Bol Med Hosp Infant Mex. 2016;73(3):147–148

Boletín Médico del
Hospital Infantil de México

www.elsevier.es/bmhim

EDITORIAL

Atypical and incomplete Kawasaki disease in the pediatric age☆

Curso atípico o incompleto de la enfermedad de Kawasaki en edades pediátricas

In Mexico, as in other Latin American countries, the number of patients with Kawasaki disease (KD) that are annually registered is unknown. Furthermore, the diagnosis of KD is late.[1] In 1977, Dr. Romeo S. Rodríguez reported the first case of KD in the *Boletín Médico del Hospital Infantil de México*.[2] Since then and until April 30, 2015, 919 cases properly registered in medical publications have accumulated, including the one that appears in this issue of the *Boletín Médico del Hospital Infantil de México*,[3] which is the second largest due to the number of cases reported, thus contributing to the better understanding of KD.[3–7]Although KD was described since 1967, its etiology is still unknown.[8] Clinically, it manifests as an acute febrile syndrome associated with vasculitis of small and medium-sized vessels that can lead to severe cardiovascular complications, including coronary aneurysms, myocarditis, pericarditis, valve injuries and myocardial infarction, and eventually involves different organs. Late diagnosis and an inappropriate treatment strongly influence the development of these complications, as well as the possibility that children course with atypical or incomplete expressions of the disease, which increases the probability of injury in the cardiovascular system or other systems.[9–12]For the etiology, the activation of the immune system triggered by an infectious process in a genetically susceptible host has been considered. The reason for the previous statement is that KD presents the characteristics of a process that is self-limited. From an epidemiological point of view, cases occur in seasonal outbreaks although an etiologic agent has not been specified. The presence of parvovirus B19 and herpesvirus in giant cell arteritis, and the human virus *New Haven coronavirus*, found in respiratory secretions of children with KD, have been reported. Ultrastructure and immunofluorescence studies have identified cytoplasmic inclusion bodies in the bronchi of patients with KD. More recently, adenovirus and bocavirus had also been identified.[13,14] Although these findings are not indicative that these agents are the specific cause of the disease, they reinforce the hypothesis of an infectious etiology of KD.

The purpose of this paper was to emphasize those atypical or incomplete manifestations of KD, which are more likely to cause cardiovascular injuries.

In published series of Mexican patients, those that collected literature data up to the year 2012 as well as those containing the largest number of cases of KD,[4–7] the percentage of presentation of the atypical or incomplete course of KD varies from 20 to 30%. In contrast, the percentages reported are 9%, 15% and 20% in other latitudes, respectively.[11,15,16] Clearly, a greater number of cases with KD evolve in an atypical course in Mexico, which turns out to be significant and makes it essential to know the prevalent (although not definitive) criteria designated so far to establish the differences in this course of the disease.

Meaning of the terms atypical and incomplete

According to the definitions, *atypical* refers to anything that deviates from the representative models due to its characteristics. *Incomplete* means that it has not been finished or completed.

The use of the term atypical KD is recommended for patients with clinical manifestations that are not usually included in the basic criteria of the disease, such as nephritis, hepatitis, gallbladder hydrops, pancreatitis, among others.

On the other hand, it is reasonable to use the term incomplete KD when there are less than four of the classically described criteria. These terms should not be used in either

DOI of original article: http://dx.doi.org/10.1016/j.bmhimx.2016.05.001

☆ Please cite this article as: Sotelo-Cruz N. Curso atípico o incompleto de la enfermedad de Kawasaki en edades pediátricas. Bol. Med. Hosp. Infant. Mex. 2016;73:147–148.

http://dx.doi.org/10.1016/j.bmhime.2017.05.001

indistinct or interchangeable manner. As long as clinical evidence accumulates, the condition of atypia is likely to be more clearly defined. The following data should be taken into account for the diagnosis of atypical course of KD: patients under one year of age or school children and adolescents, fever for more than 9 days, skin rash for long periods of time, renal or liver problems, acute abdominal pain, gallbladder hydrops, hepatitis, cholangitis, pancreatitis, aseptic meningitis, anterior uveitis, hypacusis, arthritis, urethritis, pleural effusion, facial nerves paralysis, erythema at the inoculation site of BCG (vaccine against tuberculosis).

The so-called incomplete KD cases also tend to occur in infants under one year of age or older children and are characterized by fever for more than five days and only two or three of the main signs of the disease.

Moreover, it has been shown that children with atypical or incomplete courses of KD present coronary aneurysms and other cardiac complications more often, which are manifested with increased severity.[9,15]

Considering the difficulties in the diagnosis in addition to clinical data regarding patients with suspicion of atypical or incomplete forms of KD, it is recommended to take into account the following changes in lab studies[9–11] before the decision of treatment with intravenous immunoglobulin: albumin < 3 g/dl, erythrocyte sedimentation rate (ESR) > 40 mm/h, C-reactive protein (CRP) > 3 mg/dl, hemoglobin < 10 g/dl, elevation of alanine aminotransferase (ALT), platelets > 450,000/mm^3, leukocytes < 15,000/mm^3, general urine test > 10 leukocytes/field, and echocardiographic evidence of dilatation of left anterior descending coronary artery > 2.5, decreased left ventricular function, pericardial effusion and mitral regurgitation.[9,12]

Currently, more information and notable advances in the understanding of the physiopathology of KD exist, although biological specific markers have not been identified for diagnosis. The treatment is still based on immunomodulation; however, several attempts for vaccine development have been made.

