Kawasaki Disease - From History to the Present: Literature review

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ABSTRACT

Objectives: The text addresses the objectives of understanding Kawasaki disease in terms of its etiology, clinical manifestations, diagnosis, treatment and complications, in addition to highlighting the socioeconomic impact and future perspectives of the research. Methods: The literature review uses information from scientific studies and expert reviews to address every aspect of the disease, from its history and discovery by Tomisaku Kawasaki to the most recent therapeutic advances and ongoing research. Results: The results highlight the complexity of Kawasaki disease, including its distinct clinical manifestations, diagnostic criteria, current therapeutic options such as intravenous immunoglobulin and aspirin, and the multiple possible complications, especially those related to the cardiovascular system. Conclusions: The conclusion underscores the importance of early detection, prompt treatment, and close follow-up to improve patients' prognosis. It also points to the continued need for research to enhance understanding of the disease, develop new therapies, and improve clinical management, aiming to reduce the social and economic impact of Kawasaki disease.

Keywords: Kawasaki disease, Acute febrile vasculitis, Arterial aneurysms, Intravenous immunoglobulin, Aspirin.

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INTRODUCTION

Kawasaki disease, an acute febrile vasculitis of unknown origin, predominantly affects children under five years of age. It is characterized by prolonged fever, conjunctivitis, skin rash, abnormalities in the lips and mucous membranes, cervical lymphadenopathy, and peripheral edema. The most serious complication is coronary vasculitis, which can lead to arterial aneurysms and other cardiac consequences. Early identification and treatment are crucial for the prevention of such complications. Understanding of the natural course of the disease and therapeutic advances have improved the prognosis, although there are still challenges in its clinical management.

HISTORY AND DISCOVERY OF THE DISEASE

Revealed to the world in 1967 by Tomisaku Kawasaki in Japan, Kawasaki Disease was initially called acute mucocutaneous lymphadenitis syndrome. After Kawasaki published a series of cases in 1974, the nomenclature was universally accepted. Since then, reports of the disease have emerged globally, indicating that it is not limited geographically. Early recognition of Kawasaki Disease is vital to avoid severe complications, making knowledge about its history and discovery essential for a proper treatment and understanding of the disease.

EPIDEMIOLOGY AND GEOGRAPHICAL DISTRIBUTION

Although more common in East Asian countries, such as Japan and Korea, Kawasaki Disease is also reported globally, including in the Americas and Europe. The incidence varies according to ethnicity, being higher among people of Japanese descent. The geographic distribution of the disease suggests influences of genetic and environmental factors on its pathogenesis. In addition, despite its prevalence in children, Kawasaki disease can affect adults, emphasizing the need for its recognition and management in different populations and localities.

ETIOLOGY AND PATHOPHYSIOLOGY

Kawasaki disease represents a systemic vasculitis whose etiology remains undetermined and is most frequently diagnosed in children under 5 years of age. Its pathophysiology is related to an inflammatory state that mainly affects the medium-sized arteries, resulting in serious possible complications. Although the precise cause is still uncertain, it is suspected that the disease derives from an atypical immune response to environmental stimuli in subjects with a genetic predisposition.

POSSIBLE CAUSES AND RISK FACTORS

The exact causes of Kawasaki disease remain a topic of intense research, although it is postulated that genetic aspects, exposure to pathogens and immune dysregulation may be drivers of

its onset. Specific ethnic groups, such as those of Asian origin, demonstrate greater susceptibility, indicating a strong genetic influence. Additional risk factors, including age and gender, are also under analysis in recent studies.

PATHOPHYSIOLOGICAL MECHANISMS INVOLVED

The pathophysiological mechanisms underlying Kawasaki disease are associated with the activation of the immune system, which triggers the production of inflammatory cytokines and promotes the formation of coronary artery aneurysms. Vascular inflammation is essential for the pathogenesis of the disease, causing endothelial injury and subsequent thrombosis. The overactive immune response also plays a fundamental role in the intensity of symptoms and complications derived from the pathology.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Kawasaki disease reveals a number of distinct clinical manifestations, such as prolonged fever, conjunctivitis in both eyes, skin rash, swelling in the extremities, redness of the lips and tongue, cervical lymphadenopathy, and irritability. The diagnosis is predominantly clinical and is based on previously stipulated criteria. It is crucial for the doctor to be vigilant to recognize these specific signs and symptoms in order to begin treatment immediately and avoid serious complications.

