Incomplete kawasaki disease –a diagnostic and therapeutic challenge

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ABSTRACT

Background

The diagnosis of classical Kawasaki Disease was based on clinical criteria. The conventional criteria is particularly useful in preventing over diagnosis, but at the same time it may result in failure to recognize the incomplete form of Kawasaki Disease.

Objective

To suspect incomplete Kawasaki Disease, because early diagnosis and proper treatment may reduce substantial risk of developing coronary artery abnormality which is one of the leading causes of acquired heart disease in children.

Method

Nine cases of incomplete Kawasaki Disease were diagnosed over a period of one year. The diagnosis of incomplete Kawasaki Disease was based on fever for five days with less than four classical clinical features and cardiac abnormality detected by 2D- echocardiography. A repeat echocardiography was done after 6 weeks of onset of illness. The patients were treated with Intravenous Immunoglobulin and/or aspirin.

Result

The mean age of the patients was 3.83 years and the mean duration of symptoms before diagnosis was 12.1 days. Apart from other criteria all of our patients had edema and extreme irritability. All the patients had abnormal echocardiographic finding. Five patients received only aspirin due to non-affordability of Intravenous Immunoglobulin and four patients received both aspirin and Intravenous Immunoglobulin, but the outcome was excellent in all the cases.

Conclusion

Incomplete Kawasaki Disease can be diagnosed with more awareness and aspirin alone may be used as a second line therapy in case of non affordability of Intravenous Immunoglobulin.

Key Words: Incomplete Kawasaki Disease, Echocardiography, Aspirin/ Intravenous Immunoglobulin

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INTRODUCTION:

Kawasaki disease (KD) is a self limiting acute febrile vasculitis mainly affecting the medium sized vessels. Although KD has been reported from all over the world[1] Asia has reported highest incidence in comparison to other continents.[2,3] The number of reported cases in our country is less suggesting gross under diagnosis and or under reporting or misdiagnosis as other illnesses. Incomplete KD should be considered in all children with unexplained fever for at least 5 days associated with 2 or 3 principal features of KD.[2] Clinical recognition of such cases can sometimes be quite difficult.[3] This delayed or missed diagnosis of incomplete KD is one of the major risk factor for development of coronary artery disease. In India, majority of affected patients are left untreated who subsequently develop coronary complications later in life. The aim of our study is to suspect incomplete KD because early diagnosis and proper treatment may reduce substantial risk of developing coronary artery abnormality (CAA) which is one of the leading causes of acquired heart disease in children.[2]

METHODS

All the cases below 12 years of age admitted in the Pediatric Medicine Department of Calcutta National Medical College & Hospitals, Kolkata and diagnosed as incomplete KD over a period of November 2008 to September 2009 were included in this study. Written consent was taken from the parents of the patients and the study was approved by the Institutional Ethical Committee. The criteria for diagnosis of incomplete KD included fever for at least 5 days and 2 or 3 of the following clinical features and lack of any other known disease processes, CRP >3mg/dl and/or ESR >40mm(1st hr) plus echocardiography proven cardiac abnormality. Apart from fever other clinical criteria were bilateral non-purulent conjunctival congestion; changes in extremities like edema, peeling; polymorphous rash; changes in the lips and oral cavity and cervical lymphadenopathy (>1.5cm diameter). Other important clinical feature was extreme irritability. Cases having fever with rash, conjunctivitis due to other causes and other similar illnesses were excluded from the study. Echocardiographic findings considered include combination of findings of left ventricular (LV) dysfunction, mitral regurgitation (MR), pericardial effusion, perivascular brightness, lack of tapering and aneurysm or ectasia of coronary artery. Patient having normal echocardiographic findings were excluded from the study.

Details including clinical presentation, investigation and treatment were recorded. They were followed up to six weeks and a repeat 2D echocardiography was done. Statistical analysis was not possible due to small sample size.

RESULTS

Total 9 patients of incomplete KD were diagnosed from November 2008 to September 2009 at Calcutta National Medical College, Kolkata. All the cases fulfilled case definition of incomplete KD. Age varied from 8 months to 11 years, mean age being 3.83 years. There were 6 girls (66.66%) and 3 boys (33.33%). Fever was present in all, with mean duration of 12.1 days with a range of 10 days to 2 weeks. All patients had edema of the lower limbs and they were extremely irritable .One (11.11

%) patient had cervical lymphadenopathy ,five (55.55%) patients had rash and only 2 patients (22.22%) presented with conjunctival congestion .Changes in the lips and oral cavity were seen in six patients (66.66%) (Table –I).

