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IS PERIVASCULAR ECHO BRIGHTNESS A RELIABLE MARKER OF CORONARY ARTERITIS IN ACUTE KAWASAKI SYNDROME ?

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Background: Coronary aneurysms (CAA) appear around Day 10 of Kawasaki syndrome (KS). Enhanced perivascular echo brightness (PEB) is not widely accepted as a marker of vasculitis. To explore its utility in early diagnosis of KS, we examined interobserver agreement (IOA) and prevalence. *Working definition*: Appearance of bright broad echoes surrounding the coronary lumen extending for at least 1 cm along the artery, as compared to thin parallel echoes representing normal coronary artery walls distinct from the surrounding. **Methods:** IOA: 20 randomly mixed PEB positive and negative studies were reviewed blindly by 6 pediatric cardiologists after they were coached on the definition. Mean % IOA and 95% confidence intervals (CI) were calculated for presence/absence of PEB in right and left coronary arteries (RCA, LCA). Prevalence: 50 consecutive KS pts' echoes were reviewed for PEB and concomitant or subsequent coronary ectasia or aneurysm (CAE or CAA). **Results:** *IOA*: Overall IOA was 79.2% (95% CI: 74.4, 84.0). For RCA and LCA, IOAs were 76.7% (70.2, 83.1) and 81.7 (74.6, 88.7), respectively. *Prevalence*: 28/50 pts (56%) showed PEB in one or both CAs in the first echo. 13 and 4 of those (26% and 8%) showed CAE and CAA, respectively. PEB without CAE/CAA was noted on Day 7.2 + 4.24 (m + sd); PEB with CAE or CAA was noted on Day 9.29 + 5.77 (NS). PEB was noted in 11/18 (61%) typical KS pts (TKS), in 11/14 (79%) atypical KS pts (AKS) and in 4/14 (29%) possible KS pts (PKS) ($p=0.025$). All pts who later developed CAA or CAE initially showed PEB. All PEB-negative pts remained free of CAA or CAE. **Conclusions:** (1) PEB is a sufficiently objective finding. (2) PEB is detectable in majority of pts before Day 10. (3) PEB precedes CAE or CAA in some pts.

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DIAGNOSIS OF ATYPICAL KAWASAKI DISEASES IN EARLY STAGE BY ECHOCARDIOGRAPHY

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Objective: To improve the diagnostic ability of atypical Kawasaki Diseases in early stage. Methods: Two-dimensional echocardiographic features of 24 cases with atypical Kawasaki disease in last two years were analyzed in retrospect. All the children in our study only have 3 or 4 items in the diagnostic standard revised by Japanese MCLS Research Committee in 1984. ATL HDI 5000 and/or HP 5500 color Doppler ultrasound system with transducer frequency of 3~8 MHz were used to scan the sick children. The internal diameter and shape of coronary arteries were focused in the following views: short axis of aorta, short axis of LV at mitral level, atypical longistudinal view of LV, longistudinal view of right ventricular inlet and outlet view, et al. The qualification of coronary dilatation was classified according to the "Guidelines for coronary lesion in KD" reported by Kato, based on the changes of coronary artery in coronary angiography. Results: Four kinds of two-dimensional echocardiographic features of Kawasaki diseases are described as follow. (1) Normal coronary arteries in diameter with thickening arterial wall, enhancing wall echo, and blurred internal cavity. (2) Stenosis of coronary arteries with thickening arterial wall and enhancing wall echo. (3) Slight dilation of coronary arteries with thickening arterial wall and enhancing wall echo. (4) Severe dilation of coronary arteries and coronary aneurysms developed. Conclusion: Echocardiography is of great values in diagnosing Kawasaki disease at early stage of Kawasaki disease, which plays an important role in releasing coronary arteries injure.