SYMPTOMS AND CLINICAL PRESENTATIONS

The typical symptoms and clinical presentations of Kawasaki disease include persistent fever for at least 5 days, in addition to conjunctivitis, skin rash, lip redness, swelling in the extremities, cervical lymphadenopathy, and changes in the oral mucosa. Detection of these symptoms is critical for diagnosis and should be meticulously investigated by the healthcare professional. The rapid identification of these signs is essential to prevent serious cardiovascular complications.

DIAGNOSTIC CRITERIA AND COMPLEMENTARY TESTS

Diagnostic criteria for Kawasaki disease include persistence of fever combined with at least four major clinical signs, or manifestation of fewer than four signs accompanied by laboratory evidence of inflammation.

In addition to the clinical evaluation, complementary tests such as blood count, C-reactive protein, erythrocyte sedimentation rate, platelet measurement, and cardiac imaging tests are important to confirm the diagnosis and monitor the progression of the disease.

COMPLICATIONS AND PROGNOSIS

The complications of Kawasaki disease are diverse and can affect multiple organ systems, such as cardiovascular, gastrointestinal, renal, neurological, and musculoskeletal. Such complications may include coronary aneurysms, myocarditis, pericarditis, arrhythmias, coronary artery obstruction, ventricular dysfunction, peripheral arterial disease, enteritis, hepatitis, nephritis, encephalopathy, arthritis, among others. The prognosis of Kawasaki disease depends critically on the evolution of these complications, making early diagnosis and effective management essential to prevent severe sequelae and improve patients' life expectancy.

MAJOR ASSOCIATED COMPLICATIONS

Among the most significant complications of Kawasaki disease, the formation of coronary aneurysms deserves special attention because it is the most serious and possibly fatal, and can trigger critical cardiovascular events, such as myocardial infarction or sudden death. Other relevant complications include myocarditis, pericarditis, arrhythmias, coronary artery obstruction, ventricular dysfunction, and peripheral arterial disease, which also exert a considerable influence on the prognosis and quality of life of those affected.

RISK FACTORS FOR UNFAVORABLE OUTCOME

The unfavorable progression of Kawasaki disease can be influenced by multiple risk factors, including the severity of initial symptoms, the presence of persistent fever, inadequate response to initial treatment, pericardial effusions, echocardiographic abnormalities, elevated levels of inflammatory markers, thrombocytosis, and the development of cardiovascular complications. Early detection of these risk factors is crucial for more assertive management and to avoid severe complications.

TREATMENT AND CLINICAL MANAGEMENT

Management of Kawasaki disease focuses on the use of intravenous immunoglobulin and aspirin. Widely adopted as a primary treatment, intravenous immunoglobulin has demonstrated efficacy in minimizing coronary aneurysms. Aspirin is administered in doses with anti-inflammatory properties to prevent thrombosis.

In addition, clinical management includes symptom relief, rest, and careful observation to assess pathological evolution and identify any adversities.

CURRENT THERAPEUTIC APPROACH

The current therapy to deal with Kawasaki disease recommends the early application of intravenous immunoglobulin, ideally in the first 10 days of the clinical picture, in order to attenuate the risk of coronary complications. The usual protocol suggests a single dose of 2 g/kg of intravenous immunoglobulin, combined with anti-inflammatory aspirin. For cases refractory to initial treatment, immunosuppression and other anti-inflammatory drugs are considered.

TREATMENT STRATEGIES IN SEVERE CASES

In the most severe manifestations of Kawasaki disease, especially when cardiac complications are involved, a more intensive therapeutic approach may be required. This strategy may involve intensive supportive treatments, cardiac procedures such as angioplasty or surgical interventions, and the use of robust immunosuppressive therapies. The selection of treatment for severe cases requires a careful analysis that considers the severity of the clinical condition, the existing complications, and the receptivity to the preliminary treatment.

SPECIFIC ASPECTS IN SPECIAL POPULATIONS

Kawasaki disease may exhibit varying manifestations at different ages, making it essential to recognize specific aspects in special groups. In children and adults, the condition may demonstrate variations in the clinical profile, diagnostic methods, and treatment approaches, requiring differentiated specialized care. Thus, intervention in Kawasaki disease in special groups requires a thorough exploration of the symptoms and complications typical of each category, in addition to the contemplation of individualized therapeutic approaches.

