Diagnosing Kawasaki syndrome

Sirs, We read with great interest the recent editorial on the need for a new tool for diagnosing Kawasaki syndrome/Kawasaki disease [1]. Our investigations of the history of the clinical criteria for Kawasaki syndrome [2–4] lead us to share a number of observations. Researchers have long noted that strict reliance on the classic case definition has led to delay in treatment of children who do not meet the classic criteria, yet still develop coronary artery aneurysms (CAA) [5]. Not only is the diagnosis delayed in these atypical cases, but recent North American studies report that the incidence of CAA is higher in the atypical cases than in the classic ones [6, 7].

The goal of a clinical case definition of Kawasaki syndrome should be to prevent CAA. Although this may seem obvious, the classic case definition was formulated prior to the knowledge that Kawasaki syndrome can result in CAA [2, 3]. Simonini et al. [1] have reviewed their data and identified a combination of clinical signs and laboratory findings that may help identify patients with CAA who failed to meet the classic diagnostic criteria. As the authors note, the American Heart Association’s Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease has recently issued an algorithm to better identify patients at risk of CAA [8]. Although these revised guidelines should help identify patients at risk of CAA who do not meet the classic criteria, they have not yet undergone prospective testing. We endorse Simonini et al.’s suggestion that any new guidelines undergo prospective analysis to determine their sensitivity and specificity for preventing CAA. In Japan, there has been prospective testing of the Harada scoring system, which relies on a combination of clinical and laboratory findings, for identification of patients with CAA [9]. Using the Harada criteria, Sato et al. [10] were able to successfully identify and treat those at risk of CAA in a study of 203 patients. Given its initial reliability, it seems that the Harada score is a reasonable starting point for the development of a clinical case definition to identify patients at risk of CAA.

Our other comments deal with phenotype and nosology. Because neither the agent(s) nor the pathophysiology that result in paediatric CAA are known, the illness should properly be labelled ‘Kawasaki syndrome’, not ‘Kawasaki disease’. The authors of the editorial and the Centers for Disease Control and Prevention have reverted to this nomenclature, but the American Heart Association and the Japan Kawasaki Disease Research Committee retain the term ‘Kawasaki disease’. As we have discussed in detail elsewhere [2, 3], the use of the term ‘Kawasaki disease’ came into the lexicon for political rather than scientific reasons. This distinction has important ramifications for both diagnosis and research. Only when an aetiological agent and/or pathophysiology are identified should the ‘disease’ nomenclature be adopted.

From this perspective, the adoption and use of the term ‘incomplete Kawasaki disease’ is misleading, because it presumes that all cases which develop CAA but fail to meet the classical criteria are anomalous. There are two reasons to resist such nomenclature. First, as a syndrome, the clinical signs, symptoms and laboratory findings (the phenotype) are necessarily tentative. Grouping classical and atypical presentations together as a syndrome authorizes epidemiologists and researchers to determine if these presentations comprise a single disease with a spectrum of possible outcomes or multiple diseases that share a number of common clinical presentations but have distinct causes and outcomes. The adoption of the term ‘incomplete’ assumes that the classical criteria represent and identify the essential elements that result in paediatric CAA. However, given the number of cases in which CAA develops despite the failure to meet the classical criteria, such a designation is both unhelpful and misleading. We believe that the terms ‘incomplete’ and ‘atypical’ should both be abandoned and the term ‘Kawasaki syndrome’ be adopted to denote illnesses that may result in paediatric CAA. The emphasis should be on the identification of those children at risk of CAA and not the preservation of a clinical sign complex.

The authors have declared no conflicts of interest.

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Accepted 12 July 2005

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Letters to the Editor

Rheumatology 2006;45:241
doi:10.1093/rheumatology/kei073
Advance Access publication 20 December 2005

Reply: Nomenclature of Kawasaki disease/syndrome

We thank Drs Bastian and Kushner for their helpful comments and suggestions on our editorial on Kawasaki syndrome [1].

