Incomplete and atypical presentation of Kawasaki Disease: A report of five cases

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ABSTRACT

Introduction: Kawasaki disease (KD) is an acute febrile vasculitis mainly affecting children, with two types of presentation, namely, typical and atypical. It is the most critical cause of coronary artery complications and if not treated on time and appropriately, complications may occur in up to 25% of the patients will get.

Patients: This study reports five rare cases of incomplete KD Who has been admitted with diagnosis of Bacterial Meningitis, Staphylococcal Septic Arthritis, Herpetic Gingivostomatitis, Viral Hepatitis and prolonged Fever. Since there was no response to treatment, with impression of Atypical Kawasaki patient has been evaluated and treated.

Conclusion: Atypical presentation of the disease led to misdiagnosis and prolonged process of diagnosis. Due to the increasing number of atypical Kawasaki cases and the probability of coronary artery disorder, it is recommended that atypical Kawasaki be considered in the differential diagnosis of the disease in the patients with fever of over five days without any clinical cause.

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Introduction:

Kawasaki disease (KD) was described by Tomisaka in Japan in 1967 (1). Firstly it was supposed that the disease was bounded by world east population but later it turned out to be prevalent in USA, Europe and Asia in various races. Kawasaki is an acute disease affecting most small children and infants, so 80% of parents aged under five often presents as vasculitis. Kawasaki is more in spring and winter with more outbreak of Viral Disease (2,3). Recently it is known as the most prevalent acquired cause of heart condition that in spite of death in less than 0.01, if not treated, the probability of hearth involvement will go up to 25%.(4) The disease factor is still unknown, but some different factor are effective on forming infection factors including Epstein–Barr virus, measles, rubella, Hypatits virus, para influenza, a species Streptococcus's, Treponema palladium, Leptosipra, Mycoplasma Brucella and Recktesia Staphylococcus, Yersinia and probably Adenovirus type 2 and in recent years, Diphtheroid propionobacterium Acne with higher prevalence, also immunologic factors.

Its clinical syndromes including over – four – days fever without reaction to antibiotic therapy and Conjunctivitis, redness of tongue and mouth mucus, cracked lips, inflated and red ends are rash and generalized lymphodenopathy respectively, which will result in scaling later. Symptoms found in most patients including arousal, anorexia, lethargia diarrhea, arthragia, adenitis, abdominal pains and uveitis (7). The diagnosis is clinical and

there's no preclinical specific finding in the disease but nonspecific changer might be seen in the form of,leukosytosis, high sedimentation, positive CRP, increased, increase thrombosis (in early second stage) and anemia.

The most serious disease symptom is involvement of heart coronary.

There are myocarditis in 20-30% of cases and mild changes in E.C.G in E.C.G in the long P-R and ST changes in 60% of the patients.

Asprine consumption and venous gamaglobin in high dose leads to decrease the disease symptoms in the first 10 day and before aneurysm formation coronary veins involvement (8).

Kawasaki disease appears in complete and in complete forms. In incomplete form, which has four mentioned criteria, the fever continues more than 4 days. The incomplete form is more current in infants and children above five (9). In complete Kawasaki is usually diagnosed with delay (10). The Kawasaki disease including Asprine consumption and venous gamaglobin result in decreasing disease symptoms in the first 10 days (11). In this paper, we consider to identify the patients with incomplete Kawasaki and atypical presentation contributing to awareness of physicians.

Case Presentations:

First case (Kawasaki during bacterial meningitis treatment):

The patient was a 6 – month infant with three - days fever and skin eash who was hospitalized after diagnosing meningitis.