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SEVERE MYOCARDITIS IN CHILDREN WITH KAWASAKI DISEASE

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Background: Severe myocarditis leading to heart failure is a specific entity complicating the acute phase of Kawasaki disease (KD) in children. Clinical course and response to therapy appear to differ in those children with myocarditis requiring inotropic treatment. **Objective:** To characterize specific clinical, laboratory and imaging findings in patients with severe myocarditis and delineate their response to therapeutic intervention. **Methods:** A 3 year retrospective chart review of all patients seen at the HSC (1998-2001) with the diagnosis of KD plus severe myocarditis was performed. The demographic features, clinical, lab and imaging findings and response to treatment were analyzed. **Results:** 5 patients (3female/ 2male) with a mean age at onset of 3.4years (range 1.5 to 4.4yrs) met diagnostic criteria for KD. In addition all children had significant fatigue, severe tachycardia (mean HR161/min) and hypotension (5/5 <10.perc.). Lab testing revealed elevated ESR (mean 105mm), anemia (mean HGB 112g/l), hypocalcemia (mean ion.Ca 0.99mmol/l) and hypoalbuminemia (mean 26g/l). All children received 2 doses of IVIG (2g/kg/dose). In addition to non-responsiveness to IVIG clinical signs of heart failure were aggravated (tachycardia: mean HR 195/min) supported by diagnostic findings of hemodilution and reduced heart function (anemia: mean HGB 82g/l; ECHO: mean EF 41%, range 18-59%; x-ray bilateral lung effusion). Coronary arteries showed only minor involvement. All patients required positive inotropic support (range 2-5 days). 4 out of 5 patients were treated with high dose methylprednisolone IV-therapy for at least 2 days resulting in rapid clinical improvement. All were maintained on an oral steroid regimen, which was tapered according to the clinical response. **Conclusion:** The development of severe myocarditis in KD patients leads to specific findings on clinical examination, lab testing and imaging. Multiple interventions with IVIG did not result in the resolution of the clinical features and in fact led to clinical aggravation. These observations suggest a volume-restricted strategy and a consideration of early intervention with high dose corticosteroid.

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EVOLUTION OF CORONARY ARTERIAL LESIONS DURING THE ACUTE PHASES OF KAWASAKI DISEASE IN CHILDREN AND ADOLESCENTS

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Objective: To study the evolution of coronary arterial lesions during the acute and subacute phases of Kawasaki disease by echocardiography. **Method:** The study was done retrospectively from 1st July 1994 to 30th June 2000. In our protocol, echocardiography is done for acute cases at presentation, on Day 14 (2 weeks), Day 28 (4 weeks) and Day 56 (8 weeks) of fever. Only cases that presented early, within 10 days of fever, were included. The echocardiographic findings throughout the first 8 weeks of the disease were reviewed to study the evolution of coronary arterial lesions. Those with positive coronary lesions were divided into 2 groups, one with early lesions detected at presentation and the other with lesions appearing at or after 2 weeks from the onset. Their demographics and clinical course were compared.**Results:** A total of 611 patients, mostly Chinese, aged 1.2 months to 15.4 years were identified. The majority of patients (90.2%) had received intravenous gammaglobulin (IVGG) within 10 days. Coronary arterial lesions in form of ectasia or aneurysms have been found in 112 patients (18.3%). Only 4.4% of patients had coronary lesions at presentation. Most new lesions (12.9%) were detected at 2-week echo follow-up. New lesions were rare after 4 weeks. Coronary lesions began to regress since 2 weeks from onset and continued to regress at similar rate (37-41%) at each 2-week follow-up. By the end of 8 weeks, 63.4% of all the lesions had regressed and only 6.9% of patients continued to have them. The group with early coronary arterial lesions had more male patients, required more doses of IVGG while the one with later lesions had more cases not requiring IVGG. However, their age distribution, duration of fever, frequency of atypical presentation and severity of coronary lesions were similar. These data may guide our future management plan.