Laboratory workup revealed hemoglobin within 8 to 10 gm%. Total leucocyte count was within 15,000/cmm to 25,000/cmm, mean 20,000/cmm. ESR was elevated in all the cases expect for 1 patient (11.11%). Mean value of ESR (1st hr) was 52mm with a range of 10mm to 72mm. Platelet count at second week ranges between 2.15 to 4 lakhs /cmm with mean value of 2.98 lakhs/cmm.. CRP was high in 8 cases (88.88%) ranging between 5 to 10 mg/dl, mean value 6.67 mg/dl except in one case who had also normal ESR (Table-I).

Echocardiography was performed in all the patients at presentation and after 6 weeks of illness. All of our patients had abnormal echo findings in the form of any combinations of pericardial effusion, MR, LV dysfunction, perivascular brightness, coronary artery ectasia or aneurysm. Follow up echocardiography after six weeks of illness was within normal limit in all these patients. Fig 1 (case no. 4) shows aneurysmal dilatation of LMCA and LAD which became normal after six weeks of aspirin therapy (Fig.2).

Four patients (44.44%) received intravenous immunoglobulin (IVIG) (2 gm/kg) and high dose of aspirin followed by low dose of aspirin. Five patients (55.55%) who cannot afford IVIG received only high dose aspirin (80 mg/kg/day) initially till they became afebrile. Subsequently they received 5mg/kg/day aspirin till echocardiography became normal. Any form of salicylate toxicity was not noted in these patients. All the patients became afebrile in less than 48 hours after initiation of therapy. They are under regular follow up at our clinic without any problem.

DISCUSSION

Kawasaki Disease is a self limiting acute febrile illness probably infectious in origin affecting mainly young children below 5 years of age and causes severe vasculitis of all blood vessels predominantly medium sized arteries with a predilection to coronary arteries. [2,4,5] In developed countries KD has come to be recognized as probably the most common vasculitis in the pediatric age group and is now more common than rheumatic heart disease as a cause of acquired heart disease in children.[3,6] Sudden death from myocardial infarction (MI) may occur many years later in individuals who as children had coronary artery disease due to undiagnosed KD. Many cases of fatal and non fatal MI in young adults have been attributed to "Missed KD" in childhood. The number of cases of KD reported from India has increased markedly. This increase is unlikely to be solely due to actual increase in incidence of KD but also may be due to increased awareness among health professionals as well. Accurate identification of incomplete KD cases is major clinical challenge.[2] Mean duration of illness in our study was 12.1days in comparison to 7.5 days in classical KD.[4] This delayed referral is possibly due to less awareness and suspicion regarding incomplete KD. Under reporting of incomplete KD cases is another major cause.

In a statement for health professionals from Committee on Rheumatic fever, Endocarditis and KD, Council on Cardio Vascular Disease in the

young, American Heart Association (AHA), provided a new algorithm to aid clinician in approaching a child with suspected incomplete KD who present with fever for 5 days and 2 or 3 principal features.[7] When any patient comes to us along with prolonged unexplained fever and 2 or 3 principal clinical features of KD we should always consider incomplete KD as a differential diagnosis and if the CRP is > 3 mg/dl and/or ESR(1st hr) is >40 mm we should do 2D- echocardiography to establish incomplete KD.[2]

Thus the algorithm helps us to diagnose incomplete KD easily which will be otherwise missed. Large series of studies from Japan and North America has established that coronary artery abnormalities occurs as a sequelae of vasculitis in 20-25% of untreated children. [8] Incomplete KD cases are most frequent in infants who unfortunately have the highest likelihood of developing coronary artery abnormality(CAA), [2,9,10] so early diagnosis and treatment of KD is important for prevention of complication and reducing mortality and morbidity from coronary artery disease. Other cardio vascular manifestations like myocardial involvement, pericarditis and small pericardial effusion, myocardial infarction, valvular regurgitation and systemic artery aneurysm may occur. In our study 1 case (11.15%) had pericardial effusion, MR and reduced LV contractility and another one case (11.11%) had pericardial effusion, reduced LV contractility and perivascular brightness without having coronary artery abnormality. The aim of treatment is to reduce the inflammatory process, thereby reducing the development of acquired heart disease due to KD. Early treatment with intravenous gamma globulin (IVIG) and high dose of aspirin followed by lower dose of aspirin up to 6 weeks causes resolution of fever and echocardiographic findings, thus prevents coronary heart disease.