The infant was weary and sleepy in examination. The remedy began with dexamethasne, vancomycine, ceftriaxon after lumbar puncture was (gram-staining of CSFS for diplo cocci bacteria reported positive, but the culture was negative). On the second day he was under treatment with anti-seizure drogs because of seizure but for the sake of resistant seizure, it was controlled with midazolam lastly. (Due to prolonged fever on the third day, CSF aspiration and head CT scan were evaluated in the clinical conditions. Vaccination was perfect, growth and evolution were natural without alimentary or medicine allergy. In clinical treatment, the fever resumed on the fifth day and palmar erythema, edema, tengue eruptions and scattered mucolopopular, rash were observed, hypoalbumine, Therombocytosis increasing blood sedimentation rate were observed in analysis.

In abdomina sonography, mild inflammation in left kidney and normal echo cardio graphy was reported. These findings in clinical reviewing are as following:

HB: 10/7 platelet 245000:- 7010000 WBC: 5000 PMN: 43% Lymph: 51%

ESR: 20…120 GRP: +2…. +3 U/A: Sterile pyuria U/C & B/C GSF/C: negative Albumim:2.5 CSF cell count many WBC

(90% polymorphonuclears)

CSF analysis: protein 11 mg/d1, Glucose: 10mg/d1 and ferritine at 350.

Smear showed gram positive diplococcus.

During repetition, white globule and sugar and protein were 130, 20 and 57 respectively.

In sonography mild inflammation was seen in left kidney. No finding was seen in echocardiography. Brain scanning was natural and 2 grams venial immunoglubin and asprine were prescribed per kilogram weight for him that his fever went away after 24 hours and he was discharged with normal condition.

The second case (infectious arthritis immediately after Kawasaki disease):

A three year old child with pro longed fever was referred and hospitalized. During the examination, tengue eroptions, lip redness, scattered, mucopopular, rash on body and scaling within feet and hands nails were seen. Growth was normal. No abnormal point was reported in abdominal sonography, echocardiography. The tests were as following:

ESR: 55 120 CRP: +3 U/A & B/C CSF/C: negative

Diagnosis Kawasaki, 2gr venous immunoglubin and asprine was prescribed so that the fever disappeared went after a day and discharged next 2 days.

The third case (presenting initial Kawasaki with Herpes gingiuostomatitis:

A 20-month girl with 9-day fever and Aphthous wounds in the anterior areas of mouth and tongue was hospitalized by diagnosis of herpes ostomitis and Acyclovir was sleepy with temperature 40 rectaly and she has a probably fever over 3 days and Desquamation of the perineum and redness flip and oral cavity redness, were seen in reexamination.

No special point was observed in abdominal sonography and echocardiography. Laboratory tests were as following:

HB: 8.9 platelet: 235000 WBC: 8900 PMN: 86.9%

CRP: +3 ESR: 20 U/A & B/C: negative

Diagnosing: Kawasaki, 2gr venous immunoglobin and aspirin were prescribed so as the fever disappeared after a day and turned out healthy, then the infant was discharged 2 days later.

The fourth case (Kawasaki with hepatitis):

A three-month girl with seven days fever, icterus and vomiting. Her problem had started with cough and running nose since a week ago, then icterus, vomit began on the fifth day. The fever disappeared overing 3 days, lip or oral cavity redness and unilateral anterior lymphodenopathy and strauberry tongue sized 1.5cm and scattered rash were seen in reexamination.

No special point was observed in abdominal sonography gall bladder hydrops and in echo cardiography, her test was as following:

HB: 10.2……8.3 platelet: 470000…578000 WBS: 16600… 27100 PMN:66….74.7% CRP: +3 ESR: 14 PBS:

Toxic granulation: GM HAV: negative U/A: many WBC U/C & B/C: negative

ALT: 19 AST:24 Bili:7.8 Albumin: 3.4

Diagnosing: Kawasaki, 2gr venous immunoglobin and aspirin prescribed, so, that the fever disappeared after one day, then she was discharged upon 2 days.

The fifth case (prolonged fever):

A two-month infant boy with fever and skin rash referred 3 days before and was hospitalized with probable diagnosis of sepsis / pnemonia. The disease began with fever, skin rash and rhinutis and Amoxycilin Clavulomic acid was prescribed and he was hospitalized for loss of impromvent. The body temperature was 39.5 rectally. Ampicillin and Cefotaxin began after sending required tests then Vancomycin was added because of parents dissatisfaction for CSF aspiration. The fever resumed for a week and there was no special sign except fever. Head scan was normal and mild mitral and reorgitation and were dosered during echocardiography.

