Neonatal Kawasaki Disease: Case Report and Literature Review

Cancan Li

Children's Hospital of Soochow University

Yiming Du

Children's Hospital of Soochow University

Huawei Wang

Children's Hospital of Soochow University

Gaohong Wu

Children's Hospital of Soochow University

Xueping Zhu (✉ zhuxueping4637@hotmail.com)

Children's Hospital of Soochow University

Case Report

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Abstract

Background: Kawasaki Disease (KD) is a self-limiting and acute systemic vasculitis of childhood that leads to coronary artery abnormality in about 25% of untreated cases. KD is extremely rare in neonates. The purpose of this paper is to explore the clinical features and diagnosis and treatment of Neonatal Kawasaki Disease (NKD) for early identification.

Case presentation: A boy was a 24-day-old full-term infant with no special birth history. He had fever, irritability and rash at the time of admission. After 4 days of treatment with empirical antibiotics, the rash and fever were still present, and the rash was progressively increased. It is considered that the infection was serious, and antibiotics were changed and given intravenous immunoglobulin. The temperature and rash were better than before. On day 5, he had cracking of lips, on day 9, he had lymph node enlargement in the neck, and molted fingers appeared on the 10th day. Thus the complete Kawasaki Disease (CKD) was diagnosed, and the patient was given intravenous immunoglobulin (IVIG) and aspirin. Within 48h after the start of this therapy, the fever declined, the chapped lips got better, the rash resolved, and distal extremity desquamation appeared. On day 5, 13, and 18, there was no abnormality in echocardiography and no coronary dilatation. On day 20, the chapped lips and the distal extremity desquamation got better. After discharge, the patient continued to take aspirin orally. The patient was followed up to 1 year old, with good prognosis and no carditis or coronary artery abnormalities. Our literature search revealed only a few reported cases of suspected NKD worldwide (18 cases, including 14 English literature and 4 Chinese literature) (Table 1), together with this case, 19 cases in total. Among these 19 cases, 12 were male and 7 were female, the age of onset was 1-26 days. Six patients had complete KD (31.5%), 13 patients were IKD. Clinical manifestations: there were 17 cases of fever (89.5%, 13cases of fever >5days), 13cases (68.4%) of early limb edema/swelling or peeling, 16 cases (84.2%)of skin rash, 14cases (73.7%)of oral mucosal changes (lips red/cleft or strawberry tongue), 10 cases (53%) of coronary artery changes, 7cases (36.8%) of conjunctival congestion, 3cases 15.8%of cervical lymph node enlargement. Laboratory investigations: There were 5 cases (35.7%) with elevated ESR, 9 cases normal, 5cases unknown. CRP was normal in 6 cases (33%). Thrombocytopenia occurred in 11cases (64.7%). Among the 10 patients with coronary artery changes, 1 had an unknown prognosis due to loss of follow-up (patient 15). One patient died 2 days after discharge due to multiple organ failure (patient 17). 4 cases returned to normal (patient 3.6.7.14). The coronary artery changes in 4 cases still did not return to normal and were not followed up for a long time. Of the 19 NKD patients, 16 were sensitive to IVIG, 1did not use IVIG, and 1 was not sensitive to IVIGand due to multiple organ failure, the parents gave up treatment and died two days after discharge.

Conclusion: NKD is extremely rare, and its clinical manifestation is not typical and easy to be missed. If not treated early, it will potentially give rise to coronary artery aneurysms or expansion, ischemic heart disease, and sudden death. Early diagnosis and treatment are very important.

Background

Kawasaki Disease (KD) is a self-limiting and acute systemic vasculitis of childhood that leads to coronary artery abnormality in about 20–25% of untreated cases. It is commonly seen in childhood < 5 years. It is the leading cause of acquired heart disease in children in developed countries [1–2]. KD commonly results in childhood heart disease, potentially giving rise to coronary artery aneurysms or expansion, ischemic heart disease, and sudden death [3]. In some patients, heart disease might even affect the quality of their adult lives [4]. Domestic and foreign reports of neonatal KD (NKD) are rare, and due to the lack of typical clinical manifestations, it is easy to be misdiagnosed, missed diagnosis and delayed treatment. We present a case of CKD in a neonate of Children's Hospital of Soochow University and a review of the literature on NKD. The aim is to explore the clinical features of NKD, to identify and diagnose it early, treat it as soon as possible, improve its prognosis and provide help for clinical practice.

Materials And Methods

Case presentation

A 24-day-old full-term boy, admitted to the Children's Hospital of Soochow University, due to "fever for 3 hours with a rash". The child developed fever without obvious inducement 3 hours ago, with a body temperature of 38.5°C, foaming, sneezing, decreased intake of milk, and irritability.