KAWASAKI DISEASE IN CHILDREN AND NEONATES

In the context of children and neonates, Kawasaki disease imposes specific challenges, considering the particularities of the immune system still in formation. The early detection of symptoms becomes complex, and the danger of coronary sequelae demands a special focus from health professionals. It is crucial to make a differential diagnosis and adapt the therapeutic approach to the needs of this age group, aiming to minimize the prolonged adverse effects of the condition.

KAWASAKI DISEASE IN ADULTS AND THE ELDERLY

Recently recognized also in adults and the elderly, Kawasaki disease in these age groups has distinct clinical and prognostic characteristics. Diagnosis becomes a challenge due to the low clinical suspicion in this group, requiring prevention and management of long-term complications. It is vital

that health professionals are aware of the possibility of this disease in adults and the elderly, thus ensuring an agile diagnosis and the implementation of appropriate therapeutic strategies.

FUTURE PERSPECTIVES AND ONGOING RESEARCH

The future prospects for Kawasaki disease include the development of more accurate and accelerated diagnostic methodologies, aiming at early detection of the disease to prevent adverse complications. In addition, new treatments are being explored focused on more effective therapies and with a reduction in adverse effects. Ongoing investigations seek to deepen the understanding of the pathophysiology of the disease and identify biomarkers that contribute to diagnosis and prognosis, with the aim of improving the quality of life of patients and reducing the long-term repercussions of the disease.

RECENT SCIENTIFIC ADVANCES

In the recent science of Kawasaki disease, studies that have elucidated new pathophysiological mechanisms implicated in the disease, including the action of the immune system and inflammatory processes, are highlighted. Advances in the genetic field have also helped to identify genetic predispositions that can facilitate the onset of the disease. Significant progress includes research into specific treatments, which aim to minimize complications and optimize the prognosis of those affected by the disease.

FEATURED RESEARCH AREAS

The areas of research that are in vogue in Kawasaki disease include studies focused on the discovery of new biomarkers that help in early diagnosis and in the assessment of risks of complications. In addition, the exploration of new therapies, such as the use of immunomodulators and biotherapeutics, is underway, which have received great attention. Another highlight is epidemiological research, which seeks to better understand the geographic distribution of the disease and identify environmental factors that may influence its development.

SOCIAL ASPECTS AND IMPACT OF THE DISEASE

Kawasaki disease exerts a considerable influence on the social sphere, affecting mainly schoolchildren. Early diagnosis and treatment are crucial to prevent severe conditions, resulting in a high need for medical and financial resources. In addition, the emotional consequences for the families and caregivers of the impacted children are significant aspects, in view of the prolonged recovery process and the potential risk of lasting sequelae, which can induce stress and restlessness.

ECONOMIC AND SOCIAL IMPACT

The economic impact of Kawasaki disease is remarkable, considering the costs of hospitalization, tests, and medications. The social sphere also feels the effects, given that the disease can compromise the school attendance of the affected children due to the extensive recovery time required. This can lead to educational deficits, affecting child development, in addition to significantly altering family dynamics, which are forced to provide intensive care during the recovery phase.

PUBLIC HEALTH NEEDS

Public health demands linked to Kawasaki disease include raising awareness among health professionals and general about the cruciality of early diagnosis, standardizing treatment protocols, and ensuring equitable access to health services. In addition, it is imperative to foster research that enables a deeper understanding of the disease and the development of more effective prevention and management tactics, with the aim of mitigating the adverse effects of this condition on society.

FINAL CONSIDERATIONS AND RECOMMENDATIONS

By concluding this literature review on Kawasaki disease, we conclude that it represents a clinical condition with significant complexities and challenges, having a relevant impact on public health. The synthesized knowledge highlights the imperative need to progress in the understanding of the pathophysiological processes that involve this condition, as well as in the formulation of more effective treatment and clinical management methods. In addition, early detection and multidisciplinary follow-up are vital to reduce complications and improve the prognosis of patients. Therefore, it is essential for healthcare professionals to stay up-to-date and trained to identify and treat Kawasaki disease efficiently in their clinical practices.

