Taiwan report the second and third highest incidence figures of KD – 134.4 and 82.8 per 100,000 children below 5 respectively. Incidence figures in Europe, North America and Australia vary between 4 and 25 / 100,000 children below 5. Nationwide data are not available from China and India but anecdotal reports suggest that the incidence is going up in these countries as well. In Chandigarh, the incidence of KD was estimated to be 4.54/100,000 children below 15. This figure was based on hospital admission data and is likely to be an underestimate [6].

Etiopathogenesis

While the etiology of KD remains an enigma, several novel hypotheses have been put forward. Dr. Burns described how the occurrence of this disease has recently been linked to tropospheric wind patterns [16, 17]. The occurrence of KD has been linked to these wind patterns in Japan, Hawaii and San Diego. It has been hypothesized that the putative causal agent of KD (? a fungal spore) gets transported across the Pacific region by strong winds blowing through the upper troposphere. Further evidence in favour of this hypothesis comes from sampling of the microbiome of these tropospheric winds which has yielded high concentrations of Candida species. It is believed that this fungal trigger (perhaps a toxin) triggers an abnormal host immune response in genetically susceptible individuals and this manifests as KD.

Animal Models

Dr. Phillip discussed his work on pathology of KD and described how injection of horse serum in piglets could replicate the pathological changes seen in humans [18, 19]. This work had been carried out by him at Taipei, Taiwan. He also described correlation of echocardiographic findings of induced coronary artery lesions in piglets with histopathological findings. The author concluded that piglets may serve useful experimental models for understanding the pathology of KD.

Genetics

Dr. Burns summarized three important signaling pathways in KD discovered so far [20]. The first was the calcineurin-nuclear factor involved in activation of T lymphocytes. In this pathway, a functional single nucleotide polymorphism (SNP) in the gene encoding 1,4,5-inositol trisphosphate 3-kinase C (ITPKC) on chromosome *19q13.1* perhaps contributes to host susceptibility to KD and also results in formation of coronary artery aneurysm. It is for this reason that calcineurin inhibitors like cyclosporine are now being proposed as therapy for patients refractory to conventional treatment with IVIg. The second pathway pertains to the transforming growth factor-β (TGFβ) signaling pathway. It is believed that SNPs in TGFβ2, TGFβR2, and SMAD3 contribute to risk of development of coronary artery aneurysms. Understanding of the pathophysiology of this pathway has led to the suggestion that atorvastatin may have beneficial effects during the acute stage of KD. The third pathway pertains to *FCGR2A* gene which encodes for FcγRIIa. A non-synonymous SNP in the *FCGR2A* gene has been identified in some patients with KD from Europe and has been linked to disease susceptibility. Shrestha et al., have also reported an association of this SNP in *FCGR2A* gene to susceptibility to KD [21]. Variation in a second gene encoding FcγIIB has been implicated as influencing response to treatment with IVIg. Dr. Burns highlighted the fact that genetic studies in KD hold the key to understanding of the pathogenesis of the disease.

Clinical Features [1, 22, 23]

Clinically, KD can be divided into three phases - acute, subacute and convalescent phases.

Acute Phase (Initial 10–14 d)

Fever, extreme irritability, bilateral non-exudative conjunctival injection, red oral and pharyngeal mucosa, strawberry tongue, dry cracked lips, extremity edema, various forms of rashes and cervical lymphadenopathy (usually unilateral) are the usual presenting features in

the acute phase of KD. Myocarditis is said to be common in this phase but has been underemphasized in the existing literature. Pericarditis, hydrops of the gallbladder and perineal desquamation are other early features of KD. There may be redness and crusting at the BCG inoculation site in infants, but is an uncommon finding in authors' experience.

Subacute Phase (2–4 wk)

Most of the acute symptoms subside by this time. Periungual desquamation is typically seen in this phase. In some children arthritis of one or several joints can develop. Coronary artery abnormalities (CAAs) are most commonly seen during this phase.

Convalescent Phase

By this time all the clinical signs disappear. This phase persists till the acute phase parameters (high eryhthocyte sedimentation rate, elevated C-reactive protein and raised platelet counts) return to normal. It usually lasts for 6–8 wk after onset of the illness. The characteristic Beau's lines in nails are seen at this time.

