Diagnosing Incomplete Kawasaki Disease

Sir,

Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology that occurs predominantly in infants and young children aged <5 years.[1] KD has been reported worldwide, but is most prevalent in Japan, with an annual incidence of 112 cases per 100,000 children aged <5 years.[1] In the Eastern Province of Saudi Arabia, the incidence is estimated as 7.4/100,000 children aged <5 years, with a male-to-female ratio of 1.9:1.[2] The diagnosis of KD is made based on the presence of at least four of the five clinical diagnostic criteria along with fever for ≥5 days.[1] However, its diagnosis presents challenges because the clinical diagnostic criteria are not specific for KD, and a significant proportion of children with KD do not fulfill the diagnostic criteria.[3] Patients with incomplete KD are usually treated for infection until the disease begins to manifest clinically,[1,4] which results in a delay in diagnosis and significantly increases the risk of complications. Coronary artery aneurysms are the most significant complications, developing in 1 of 5 children with KD if treatment with intravenous immunoglobulin (IVIG) is not initiated early.[1]

In Saudi Arabia, Lardhi[2] found coronary artery abnormalities in 37% of the patients despite treatment with IVIG, likely due to delay in recognition of the disease, and thus in starting management.[2] Similarly, Muzaffer and Al-Mayouf[4] found that 30% of their patients with KD had coronary aneurysm and unusual complications, while Alsaggaf[3] found that 48.2% of the KD patients had coronary artery lesion, of which 51.8% had incomplete KD. Therefore, early diagnosis and treatment are of considerable significance for patients with KD.

Several studies have recently investigated the predictive value of brain natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) in differentiating KD from other febrile illnesses.[5-7] Elevated levels of NT-proBNP during the acute phase of KD are indicative of systemic inflammatory responses and increased vascular permeability, with or without overt myocarditis.[7] It should be noted that subclinical myocarditis is a common feature of early KD, regardless of the presence or absence of major coronary artery involvement,[1] and NT-proBNP is a marker of myocardial, rather than coronary artery, involvement in KD.[6]

In a recent study, at cutoff points 514 pg/ml and 1025 pg/ml, the sensitivity of NT-proBNP in diagnosing KD was found to be 100% and 88%, respectively, while the specificity was 80% and 96%, respectively.[5] However, serum levels of BNP and NT-proBNP vary with age during childhood (i.e., higher in neonates and infants than in children >3 years of age).[8] Therefore, use of a single cutoff value for all ages would be inappropriate, and age should be considered as a factor in interpreting the concentrations of these peptides.[8]

An 18-month-old Saudi boy was admitted to Qatif Central Hospital with a history of fever for the past 5 days, bilateral nonpurulent conjunctivitis and transient rash over his abdomen. On examination, the patient was found to have swollen, dry, peeling lips without redness or cracking. His complete blood count was 355 × 10^3/ul, erythrocyte sedimentation rate (ESR) 48 mm/hr and C-reactive protein (CRP) 3.2 mg/dl. NT-Pro-BNP was used as a biological marker for KD and was found to be considerably higher (1510 pg/ml) than the 97th percentile of NT-pro-BNP for the patient's age (675 pg/ml).[9] Based on these results and the clinical status of the patient, incomplete KD was considered as a possible diagnosis, and 2 g/kg of IVIG was administered to the patient over 2 days. After 24 h, the patient became afebrile, with normal echocardiogram results. On Day 7 of admission, the patient developed peeling of palms along with marked thrombocytosis (628 × 10^3/μl), findings that support the diagnosis of incomplete KD. One month later, NT-pro BNP decreased to 80.2 pg/ml, with negative ESR and CRP.

This is the first report in Saudi Arabia on the use of age-dependent reference range of NT-proBNP to support the diagnosis of incomplete KD. Given its considerable diagnostic value for KD, this reference range of NT-pro-BNP may help clinicians in early decision-making, and thus decrease KD complications. Although elevation of inflammatory markers such as ESR and CRP is universal in KD, they are not specific.[1]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parent has given his/her consent for his/her child's images and other

clinical information to be reported in the Journal. The patient's parent understands that his/her child's name and initials will not be published and due efforts will be made to conceal the child's identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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