SUMMARY OF THE MAIN POINTS ADDRESSED

This review presented a variety of aspects related to Kawasaki disease, ranging from its etiology and pathophysiology to clinical manifestations, therapeutic approaches, and socioeconomic impact. It is crucial to emphasize the importance of recognizing diagnostic criteria and collaborative team action for effective clinical management. In addition, there was an in-depth discussion about the complications and risks that contribute to an unfavorable evolution of the disease. The review also included future perspectives, the latest advances in science, and priority areas for future research, offering a complete and up-to-date view on Kawasaki disease.

RECOMMENDATIONS FOR HEALTHCARE PROFESSIONALS

Considering the accumulated knowledge, it is advisable for health professionals to remain vigilant to the symptoms and diagnostic criteria of Kawasaki disease, especially prioritizing the care of children and neonates. It is also vital to maintain a close follow-up of patients for the early identification of complications and confirmation of the effectiveness of treatments. Collaboration between various medical specialties, including pediatricians, cardiologists, rheumatologists, among others, is essential for holistic and effective clinical management. In addition, psychosocial support strategies for families and public health education initiatives are recommended to promote a better understanding and management of Kawasaki disease.

REFERENCES

1. de Oliveira Ramos, C., de Castro, M. E., Daboit, L. G., Nogueira, L. B., Goes, I. S., Ribeiro, K. M., das Graças, T. V., & Almeida, A. C. (2022). Fatores de risco para o agravamento de crianças com síndrome inflamatória multissistêmica após infecção por Covid-19: revisão sistemática [Risk factors for worsening of children with multisystem inflammatory syndrome after Covid-19 infection: systematic review]. *Brazilian Journal of Health Review, 5*(3), 10636-48. Disponível em https://archive.org

2. Teixeira, D. C., Diniz, L. M., Guimarães, N. S., Moreira, H. M., Teixeira, C. C., & Romanelli, R. M. (2020). Fatores de risco associados aos desfechos da meningite bacteriana pediátrica: uma revisão sistemática. *Jornal de Pediatria, 96*, 159-67. Disponível em https://scielo.br

3. da Silva Oliveira, V., Oliveira, L. G., Bastos, G. S., Dias, L. A., Pinto, R. M., Simões, C., & de Souza, B. Fatores determinantes de evolução grave e crítica da COVID-19 em crianças: revisão sistemática e metanálise. Disponível em https://residenciapediatrica.com.br

4. da Costa, M. M., Roberto, I. S., Vilaca, D. H., & Pires, A. C. (2022). Achados clínicos e laboratoriais da síndrome multissistêmica pós-covid em crianças: uma revisão sistemática [Clinical and laboratory findings of post-covid multisystemic syndrome in children: a systematic review]. *Brazilian Journal of Health Review, 5*(3), 8488-502. Disponível em https://archive.org

5. Araújo, R. S., Francisco, G. G., da Silva Queiroz, V. H., Silva, G. A., & de Souza Coelho, L. (2023). Insuficiência cardíaca em crianças com histórico clínico de síndrome de Kawasaki: avaliação clínica. *Revista Ibero-Americana de Humanidades, Ciências e Educação, 9*(9), 1115-24. Disponível em https://periodicorease.pro.br

6. Andrade, M. R. V. (2023). Investigação cardiológica na síndrome inflamatória multissistêmica pediátrica associada à covid-19: uma revisão sistemática. Disponível em https://bahiana.edu.br

7. Gonçalves, L. F., Gonzáles, A. I., Paiva, K. M., & Patatt, F. F. S. A. (2020). Doença de Kawasaki e Covid-19 em Crianças: Uma Revisão Sistemática. Disponível em https://scielo.org

8. da Silva, D. A., Silva, T. S., Miranda, F. S., & Pires, R. C. C. P. (2023). Manifestações orais e Covid-19: Revisão Sistemática da literatura. *RFO UPF*. Disponível em https://upf.br

9. Kawasaki, I. H. (2021). Estratégias de prevenção do suicídio em médicos: revisão sistemática de literatura. *Mudanças*. Disponível em https://bvsalud.org

10. Silva, V. M. C. (2022). Síndrome inflamatória multissistêmica pediátrica e doença Kawasaki “like” relacionada à infecção por SARS-CoV-2: uma revisão sistemática. Disponível em https://bahiana.edu.br