Clinical Criteria for Diagnosis of Kawasaki Disease [1, 22, 23]

- Fever persisting for atleast 5 d
- Presence of atleast 4 of the following principal features:
  - Changes in extremities:
    - Acute: Erythema of palms, soles; edema of hands, feet
    - Subacute: Periungual peeling of fingers, toes in wk 2 and 3
  - Polymorphous exanthema
  - Bilateral bulbar conjunctival injection without exudate
  - Changes in lips and oral cavity: Erythema, lip cracking, strawberry tongue. Diffuse injection of oral and pharyngeal mucosa
  - Cervical lymphadenopathy (> 1.5 cm diameter), usually unilateral
- Exclusion of other diseases with similar findings

*Patients with fever for atleast 5 d and <4 principal criteria can be diagnosed with KD when CAAs are detected by two dimensional echocardiography.

#In the presence of 4 or more principal criteria, KD diagnosis can be made on day 4 of illness.

Fever

This is usually high grade and is often the first manifest clinical finding. It is unresponsive to antimicrobials and may be accompanied by extreme irritability.

Conjunctival Injection

This is non-exudative and may have a characteristic perilimbal sparing. It may not be prominent and can be easily missed if not specifically looked for. It can disappear within a few days.

Mucosal Changes

The typical changes include redness of lips, oral and pharyngeal mucosa and red strawberry tongue.

Rash

Rash can be very variable and may present with macular or maculopapular lesions which can, at times, be erythema multiforme like. The rash may have '*perineal accentuation*'. Vesicular rashes are, however, unusual in KD. The perineal rash can desquamate during first few days of the illness.

Extremity Changes

These include erythema of hands and feet in the acute stage of the disease often accompanied by a pathognomonic 'indurative edema' on the dorsal aspects of hands. The characteristic periungual desquamation of fingers and toes begins in the subacute phase of KD. Beaus's lines develop several weeks after the acute illness. These are transverse grooves at the base of the nails of fingers and toes and move distally as the nails grow. These develop because of arrested nail growth during the acute phase of the disease.

Cervical Lymphadenopathy

This is usually unilateral and non-suppurative but it may be seen on both sides of the neck. It is seen only in 50–75 % of cases. The size should be atleast 1.5 cm. but this limit is rather arbitrary. Occasionally a markedly enlarged solitary cervical lymphadenopathy can be the presenting feature of KD and is often unresponsive to antimicrobials.

Atypical and Incomplete KD

The terms 'atypical' or 'incomplete' KD are used when a patient presents with less than the required number of criteria for diagnosis of the disease. These terms, however, should not be used interchangeably [1, 23]. The term 'incomplete' is preferred when

there are 4 or less principal criteria and 'atypical' is preferred when presentation is unusual (as for *e.g.*, with stroke, nephritis, or hepatitis). Incomplete KD is more common in young infants and may often be associated with CAAs [1, 22, 23].

Cardiovascular Findings in KD [1, 22, 23]

KD is a pancarditis and can involve all three layers of the heart, in addition to the coronary arteries. In early phase of the disease there may be hyperdynamic precordium, gallop rhythm and flow murmurs. Myocarditis is almost universal in KD but may not be clinically significant. It can manifest as tachycardia out of proportion to fever and diminished left ventricular systolic function. Mild valvular regurgitation is not unusual during the acute phase of KD. Pericarditis with pericardial effusion can be detected in the early part of the disease. CAAs are the most significant cardiovascular complication of KD. These can develop in approximately 25 % of untreated patients. Giant aneurysms (>8 mm internal diameter) have a risk of rupture and development of thrombosis during the acute stage, and may evolve onto coronary stenoses later in life. KD is an important cause of myocardial infarction in children.

Other Organ Systems

As KD is essentially a vasculitis, several organ systems can get involved. This can result in clinical presentations which may be very variable and may mislead the unwary clinician. Several patients with KD, for instance, can have arthralgia and/or arthritis involving small and large joints. These joint manifestations may be seen at presentation but can also come up during convalescence. Joint involvement after the first 2 wk of illness is usually limited to large joints like the ankles and knees. Children with KD can present with gastrointestinal manifestations like diarrhea, vomiting and pain abdomen. KD has, on occasion, been known to present as an acute abdomen. Hydrops of the gall bladder can be seen in up to 15 % of cases of KD and is a characteristic finding in this disease. Neurological involvement in KD can present as extreme irritability, acute unilateral facial nerve palsy and transient sensorineural hearing loss during the acute phase of the disease. Other presentations include pleural effusion (occasional hemorrhagic), testicular swelling and macrophage activation syndrome [1, 22, 23].