Whereas diagnosis rests primarily on a clinical basis, pediatricians need to be aware of how KD is manifested in children of different ages.

References

1. Ulloa-Gutiérrez R, Salgado PA, Tremoulet AH. Kawasaki disease in Latin American children: past, current, and future challenges. J Pediatric Infect Dis Soc. 2014;3:280–1, http://dx.doi.org/10.1093/jpids/piu105.
2. Rodríguez R. Síndrome linfomucocutáneo. Bol Med Hosp Infant Mex. 1977;34:53–7.
3. García RF, Flores PA, Villarreal Treviño A, Salinas ED, Lara HP, Maldonado VM, et al. Enfermedad de Kawasaki en un hospital pediátrico en México. Bol Med Hosp Infant Mex. 2016;73:166–73.
4. Sotelo-Cruz N. Revisión de la enfermedad de Kawasaki en México desde la perspectiva de las publicaciones médicas (enero de 1977 a mayo del 2012). Arch Cardiol Mex. 2013;83:214–22.
5. Gámez-González LB, Murata CH, Muñoz-Ramírez M, Yamazaki-Nakashimada M. Clinical manifestations associated with Kawasaki disease shock syndrome in Mexican children. Eur J Pediatr. 2013;172:337–42, http://dx.doi.org/10.1007/s00431-012-1879-1.
6. Arias Cabello B, Fernández Álvarez H, Ordaz Favila JC. Manifestaciones oculares en enfermedad de Kawasaki. Experiencia en el Instituto Nacional de Pediatría. Rev Mex Oftalmol. 2016;90:3–8.
7. Coria-Lorenzo JJ, Sotelo-Cruz N, Martínez-Medina L, Enríquez-Cisneros O, Díaz-Luna JL, Unda-Gómez JJ. Manifestaciones no mucocutáneas de la enfermedad de Kawasaki en población mexicana. Rev Enf Infecc Pediatr. 2015;28:676–81.
8. Kawasaki T, Kosaki F. [Febrile oculo-orocutaneous acrodesquematous syndrome with or without acute none suppurative cervical lymphadenitis in infancy and childhood: clinical observations of 50 cases]. Arerugi. 1967;16:178–222.
9. Rowley AH. The complexities of the diagnosis and management of Kawasaki disease. Infect Dis Clin North Am. 2015;29:525–37, http://dx.doi.org/10.1016/j.idc.2015.05.006.
10. Sánchez-Maubens J, Bou R, Anton J. Diagnosis and classification of Kawasaki disease. J Autoimmun. 2014;48-49:113–7, http://dx.doi.org/10.1016/j.jaut.2014.01.010.
11. Saguil A, Fargo M, Grogan S. Diagnosis and management of Kawasaki disease. Am Fam Physician. 2015;91:365–72.
12. Singh S, Sharma D, Bhattad S, Phillip S. Recent advances in Kawasaki disease—Proceedings of the 3rd Kawasaki Disease Summit, Chandigarh, 2014. Indian J Pediatr. 2016;83:47–52, http://dx.doi.org/10.1007/s12098-015-1858-4.
13. Song E, Kajon AE, Wang H, Salamon D, Texter K, Ramilo O, et al. Clinical virologic characteristics may aid distinction of acute adenovirus disease from Kawasaki disease with incidental adenovirus detection. J Pediatr. 2016;170:325–30, http://dx.doi.org/10.1016/j.jpeds.2015.11.021.
14. Bajolle F, Meritet JF, Rozenberg F, Chalumeau M, Bonnet D, Gendrel D, et al. Markers of a recent bocavirus infection in children with Kawasaki disease: ''a year prospective study''. Pathol Biol (Paris). 2014;62:365–8, http://dx.doi.org/10.1016/j.patbio.2014.06.002.
15. Falcini F, Ozen S, Magni-Mazoni S, Candelli M, Ricci L, Martini G, et al. Discrimination between incomplete and atypical Kawasaki syndrome versus other febrile disease in childhood: results from an international registry-based study. Clin Exp Rheumatol. 2012;30:799–804.
16. Saundakar J, Yim D, Itotoh B, Payne R, Maslin K, Gayatri J, et al. The epidemiology and clinical features of Kawasaki disease in Australia. Pediatrics. 2014;133:e1009–14.

Norberto Sotelo-Cruz
Departamento de Medicina, Universidad de Sonora, Hermosillo, Sonora, Mexico
E-mail address: norbertosotelo5@hotmail.com