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Yerusinia infection with symptoms of Kawasaki disease in Japan

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Yersinia pseudotuberculosis (*Y. pstb*) infection is mainly reported from the Seto Inland Sea coast in Japan and is thought to be localized. That is why *Y. pstb* infection seems to be of low interest throughout the country. However, in the past there has been an outbreak of *Y. pstb* infection in Aomori Prefecture, which is far from the Seto Inland Sea. The national distribution of the sporadic cases is unclear, and it is highly likely to be present throughout Japan.

Y. pstb infections have the same symptoms as Kawasaki disease (KD), including coronary artery aneurysm, and there are reports that approximately 10% of cases were clinically indistinguishable from KD [1-3]. On the other hand, it has been reported that about 10% of cases diagnosed with KD are suspected to have *Y. pstb* infection due to antibody elevation [4,5].

Y. pstb is capable of producing the superantigen *Y. pstb*-derived mitogen (YPM) [6,7]. Generally, many bacteria are found to have the ability to produce superantigen, but the rate of actually producing superantigen is considered to be small. However, it has been reported that about 60% of *Y. pstb* infections show an increase in YPM antibodies [7]. On the other hand, it has been reported that about 3% of *Y. pstb* infection with KD symptoms showed an increase in YPM antibody [5].

According to the report of Tahara et al. [4], among 375 cases diagnosed with KD, 42 cases were positive for *Y. pstb* antibody and 333 cases were negative. The positive group of *Y. pstb* antibody tends to have a significantly higher age of onset compared to the antibody negative group (3.1 ± 2.2 and 2.3 ± 2.1 years old), and cases of additional intravenous immune globulin (IVIG) administration (13/36, 36.1% and 41/256, 36.1%), and cases of coronary involvements (22/42, 52.4% and 105/330, 31.8%) were also significantly higher ($p = 0.03$, $p = 0.004$, and $p = 0.001$, respectively).

According to Horinouchi et al. [5], out of 108 cases, there were 10 cases where *Y. pstb* antibody was elevated, and 98 cases where no rise was observed. Coronary artery complications (2/10, 20% and 1/98, 1.0% respectively; $p < 0.03$) were significantly more frequent in patients with elevated antibodies.

We also experienced one case of elevated *Y. pstb* antibody among 3 cases where symptoms such as fever were prolonged due to refractory IVIG and we had to be diagnosed with Juvenile Idiopathic Arthritis (JIA).

The existence of *Y. pstb* infection with KD symptoms was once noted in the superantigen etiology of KD. At present, as mentioned above, *Y. pstb* antibody positive seems to be a risk factor for IVIG treatment of Kawasaki syndrome (KS) and coronary artery disease development.

Y. pstb antibody tests and Loop-Mediated Isothermal Amplification (LAMP) tests may be essential tests for medical care of KS not only in Japan but also worldwide.

The existence of *Y. pstb* infection with KD symptoms was once noted in the superantigen etiology of KD. At present, as mentioned above, *Y. pstb* antibody positive seems to be a risk factor for IVIG treatment of KS and coronary aneurysm development. *Y. pstb* antibody tests and Loop-Mediated Isothermal Amplification (LAMP) tests may be essential tests for medical care of KS not only in Japan but also worldwide.

Y. pstb infections and superantigens are likely not the etiology of KD itself. However, it may play an important role in determining the severity and treatment of KS. It is accepted without contradiction with the intestinal dysbiosis with translocation of gut flora theory [8-10] regarding the pathogenesis of our KD. The pursuit is thought to be necessary not only to better understand of KS but also to prevent complications.

The morbidity status of KS in Japan is tabulated separately every two years by prefecture. Although there is a difference in morbidity in each prefecture, it does not tend to be high on the Seto Inland Sea coast but is scattered throughout the country. If the *Y. pstb* infection is localized only in a limited area, the prevalence and age distribution of KS and the frequency of coronary artery aneurysm may be different, and its epidemiological study may also be necessary.

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