Imaging in KD

Dr. Kohli spoke on echocardiography in children with KD and explained how it is crucial that the evaluation be done by a skilled and experienced pediatric cardiologist. It is also important that the coronaries be assessed using 'Z' scores. Dr.Rohit shared his experience on giant aneurysms in children with KD who are being followed at Chandigarh. Although several of these aneurysms show a decrease in size over time, the risk of serious cardiovascular sequelae are not abated as coronary stenosis tend to develop after remodeling. Dr. Singhal deliberated upon Dual-source CT coronary angiography as a new diagnostic modality in KD. This is an upcoming imaging technique with minimal radiation exposure (< 0.5 mSv) and has provided greater understanding of the coronary anatomy than was hitherto possible with only echocardiography. The major advantage over echocardiography is its ability to detect proximal as well as distal arterial abnormalities [24].

Management

There is no gainsaying the fact that IVIg continues to remain the cornerstone of management of KD [1, 22, 23]. This was reemphasized by Dr. Petty. The standard of care is 2 g/kg IVIg given over 12–24 h. IVIg should be initiated slowly and increased gradually. This fact cannot be overemphasized as infusion reactions, although rare, may be serious. Aspirin is initially administered at 30–50 mg/kg/d and is continued as long as the child is febrile. This dose is associated with far fewer side-effects than the higher doses used hitherto. Subsequently the dose is reduced to 3–5 mg/kg/d and is continued for 4–8 wk at which time repeat echocardiography is carried out. Aspirin may be discontinued if this follow-up echocardiography examination does not show CAA.

Although aspirin has been in use for long, robust evidence for its usefulness as an anti-inflammatory agent in KD is lacking. Its use as an anti-platelet agent, however, seems rational.

Approximately 15–20 % of children with KD are resistant to IVIg. There is no consensus on management of such patients. Therapeutic modalities that have been used in such circumstances include a second dose of IVIg, intravenous pulse methylprednisolone and cyclosporine [25–31]. Dr. Burns stressed on the role of the anti-TNF agent, infliximab, in KD. Infliximab has recently also been tried as an add-on agent along with IVIg in patients with KD.

Disease Severity Scores

The Japanese workers have developed several scoring systems like Kobayashi, Egami and Sano scores to determine the severity of KD and risk of IVIg resistance. Although these scores have been found to be beneficial in the Japanese setting, their evaluation in other regions of the world have not yielded consistent results [32]. The Harada score has been evaluated in North American settings and was found to have

90 % sensitivity for predicting high risk of CAAs in KD [33]. Dr. Melish emphasized that these scores may not be very useful in the non-Japanese setting. In her experience, it is the clinical assessment and repeat echocardiography examinations during the initial admission which yield the best results. She reiterated that a normal echocardiography examination early in the disease should not give way to complacency as CAAs may take some time to evolve.

Complications/ Follow-up

Echocardiography should be performed at 2–3 wk and again at 6–8 wk after onset of the disease. Further evaluation of coronary arteries depends upon their status on follow-up. Angiographic resolution of coronary aneurysms is observed in 50–67 % of patients by 1–2 y after the illness [1, 22, 23]. The likelihood of resolution is greater if the size is small, age at onset is less than 1 y, aneurysm is fusiform in shape and is located in a distal rather than a proximal coronary segment. Giant aneurysms are unlikely to resolve and most of them lead to thrombosis or stenoses or both. Highest risk of myocardial infarction occurs during the first year after onset of illness [1, 22, 23]. All children with KD and CAAs should be kept on long-term follow-up. The is no consensus on the precise duration of follow-up that is required.