HB:812 Platelet: 959000 … 755000 … 984000 WBC:9800 …. 124 … PMN: 59 … 51.7% CRP: +3ESR: 93 T4: 15.5 TSH: 1.8 ALT: 13 AST: 21 PCT: 0.86 LPH: 367

Albumin:3.7 B/C x 3 times & venous immunoglobin and aspirin were prescribed on the seventh day. The fever resplved after 2 days and he was discharged 4 days later. It was reported natural in echo 6 days later.

Conclusion:

KD and vasculitis with ambiguous source were presented by Tomy Socho Kawasaki and et al in 1988 (7). Diagnosing KD was based on over 4 days fever and 4 cases of clinical findings includes as:

1. Boolbar conjunctiva injection 2. ‹ papilla lip redness of tongueness of 3. 4. Changes of limbs ends and 5. Nuchal adenopathy.

Other clinical and Laboratory findings consisted of heart involvement like coronary veins respiratory and digestive finding, leukocytosis with shift to the left, hypoalbumine, anemia, redness in the place of prior B, C, J scar and venial findings (8). Presenting heart symptoms is 20% in children and 13.6% in adults, if not treated. This is why echocardiography role is undeniable in KD (12). The potential pathogens, materials, or particular antibodies in other inflammatory diseases were characterized in some cases of KD (13-17).

During incomplete KD period, the patient experienced over 4 days fever along with four

above clinical findings, and numerous studies indicated no cause. In this case, applying Laboratory gaining such as anemia, hypoalbumin, enhancing Liver enzymes, thrombocytosis, leukocytosis, sterile pyoria along with echocardiography are helpful.

According to various studies, incomplete KD is apart of KD possessing similar pathogen (18). All studies patients were clinically diagnosed as incomplete KD in our report representing in 3 cases with bacterial infection and a case as hepatitis, and these cases are following as meningitis pneumococal meningitis, septic staplylococcal arthritis referred to as quasi Kawasaki disease (quasi KD) or imitator KD (19). All reported 5 patients with incomplete KD had not suitable reaction to initial treatments and due to prolonged fever and the emergence of clinical findings, they underwent the treatment with high dose of venous immunoglubin and aspirin and reacted quickly, without coronary veins involvement, appeared in initial echocardiography within next 2 months arising from rapid diagnosis and treatment. These results showed that infectious factor (heprpes, pneumococci, staphylococci) is characterized in 3 case of patients suffering from incomplete KD called as an imitator KD (20).

Different studies indicate infectious factors in etiology of KD (6). It is an essential point for KD as hepatitis that this type of emergence is more and the clinical cooperators must take this point into account specially when the fever is more prolonged than expected along with skin rash.

USA children heart association suggested to do echocardiography for under 6 months with over 7 days fever withous obvious cause (21), that in infants, besides increasing platelets, there was a mild involvement which in next follow-up, fever as well as mild heart involvement was gone. Kawasaki disease turned out to play an important role in prolonged prognosis by creating coronary veins aneurysm resulted from venous inflammation (27).

