Difficulties in the Diagnosis of Kawasaki Disease

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This study aims to highlight the difficulties faced in the clinical diagnosis of Kawasaki Disease (KD) presenting beyond the first week. This is a retrospective study of 25 cases of which only 36% met the criteria for classical and 8 % was incomplete KD. Majority (56%) did not meet the criteria for classical KD; at the same time they were not incomplete / atypical cases. Difficulties arise in diagnosis of the cases presenting in the second week, as by that time many of the classical findings disappear or probably have not been present at all. In this scenario high index of suspicion for KD in a child presenting with fever, looking not that sick ("Non toxic look") with bulbar conjunctivitis and oral mucositis helped us to reach the diagnosis. We incidentally observed "Hyperemia of the Upper Eyelids" in 32% of our cases, which might assist in the diagnosis.

Key words: *Coronary aneurysms, IVIG, Kawasaki Disease.*

KAWASAKI Disease (KD), a multi-system vasculitis syndrome (1) is a well known clinical entity, which has become the leading cause of acquired heart disease in children in the developed countries(2,3). In USA, the annual incidence is 17.1/100,000 children(4) and in Japan, it is 111.7 / 100,000 children(5). It is being felt by the authors that the incidence of KD is increasing in India.

In our country pediatricians often encounter the cases late in the second week with prolonged fever, and by that time many clinical signs have disappeared. It is of utmost importance to diagnose them early, so as to bring down the ultimate morbidity and mortality.

This study aims at highlighting the diagnostic difficulties in this scenario. The cases reported in the series should not be confused with incomplete KD(6) as per American Heart Association guidelines because coronary aneurysms are essential diagnostic criteria for the same.

Subjects and Methods

This is a retrospective study involving analysis of case reports of all cases diagnosed and treated as KD at our Institute, over a period of three and half years, from September 2001 to March 2005 (total 25 cases).

Inclusion criteria

A high index of suspicion in cases presenting with prolonged fever and a non-toxic look at presentation having clinical features or history of features suggestive of KD. We also considered supportive laboratory parameters, echocardiographic findings and resolution of clinical features with high dose aspirin and IVIG. The classical set of criteria(1) as per AHA guidelines for KD was not mandatory for diagnosis in our series. Others(7) have stressed upon a similar point of view.

Results

In our series, amongst the 25 cases, 84% presented beyond the first week (most were

referred, undiagnosed cases). In more than 50% cases, signs like unilateral cervical lymphadenopathy, rash and edema of the extremities were absent. Consistently present clinical features were persistent fever, extreme irritability, non-purulent bulbar conjunctivitis and mucositis as shown in *Fig. 1*.

Of all the cases, 36% met the criteria for classical KD, 8% of the cases were incomplete KD and 56% cases did not meet the criteria for even incomplete KD (they met three of five clinical criteria but did not have echo-cardiographic changes.). All the cases responded dramatically to a single course of IVIG (2 g/kg single dose over 12 hrs) and high dose aspirin (100 mg/kg till day14 of illness) and then low dose aspirin was continued for 6 weeks or longer in cases with coronary aneurysms.

Clinical features noticed by us (not sufficiently stressed in the literature so far):

1. "Non toxic look" was noted in 100% of our cases ("Toxic look" is a subjective clinical finding described as an ill looking appearance). We feel this can be an important clinical finding. To appreciate it let us compare two cases of similar age one with KD and the other with "Enteric fever" running fever for two weeks. A clinician with sufficient experience will immediately recognize that the child with enteric fever will look definitely sick (toxic) while the child with KD will not look that sick (Non-toxic).
2. "Hyperemia of the upper eyelids" noted in 32 % of the cases may contribute to the clinical diagnosis. It appeared in the late first to early second week and persisted till the administration of IVIG (the first sign to disappear in our series, even before disappearance of irritability and conjunctivitis). Thus, the observed sign, as it extends into the second week, can be an important pointer to KD, especially in those cases presenting late.