That KD can no longer be considered to be merely a one-time disease of childhood was made amply clear by the long-term follow-up studies of Dr. Burns and Dr. Gordon, San Diego, USA. The sequelae of KD in childhood can have consequences later in life [34]. Coronary artery abnormalities may show remodeling but may not regain the normal architecture. Dilatations, aneurysms and stenoses are common long-term sequelae of KD. The clinical correlates of these abnormalities include congestive heart failure, arrhythmias, dilated cardiomyopathy and myocardial ischemia [35]. Dr. Gordon also explained how coronary interventions in complications related to KD are very different from the ones done in patients with atherosclerotic coronary artery disease. Damage because of KD is associated with calcium deposition in the walls of the coronary arteries and may require coronary rotational atherectomy for its resolution. Similarly bypass surgery for coronary occlusion in KD is technically difficult.

Conclusions

KD is the most common cause of acquired heart disease amongst children in Japan, North America and Europe. Emerging data from China and India suggest that it may soon replace rheumatic fever as the commonest pediatric heart disease in these countries as well. KD can have several long-term sequelae and can no longer be viewed as a one-time disease of childhood. The speakers highlighted the importance of obtaining coronary 'Z-scores' at echocardiography. CT coronary angiography is an emerging new modality of investigation in KD. As the numbers are increasing rapidly, KD and its sequelae are likely to have important implications for health planners and administrators in these countries. Early recognition and timely therapy are pivotal in preventing the long-term complications associated with this condition.

Acknowledgments The authors express their gratitude to Dr. Jane Burns, Dr. Marian Melish, Dr. Ross Petty, and Dr. John Gordon who participated as faculty from overseas in the 3rd. Kawasaki Disease Summit, Chandigarh, October 2014.

Guarantor SS will act as guarantor for this paper.

Conflict of Interest None.

Source of Funding None.

References

1. Sundel RP, Petty RE. Kawasaki disease. In: Cassidy JT, Petty RE, Laxer RM, Lindsley CB, editors. Textbook of Pediatric Rheumatology. 6th ed. Philadelphia: Elsevier Saunders; 2011. p. 505–20.
2. Uehara R, Belay ED. Epidemiology of Kawasaki disease in Asia, Europe, and the United States. J Epidemiol. 2012;22:79–85.
3. Kumar RK, Tandon R. Rheumatic fever & rheumatic heart disease: the last 50 years. Indian J Med Res. 2013;137:643–58.
4. Burns JC, Kushner HI, Bastian JF, et al. Kawasaki disease: a brief history. Pediatrics. 2000;106:E27.
5. Singh S, Kawasaki T. Kawasaki disease-an Indian perspective. Indian Pediatr. 2009;46:563–71.
6. Singh S, Aulakh R, Bhalla AK, Suri D, Manojkumar R, Burns JC. Is Kawasaki disease incidence rising in Chandigarh, North India? Arch Dis Child. 2011;96:137–40.
7. Singh S, Aulakh R, Kawasaki T. Kawasaki disease and the emerging coronary artery disease epidemic in India: is there a correlation? Indian J Pediatr. 2014; 81: 328-32.
8. Singh S, Bansal A, Gupta A, Kumar RM, Mittal BR. Kawasaki disease: a decade of experience from North India. Int Heart J. 2005;46:679–89.
9. Kawasaki T Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. Arerugi. 1967;16:178–222.
10. Dean AG, Melish ME, Hick R, Palumbo NE. An epidemic of Kawasaki syndrome in Hawaii. J Pediatr. 1982;100:552–7.
11. Yanagawa H, Nakamura Y, Ojima T, Yashiro M, Tanihara S, Oki I. Changes in epidemic patterns of Kawasaki disease in Japan. Pediatr Infect Dis J. 1999;18:64–6.
12. Yanagawa H, Yashiro M, Nakamura Y, Kawasaki T, Kato H. Results of 12 nationwide epidemiological incidence surveys of Kawasaki disease in Japan. Arch Pediatr Adolesc Med. 1995;149: 779–83.
13. Yanagawa H, Yashiro M, Nakamura Y, Kawasaki T, Kato H. Epidemiologic pictures of Kawasaki disease in Japan: from the nationwide incidence survey in 1991 and 1992. Pediatrics. 1995;95:475–9.
14. Yanagawa H, Nakamura Y, Yashiro M, Ojima T, Koyanagi H, Kawasaki T. Update of the epidemiology of Kawasaki disease in Japan: from the results of 1993–1994 nationwide survey. J Epidemiol. 1996;6:148–57.