The heart symptom was not observed in our patients because of immediate diagnosis and treatment. KD tends to present nearly at the age of one year when passive immuniaty taken from mother decreases that in our cases, all were above 1 year old except one. In various studies, incomplete KD was seen more in boys which was true about our cases (22-25). In many male studies, the age above 5 and delay in diagnosis are risk factors in creating heart involvement (11). The considerable point in incomplete KD is uncommon presentation and extensive clinical findings leading to regardlessness of KD diagnosis (26). The variety of factors was seen in incomplete KD consisting of: skin rash, arthragia or arthritis, non (un) infectious meningitis, diarrhea and vomiting, icterus, hepatomegaly, abdominal distension and acute abdominal pain (28). In our study, the first patient got KD following meningitis, and in the second patient pelvic infectious arthritis presented simultaneously with KD improvement in both which the role of microbial factors as super antigen is considerable. The third case began by presenting herpes gingivosteotitis whether the initial infection was herpes or presented as herpes lesion arising from KD is not obvious yet. Therefore, there is a high probability of emerging KD by mentioned indirect or direct infections. In the fourth case, KD is presented as infectious hepatitis in a rare type. There is more susceptibility to infection in intensive cases with declining immune system activity specially T cell immune system. In spite of most researchers belife, the micro-organism of the disease factor has remained uncertain yet. In some studies, super antigens are introduced as the etiologic factor of disease which are observed in microorganisms like staphylococci.

Super antigens include antigens causing activation of a great number of T Cells which leads to cytokines overproduction of course, some studies dedicate a minor role to superantigenes (28). The diseases developed by the intervention of superantigenes like shock toxic syndrome are created in individuals with a poor reaction to shock toxic syndrome toxin. Gupta, et al posed this assumption that antibody production against staphylococci toxin has deficiency in children with KD (29). Laboratory tests in the diagnosis of KD is not particular, but is helpful to reject other diseases. In different studies, leukocytosis, thrombocytosis and mild anemia were reported that in our study leukocytosis in one case (neutrophil percent was higher 60% in 3 cases),

thrombocytosis in 3 cases and mild anemia in all cases, were reported. Anemia is likely to be related with nutritive issues existing in our region and its intensity in 2 month infants relates to physiological anemia. Diagnosing incomplete KD is often postpones because of atypical findings. So this diagnosis should be considered in children with prolonged fever, because there is a high risk of heart disease involvement specially coronary veins in these cases and by exact diagnosis and accurate treatment of the probable heart involvement, it can be decreased from 20-25% to about 1.3%.

Lastly it can be concluded that the immediate diagnosis in complete KD can help to reduce the risk of heart involvement and to prevent many additional diagnosis and treatment efforts.

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کاوازاکی ناکامل و تظاهر نامعمول: گزارش موارد و مرور مقالات

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چکیده

مقدمه: *کاوازاکی یک بیماری سیستمیک حاد است که بیشتر شیرخواران و بچه‌های کوچک را مبتلا می‌کند و اغلب به صورت یک واسکولیت تظاهر می‌کند. عامل این بیماری هنوز ناشناخته است. با توجه به اینکه بیماری کاوازاکی امروزه به عنوان شایع‌ترین علت اکتسابی بیماری قلبی مطرح گشته که علیرغم مرگ کمتر از ۰/۱ درصد، در صورت عدم درمان احتمال درگیری قلبی تا ۲۵ درصد و مرگ ۱ تا ۲ درصد را دارد. مقاله حاضر گزارش موارد بیماری کاوازاکی با تظاهرات نادر می‌باشد.*

گزارش مورد: *گزارش ۵ مورد بیمار که در بررسی اولیه با به تشخیص مننژیت باکتریال، ژنژیواستوماتیت هرپسی، آرتریت سپتیک استافیلوکوکی هپاتیت ویروسی و تب طول کشیده بستری شدند و در سیر درمان به دلیل عدم پاسخ به درمان با شک به کاوازاکی بررسی و تحت درمان قرار گرفتند و پس از بهبودی ترخیص شدند. در این بیماران شکل غیرمعمول بیماری باعث اشتباه در تشخیص و طولانی شدن روند تشخیص شد.*

نتیجه‌گیری: *توصیه می‌شود با توجه به افزایش موارد بیماری ناکامل و غیرمعمول کاواساکی و افزایش احتمال درگیری عروق کرونر درمواردی که تب در بیماری طولانی شود، بایستی به کاواساکی ناکامل توجه نمود.*

کلیدواژه‌ها: *بیماری کاوازاکی – مننژیت – هپاتیت – آرتریت سپتیک*

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