Cost of IVIG is a limiting factor for our country in some cases. We have treated 4 patients (44.44%) with IVIG along with high dose aspirin, other 5 cases (55.55%) were treated with high dose aspirin only due to unavoidable circumstances. But surprisingly both the groups had normal echocardiographic finding after six weeks of illness. So aspirin therapy alone had equal efficacy as dual therapy with IVIG plus aspirin in our study population. Due to small sample size statistical significance cannot be made in this regard.

CONCLUSION

Awareness, early suspicion and early treatment may reduce a large number of acquired heart diseases due to incomplete KD which otherwise remains undiagnosed. IVIG is now the gold standard therapy for the treatment of KD. Studies comparing efficacy of IVIG along with aspirin versus aspirin alone in the treatment of KD are not available. To compare the efficacy between the two groups ideally a prospective randomized control trial should be done where some patients will not receive IVIG, which will be highly unethical. So, though IVIG is the standard mode of therapy in KD , high dose aspirin alone as an anti inflammatory drug should be used in those patients who cannot afford costly IVIG. A retroprospective study with a large sample size where IVIG could not be given to some KD patients due to financial constraints could prove it.

Table I : Showing clinical features, principal investigations & treatment given to the nine cases

Table: 1

	Case 1 M,11 yrs	Case 2 M,2yrs	Case 3F,2yr 6m	Case 4 F,1 yr 5m	Case5 3yr,F	Case6 M,8m	Case7 F,5yr	Case8 F,5yr	Case9 F,4yrs
Fever	13 days	2 wks	11 days	10 days	12days	11days	10days	2wks	2wks
Changes extremities-edema	+	+	+	+	+	+	+	+	+
Rash	+	+	_	_	+	_	_	+	+
Conjunctival injection	+	_	+	_	_	_	_	_	_
Changes in lips and oral cavity(strawberry tounge)	_	+	_	+	_	+	+	+	+
Cervical lymphadnopathy	_	_	_	_	_	_	_	_	+
Extreme irritabilitiy	+	+	+	+	+	+	+	+	+
ESR(mm/1st hr)	65	50	55	50	72	45	55	65	10
CRP(mg/dl)	8	6	7	5	9	6	7	10	2
Hb (mg/dl)	10	8	9	8	8	9	9	9	9
TC (/mm^3)	22000	17000	22000	15000	19000	17000	23000	20000	25000
Platelet (Lac/cmm)	3.5	3	2.8	4	3.1	2.7	2.8	2.15	2.8
ECHO	LVdila^n, Systolic dys,MR, ADLMCA, ADLAD, ADRCA	Ectasia of LMCA, P/Eff.MR	ADLMCA	ADLMCA, ADLAD	ADLMCA	ADLMCA Periv.	P/Eff LVC. red, Bright	P/Eff. MRLVC. red,	ADLMCA, P/Eff.
R$_X$	Aspirin	IVIG+ Aspirin	IVIG+ Aspirin	Aspirin	IVIG+ Aspirin	Aspirin	Aspirin	IVIG+ Aspirin	Aspirin

AD- Aneurysmal dilatation, LMCA- left main coronary artery, LAD- left anterior descending artery, RCA- right coronary artery, MR- mitral regurgitation, P/Eff- pericardial effusion, ESR – Erythrocyte sedimentation rate, CRP – C-reactive protein, Hb – Hemoglobin,IVIG- Intavenous immunoglobin, TC-total leucocyte count, LVC- left ventricular contractility.

Fig 1. Echocardiography showing aneurysmal dilation of LMCA (2.7 mm) & LAD (2.8 mm)[two dilated segments]

Fig 2. Follow-up Echo after treatment with aspirin of the same patient showing normal anatomy of the left coronary arteries

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