We agree with their suggestion that the term Kawasaki syndrome (KS) is more appropriate than Kawasaki disease until we have a better understanding of the exact aetiology and pathogenesis of this vasculitic syndrome. Drs Bastian and Kushner state that ‘the goal of a KS clinical case definition should be to prevent coronary artery aneurysm. In our view this goal can be accomplished by developing a broader definition of the syndrome to ensure identification of all children who would benefit from iv Ig treatment’ [1].

Modifying case definition and classification criteria will not help. The terms ‘atypical’ and ‘incomplete’ are introduced to modify and supersede a rigid rule requiring a categorical answer!

The current criterion for diagnosing KS is based on case definition criteria created for epidemiological surveys [2, 3]. In many respects case definition has the same weakness as classification criteria. These tools work well for groups of patients, but not in the evaluation of individual patients [4]. Also, application of case definition criteria and classification criteria results in ‘yes’ or ‘no’ answers only. Therefore they function poorly in diagnosing individual patients.

Unfortunately, physicians often use case definition and classification criteria for diagnostic purposes. Since the complications of untreated KS can be fatal and since this can be greatly reduced with timely treatment, there is an urgent need for the physician to diagnose this condition early. However, the disease evolves over a few days to weeks and mimics several other common childhood diseases. Therefore, they need a different set of criteria capable of minimizing over- and underdiagnosis. Such diagnostic criteria should be able to exclude other diseases as much as possible (specificity) but, even more importantly, to include patients with probable KS (sensitivity). That is why we have been working on a more comprehensive set of diagnostic criteria that will group and label patients as having definite or probable KS.

Drs Bastian and Kushner also suggest that the Harada score may be a good start for developing a clinical case definition. We have already outlined our objection to using case definition for diagnostic purposes. Also, in the study by Sato and colleagues [5] referred to by Drs Bastian and Kushner, the Harada score was applied after patients had been diagnosed as having KS based on case definition criteria. Also, other than the age and sex of the patients, all the other items included in the score are laboratory values. We believe that any new diagnostic criteria should include a spectrum of clinical and laboratory values.

The authors have declared no conflicts of interest.

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Rheumatology 2006;45:241–242
doi:10.1093/rheumatology/kei194
Advance Access publication 22 November 2005

Dementia associated with antiphospholipid antibodies

Sir, Gomez-Puerta and colleagues [1] recently summarized the clinical and radiographic characteristics of dementia associated with the antiphospholipid syndrome. Their computer-assisted literature search failed to detect a group of patients we presented with dementia associated with Sneddon’s syndrome (SS), most of whom expressed anticardiolipin antibody [2]. The presence of a hypercoagulable state implicates cerebral ischaemia as the pathophysiological mechanism. Clinical stroke, with abrupt onset of focal deficits, may be absent, however; a point emphasized by our report and confirmed by Gomez-Puerta et al. We recently encountered another similar patient in whom dementia was associated with lupus anticoagulant (LA) but no focal symptoms or signs.

A 66-yr-old woman presented with abrupt onset of cognitive impairment after falling and sustaining minor traumatic injuries. Past medical history included treated hypertension and Raynaud’s phenomenon but no venous thromboembolic events or prior pregnancy complications. Uncharacteristic behaviours were initially attributed to opioid analgesics, though problems persisted after treatment was discontinued. Her family noted prominent apathy and reduction of activity level; she rarely completed tasks that she started. Other problems consisted of apraxia, with difficulty operating seatbelts, opening doors and dressing. The patient reported right–left confusion as well as difficulty reading and writing. Associated symptoms included brief crying spells superimposed on consistently flat affect and gait disturbance leading to several additional falls. General physical examination showed acrocyanosis and faint livedo reticularis on her trunk. The patient was alert and cooperative with prominent psychomotor slowing. Impersistence made assessment of strength and coordination difficult to interpret but muscle tone was normal and tendon reflexes were symmetrically brisk, with positive crossed adductor response. Gait was remarkable for slightly broad base and minimal flexion posture of the left arm. Laboratory tests revealed prolonged partial thromboplastin time (54 s), a low titre of ANA (1:160, mixed homogeneous nucleolar pattern),