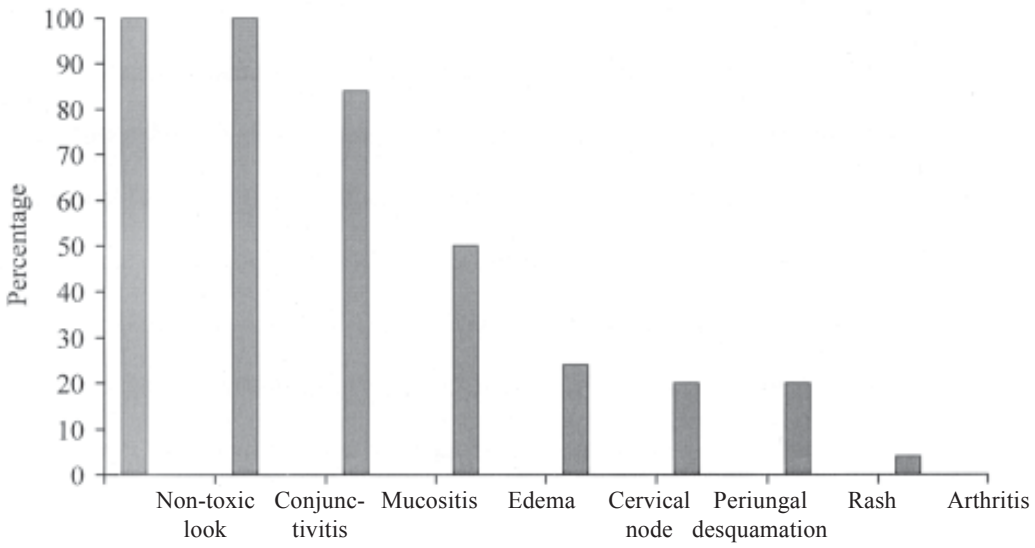

Fig. 1. Major clinical features in patients with KD presenting beyond the first week.

Key Messages

- Kawasaki Disease should be strongly considered in a child presenting with fever for more than one week, looks "Non-toxic" (Not that sick), has non-purulent bulbar conjunctivitis and oral mucositis.
- "Hyperemia of the upper eyelids", could be an important pointer to diagnose Kawasaki Disease especially in cases presenting beyond the first week.

Discussion

It will be evident that this study aims at focusing on the Indian perspective of KD, i.e. the ground realities throughout the country. The cases are often diagnosed late and are treated as "Pyrexia of Unknown Origin" extending into weeks. The result is prolonged hospitalization, unnecessary use of antibiotics, anxiety and loss of workdays for the parents. In addition to that, there is definite increase in morbidity with delay in treatment like development of coronary aneurysms and myocardial complications (myocarditis and arrhythmias)(9). Early detection and treatment would have prevented all such complications.

Thus, our effort was to highlight the difficulties in the clinical diagnosis of KD in the second week when a pediatrician often first encounters the case and by that time many clinical signs may disappear. Indian publications on Kawasaki disease till date are based on classical recommendations for diagnosis of KD (AHA guidelines)(10-12). We strongly feel that in the present scenario, following these guidelines would mean missing many cases.

Results of our study will stand out in contrast to the earlier published series from India(11,12). We noted though fever and non purulent bulbar conjunctivitis were present in 100% and oral mucosal changes were seen in 84% of our cases as reported earlier, yet the other clinical features noticed by previous authors (such as cervical lymphodenopathy, rash) were absent in majority of cases of our series. The possible cause of absence of other features could be that, the cases presented late after disappearance of many of the clinical features or they were not present at all.

Of late, many cases have been reported which do not meet all the criteria for diagnosis of Incomplete/atypical KD(8,13-15). It is prudent to mention here that in our series, majority (56%) did not meet the criteria for classical KD; at the same time they were not incomplete/ atypical cases.

In any individual child, all the criteria need not be present at the same time. They may appear sequentially. Some features, such as conjunctivitis, may disappear while others appear. Therefore, the clinician may have to rely on history and not insist on seeing all the classical features of KD personally. Furthermore, not all children with KD develop the complete picture before coronary involvement is recognized. Also, patients with atypical onset KD may not develop the typical features for a long time, thus risking delay in diagnosis(8).

An effort has been made by US Center for Disease Control to lay down clinical criteria for diagnosis of KD, which may act as a useful guide to the clinician for epidemiological survey of the disease(7,8,16). We feel that the two new clinical findings observed by us will go a long way in the diagnosis of KD. A "Non toxic look" simply would mean the child not

appearing sick, despite having prolonged high grade fever. The hyperemia of the upper eyelids could be the result of the generalized inflammatory process (vasculitis), the basic pathology of KD. We would insist that guidelines for diagnosis of KD be debated and revised.

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