A physical examination on admission, the child was acutely ill, with a body temperature of 37.7°C, a pulse rate of 138 beats/min, and a respiratory rate of 44 beats/min. Polymorphous erythema was noted over the boy's facial ministry. His lung and heart were unremarkable at the examination. The umbilicus was clean and dry, and his extremities were felt warm.

Laboratory investigations included white blood cells ($13.6 \times 10^9/L$, neutrophils 56%), hemoglobin (132g/L), platelets $434 \times 10^9/L$, and C-reactive protein (CRP) 3.1mg/L. Erythrocyte sedimentation rate (ESR) fluctuated between 18-42mm/hr. The blood and cerebrospinal cultures were negative. He was negative for influenza, parainfluenza, Respiratory Syncytial Virus, mycoplasma antibodies, EV71-IgM, TORCH, tuberculosis antibodies and autoantibodies. Humoral immune index: IgA 0.05g/L, IgG 4.16g/L, IgM 0.21g/L. Cellular immune index: CD3+63%, CD4+40.6%, CD8+20.6%, CD4+/CD8+2.0, CD19 CD23 11.5%. Craniocerebral and abdominal ultrasound showed no abnormalities. B-mode ultrasonography of the neck revealed several enlarged lymph nodes on the left side, up to about 15×7 mm. X-ray chest showed pneumonia and abdominal distension. Echocardiography showed normal.

Diagnosis and treatment: After admission, cephalosporin was given anti-infection and supportive treatment, and fever remained after 2 days treatment, with a peak of 39°C, and the rash gradually increased and faded under pressure, mainly in hands, feet, card around scar, shoulders and front chest (figure 1A/B). Polymorphous erythema was noted over the boy's entire body on the third day, and the CRP levers rose to 44.2mg/L, procalcitonin (pct) rose to 0.63ng/ml, and the antibiotic was changed to cefoperazone sulbactam, and methylprednisolone 1mg/kg was used. The rash and fever persisted, the antibiotic was changed to Meropenem (40mg/kg), methylprednisolone was added to 2mg/kg, and he was given intravenous immunoglobulin (IVIG) 800mg/kg one time for supportive treatment. The temperature of the child gradually decreased (36.4-37.6°C), the rash subsided, but not completely disappeared, and cracked lips appeared on the 5th day (figure 1C). On the 7th day, the body temperature was higher than before, on the 9th day, appeared several enlarged lymph nodes on the left side,

on the 10th day, appeared periungual desquamation, and the platelet count progressively increased from $434 \times 10^9/L$ (day 1) to $762 \times 10^9/L$ (day 10). He was suspected of CKD. The patient was given IVIG (2g/kg) and aspirin. Within 48h after the start of this therapy, the fever declined, the chapped lips got better, and the rash resolved, and distal extremity desquamation has appeared (figure 1D/E). On the 5th, 13th, 18th day, echocardiograms were normal with no carditis or coronary artery abnormalities. After 20 days of hospitalization, he was discharged to continue taking aspirin orally. The patient was followed for 3 months, and no abnormality was found in the blood routine and CRP. Follow-up echocardiography examinations showed normal on the 3rd and 12th month.

Methods

The clinical characteristics, laboratory examination, treatment and follow-up of one case of NKD in Children's Hospital of Soochow University in December 2018, were retrospectively analyzed. Our literature review encompassed a thorough search of the electronic databases of PubMed and Chinese databases for KD presenting in the neonatal period from January 2000 to December 2019. The key terms used in the search included newborns, neonates, Kawasaki Disease and Mucocutaneous lymph node syndrome. English and Chinese articles were reviewed. Clinical, laboratory, therapeutic and outcome data were collected.

