Kawasaki Disease

Subjects: Genetics & Heredity
Contributor: Camila Xu

Kawasaki disease is a sudden and time-limited (acute) illness that affects infants and young children.

genetic conditions

1. Introduction

Affected Kawasaki disease children develop a prolonged fever lasting several days, a skin rash, and swollen lymph nodes in the neck (cervical lymphadenopathy). They also develop redness in the whites of the eyes (conjunctivitis) and redness (erythema) of the lips, lining of the mouth (oral mucosa), tongue, palms of the hands, and soles of the feet.

Without treatment, 15 to 25 percent of individuals with Kawasaki disease develop bulging and thinning of the walls of the arteries that supply blood to the heart muscle (coronary artery aneurysms) or other damage to the coronary arteries, which can be life-threatening.

2. Frequency

In the United States and other Western countries, Kawasaki disease occurs in approximately 1 in 10,000 children under 5 each year. The condition is 10 to 20 times more common in East Asia, including Japan, Korea, and Taiwan.

3. Causes

The causes of Kawasaki disease are not well understood. The disorder is generally regarded as being the result of an abnormal immune system activation, but the triggers of this abnormal response are unknown. Because cases of the disorder tend to cluster geographically and by season, researchers have suggested that an infection may be involved. However, no infectious agent (such as a virus or bacteria) has been identified.

A variation in the *ITPKC* gene has been associated with an increased risk of Kawasaki disease. The *ITPKC* gene provides instructions for making an enzyme called inositol 1,4,5-trisphosphate 3-kinase C. This enzyme helps limit the activity of immune system cells called T cells. T cells identify foreign substances and defend the body against infection. Reducing the activity of T cells when appropriate prevents the overproduction of immune proteins called cytokines that lead to inflammation and which, in excess, cause tissue damage. Researchers suggest that the

ITPKC gene variation may interfere with the body's ability to reduce T cell activity, leading to inflammation that damages blood vessels and results in the signs and symptoms of Kawasaki disease.

It appears likely that other factors, including changes in other genes, also influence the development of this complex disorder.

3.1. The gene associated with Kawasaki disease

- ITPKC

4. Inheritance

A predisposition to Kawasaki disease appears to be passed through generations in families, but the inheritance pattern is unknown. Children of parents who have had Kawasaki disease have twice the risk of developing the disorder compared to the general population. Children with affected siblings have a tenfold higher risk.

5. Other Names for This Condition

- acute febrile mucocutaneous lymph node syndrome
- Kawasaki syndrome
- KD
- mucocutaneous lymph node syndrome

References

1. Burns JC. Kawasaki Disease update. Indian J Pediatr. 2009 Jan;76(1):71-6. doi:10.1007/s12098-009-0031-3.
2. Harnden A, Takahashi M, Burgner D. Kawasaki disease. BMJ. 2009 May5;338:b1514. doi: 10.1136/bmj.b1514. Review.
3. Hata A, Onouchi Y. Susceptibility genes for Kawasaki disease: towardimplementation of personalized medicine. J Hum Genet. 2009 Feb;54(2):67-73. doi: 10.1038/jhg.2008.9.
4. Kuo HC, Yang KD, Juo SH, Liang CD, Chen WC, Wang YS, Lee CH, Hsi E, Yu HR,Woon PY, Lin IC, Huang CF, Hwang DY, Lee CP, Lin LY, Chang WP, Chang WC. ITPKCsingle nucleotide polymorphism associated with the Kawasaki disease in aTaiwanese population. PLoS One. 2011 Apr 14;6(4):e17370. doi:10.1371/journal.pone.0017370.

5. Lin MT, Wang JK, Yeh JI, Sun LC, Chen PL, Wu JF, Chang CC, Lee WL, Shen CT,Wang NK, Wu CS, Yeh SZ, Chen CA, Chiu SN, Wu MH. Clinical Implication of the CAllele of the ITPKC Gene SNP rs28493229 in Kawasaki Disease: Association WithDisease Susceptibility and BCG Scar Reactivation. Pediatr Infect Dis J. 2011Feb;30(2):148-52. doi: 10.1097/INF.0b013e3181f43a4e.
6. Onouchi Y, Gunji T, Burns JC, Shimizu C, Newburger JW, Yashiro M, Nakamura Y, Yanagawa H, Wakui K, Fukushima Y, Kishi F, Hamamoto K, Terai M, Sato Y, Ouchi K, Saji T, Nariai A, Kaburagi Y, Yoshikawa T, Suzuki K, Tanaka T, Nagai T, Cho H,Fujino A, Sekine A, Nakamichi R, Tsunoda T, Kawasaki T, Nakamura Y, Hata A. ITPKCfunctional polymorphism associated with Kawasaki disease susceptibility andformation of coronary artery aneurysms. Nat Genet. 2008 Jan;40(1):35-42.
7. Onouchi Y. Molecular genetics of Kawasaki disease. Pediatr Res. 2009 May;65(5 Pt 2):46R-54R. doi: 10.1203/PDR.0b013e31819dba60. Review.
8. Rowley AH, Shulman ST. Pathogenesis and management of Kawasaki disease. ExpertRev Anti Infect Ther. 2010 Feb;8(2):197-203. doi: 10.1586/eri.09.109. Review.
9. Yeung RS. Kawasaki disease: update on pathogenesis. Curr Opin Rheumatol. 2010 Sep;22(5):551-60. doi: 10.1097/BOR.0b013e32833cf051. Review.