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OXYGEN RADICALS ACTIVITY AS A PREDICTOR OF CORONARY ARTERY LESIONS IN KAWASAKI DISEASE

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Background Neutrophil-derived Oxygen radicals (OR) play a role in a wide variety of diseases including vasculitis syndrome, however, little is known about causal relation between coronary artery lesions (CAL) in Kawasaki disease (KD) and OR activity.Objective To investigate a role of OR in CAL. Methods 27 patients with KD were enrolled within 7 days from the onset of illness. All patients were treated orally with aspirin (ASA), and 21 patients, selected by Harada scoring system, also received intravenous gammaglobulin therapy (IVGG). IVGG was administered as daily infusions of 200mg/Kg for five consecutive days. Patients were retrospectively divided into the following three groups according to IVGG and CAL: Severe group, patients with CAL treated with IVGG (n=3); Moderate group, patients without CAL treated with IVGG (n=18); and Mild group, patients without CAL not needed IVGG (n=6). 15 healthy children were studied as controls. Neutrophil-derived OR were measured as intracellular chemilluminescense (ICCL) of whole blood by luminol-dependent chemilluminescense method using luminol-binding microsheres. Serial changes in ICCL values were monitored from acute to convalescent phases in every patient.Results Significant differences were observed in pretreatment ICCL values among the three groups with KD ($p<0.05$). The mean ICCL values in mild, moderate and severe groups of KD were $13.7\pm5.5x10^5$cpm, $34.8\pm9.3x10^5$cpm, and $71.2\pm10.1x10^5$cpm, respectively, while that in control was $3.1\pm1.2x10^5$cpm ($p<0.01$). In IVGG groups, the ICCL values were significantly decreased at 1 and 4 weeks after treatment: $19.2\pm8.4x10^5$cpm and $8.1\pm3.3x10^5$cpm in moderate group ($p<0.05$), and $39.8\pm7.7x10^5$cpm and $20.3\pm9.2x10^5$cpm in severe group ($p<0.05$). Thus, patients with CAL (severe group) had persistently much higher ICCL values than patients without CAL (mild and moderate groups)($p<0.05$).Conclusions OR activity was well correlated with severity of KD in acute phase and decreased in parallel with IVGG. OR activety appears to be useful for predicting the risk of CAL despite IVGG, and possibly helping earlier decision on an alternative treatment.

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S-100 PROTEIN LEVELS IN CHILDREN WITH KAWASKI DISEASE: CORRELATION WITH IRRITABILITY

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Kawasaki Disease (KD) is a systemic vasculitis with central nervous system (CNS) manifestations including irritability, cerebrospinal fluid pleocytosis and cerebral hypoperfusion. S-100, a dimeric protein present in glial cells, is elevated in patients with brain tumors and stroke and following cardiopulmonary bypass. The purpose of this study was to determine if serum S-100 protein levels are abnormally elevated in children with KD and to correlate these measurements with markers for systemic and CNS inflammation. We measured S-100 levels in 15 children with classical KD, mean age 3.0 years (range 7 months-6 years), at 3 intervals: presentation, 11-21 days from onset of disease and 22-63 days from onset. Elevated S-100 levels ($>0.2\mu g/L$) were found in 3/15 (20%) both at presentation, and at 11-21 days, and 4/15 (26.7%) at 22-63 days. The subjects were subdivided into Group I (n=8), at least 1 abnormal S-100 measurement and Group II (n=7), normal S-100 at all times. The groups were compared for, age, duration of fever, echocardiographic changes, irritability and systemic inflammatory markers at each time period. Clinical associations were made independent of knowledge of S-100 levels. There was no difference in clinical signs or echo findings between the groups following treatment. Patients in Group I were younger at presentation (1.7 ± 1.4 yrs. vs. 4.1 ± 1.9 yrs., $p=0.05$) and more irritable at diagnosis (71% vs. 13% $p=0.04$). Fever persisted longer in Group II (9.6 ± 2.8 days) following treatment than in Group I (6.1 ± 1.8 days, $p=0.035$). The findings show that S-100 protein was elevated in a number of patients with KD who were younger and more irritable at presentation. We speculate that inflammatory changes of the CNS can lead to increased levels of S-100 which can serve as a marker for CNS inflammation.