15. Yanagawa H, Nakamura Y, Yashiro M, et al. Results of the nationwide epidemiologic survey of Kawasaki disease in 1995 and 1996 in Japan. Pediatrics. 1998;102:E65.
16. Rodo X, Ballester J, Cayan D, et al. Association of Kawasaki disease with tropospheric wind patterns. Sci Rep. 2011;1:152.
17. Burns JC, Herzog L, Fabri O, et al. Kawasaki Disease Global Climate Consortium. Seasonality of Kawasaki disease: a global perspective. PLoS One. 2013;8:e74529.
18. Philip S, Lee W-C, Liu S-K, Wu M-H, Lue H-C. A swine model of horse-serum induced coronary vasculitis: an implication for Kawasaki disease. Pediatr Res. 2004;55:211–9.
19. Philip S, Lee W-C, Wu M-H, Cherian KM, Lue H-C. Histopathological evaluation of horse serum induced immune complex vasculitis in swine: implication to coronary artery lesions in Kawasaki disease. Pediatr Neonatol. 2014;55:297–305.
20. Burns JC, Newburger JW. Genetics insights in to the pathogenesis of Kawasaki disease. Circ Cardiovasc Genet. 2012;5:277–8.
21. Shrestha S, Wiener H, Shendre A, et al. Role of activating FCVR gene polymorphisms in Kawasaki disease susceptibility and intravenous immunoglobulin response. Circ Cardiovasc Genet. 2012;5:309–16.
22. Son MB, Newburger JW. Kawasaki disease. In: Kliegman, Stanton, St. Geme Schor, Behrman A, editors. Nelson Textbook of Pediatrics. 19th ed. Philadelphia: Elsevier Saunders; 2011. p. 862-7.
23. Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment and long-term management of Kawasaki disease. Circulation. 2004;110:2747–71.
24. Achenbach S, Marwan M, Ropers D, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. Eur Heart J. 2010;31:340–6.
25. Dominguez SR, Anderson MS. Advances in the treatment of Kawasaki disease. Curr Opin Pediatr. 2013;25:103–9.
26. Okada K, Hara J, Maki I, et al. Pulse methylprednisolone with gammaglobulin as an initial treatment for acute Kawasaki disease. Eur J Pediatr. 2009;168:181–5.
27. Okada Y, Shinohara M, Kobayashi T, et al. Effect of corticosteroids in addition to intravenous gamma globulin therapy on serum cytokine levels in the acute phase of Kawasaki disease in children. J Pediatr. 2003;143:363–7.
28. Newburger JW, Sleeper LA, McCrindle BW, et al. Randomized trial of pulsed corticosteroid therapy for primary treatment of Kawasaki disease. N Engl J Med. 2007;356:663–75.
29. Tremoulet AH, Jain S, Jaggi P, et al. Infliximab for intensification of primary therapy for Kawasaki disease: a phase 3 randomised, double-blind, placebo-controlled trial. Lancet. 2014;383:1731–8.
30. Lau AC, Duong TT, Ito S, Wilson GJ, Yeung RS. Inhibition of matrix metalloproteinase-9 activity improves coronary outcome in an animal model of Kawasaki disease. Clin Exp Immunol. 2009;157:300–9.
31. Suzuki H, Terai M, Hamada H, et al. Cyclosporin a treatment for Kawasaki disease refractory to initial and additional intravenous immunoglobulin. Pediatr Infect Dis J. 2011;30:871–6.
32. Sleeper LA, Minich LL, McCrindle BM, et al. Evaluation of Kawasaki disease risk scoring systems for intravenous immunoglobulin resistance. J Pediatr. 2011;158:831–5.
33. Tewelde H, Yoon J, Van Ittersum W, Worley S, Preminger T, Goldfarb J. The Harada Score in the US population of children with Kawasaki disease. Hosp Pediatr. 2014;4:233–8.
34. Rizk SR, El Said G, Daniels LB, et al. Acute myocardial ischemia in adults secondary to missed Kawasaki disease in childhood. Am J Cardiol. 2015;115:423–7.
35. Gordon JB, Kahn AM, Burns JC. When children with Kawasaki disease grow up: myocardial and vascular complications in adulthood. J Am Coll Cardiol. 2009;54:1911–20.