Discussion And Conclusions

Our literature search revealed only a few reported cases of suspected NKD worldwide (18 cases, including 14 English literature and 4 Chinese literature) (Table 1) [5–20], together with this case, 19 cases in total. In all the presented cases including ours, 12 were male and 7 were female, the age of onset was 1–26 days. Six patients had complete KD (31.5%), 13 patients were IKD. Clinical manifestations: there were 17 cases of fever (89.5%, 13 cases of fever > 5 days), 13 cases (68.4%) of early limb edema/swelling or peeling, 16 cases (84.2%) of skin rash, 14 cases (73.7%) of oral mucosal changes (lips red/cleft or strawberry tongue), 10 cases (53%) of coronary artery changes, 7 cases (36.8%) of conjunctival congestion, 3 cases (15.8%) of cervical lymph node enlargement. Laboratory investigations: There were 5 cases (35.7%) with elevated ESR, 9 cases normal, 5 cases unknown. CRP was normal in 6 cases (33%). Thrombocytopenia occurred in 11 cases (64.7%). Among the 10 patients with coronary artery changes, 1 had an unknown prognosis due to loss of follow-up (patient 15). One patient died 2 days after discharge due to multiple organ failure (patient 17). 4 cases returned to normal (patient 3, 6, 7, 14). The coronary artery changes in 4 cases still did not return to normal and were not followed up for a long time. Of the 19 NKD patients, 16 were sensitive to IVIG, 1 did not use IVIG, and 1 was not sensitive to IVIG, and due to multiple organ failure, the parents gave up treatment and died two days after discharge. KD is an acute systemic vasculitis of childhood, and 76% of affected children are < 5 years of age, boys with the disease outnumber girls by about 1.5–1.7:1 [20–22]. Approximately 4–17% of patients are < 6 months of age [23–24]. The Japanese survey found that baby KD (including newborns) showed an atypical clinical manifestation [23]. The incidence of KD varies greatly in the world. NKD is rare, and even in Japan with a high incidence of KD, NKD has not been reported much. According to Hangai et al. [5], between January 2001 and December 2012, only 23 of the 130243 KD children in Japan were newborns (1/5500). In 19 cases including ours, six patients had complete KD (31.5%), 13 patients were IKD. Similar to Altarmmar et al. [7] (complete KD 25%) and Hangai et al. [5] (complete KD 35%) reported. The proportion of KD in infants < 12 months was 1/1500, IKD 15(65%) in 23 cases, combined with coronary changes in 4 cases (17%). Coronary artery aneurysms or coronary dilation was present in 15–25% of children with KD [25], and these conditions might give rise to ischemic heart disease or sudden death [13–15]. IVIG treatment could reduce the incidence of CAAs to about 3–5% [2, 25], but approximately 20–30% of KD patients had no response to IVIG [29–30]. KD has seasonal epidemiological features. In Japan, a distinct peak of KD incidence was observed in January, as well as a more gradual increase in summer. This pattern supports the hypothesis that the disease is caused by multiple infectious agents, one prevalent in winter and another in summer [31]. Genetic determinants have been suggested to contribute to KD susceptibility. Firstly, the risk of KD in siblings of affected children was ten times higher as compared with the general population [32]. Secondly, it was twice as high in children born to parents with a history of KD compared with the general population [33]. Thirdly, populations in Asian countries have higher incidence rates of KD than those in Western countries: Japan had the highest annual incidence rate [34], followed by Korea [35]. In this article, we retrieved 4 cases of NKD in China, including our case, there were 5 cases in total, 4 were male and 1 was female, 2 patients had complete KD (40%), 3 patients were IKD. They all had fever, a total of 4 cases were late neonates (80%), 3 cases (60%) of peeling, 3 cases (60%) of skin rash, 4 cases (80%) of oral mucosal changes (lips red/cleft or strawberry tongue), 4 cases (80%) of coronary artery changes, 2 cases (40%) of conjunctival congestion, 3 cases (60%) of cervical lymph node enlargement, 2 cases (40%) of limb edema. One patient died. 3 cases were normal (60%). The coronary artery changes in 1 case still did not return to normal when she was 3-year-old. The ratio of cervical lymph node enlargement and coronary artery dilation was significantly different from that of 19 cases, which was considered to be related to the small number of NKD in China.

Literature Review: Summary of the cases										Tat
Pt	1	2	3	4	5	6	7	8	9	10
Ref	7	6	19	5	18	8	17	9	9	9
Diagnosis	IKD	IKD	IKD	IKD	IKD	IKD	IKD	IKD	IKD	IKD
Age at onset/d	15	19	26	22	24	1	9	21	14	16
Sex	M	M	M	F	F	M	M	F	F	M
Fever duration(days)	5	0	10	4	12	0	19	4	3	4
Rash	+	+	+	+	-	-	-	+	+	+
Oral changes ¹⁾	-	+	-	-	+	-	+	+	+	+
Extremity edema	+	+	+	-	-	-	-	+	+	+
peeling	+ 4)	UN	+ 4)	+ 4)	-	-	+4)	UN	+ 4)	UN
Conjunctival congestion	+	+	-	-	+	-	-	-	-	-
Cervical lymph node enlargement	-	-	-	-	-	-	+	-	-	-
CAA ³⁾	-	-	LCA+	-	BCA+	BCA+	LCA+	-	-	-
CRP	N	H	H	H	H	UN	H	N	N	N
ESR	N	N		N	N	N	H	N	N	N
Other	Apnea, AL rise	Asphyxia, RDS	Anemia, Hypoalbuminemia	-	meningitis	Anemia, jaundice	N	vomit	ALT rise	ALT rise
Platelet	H	N	H	N	H	decline	H	UN	N	N
IVIG response	+	+	+	+	+	Not use	+	+	+	+
CA outcome	N(1yrs)	N(163d)	N(3yrs)	N(3mos)	AB(3yrs)	N(1yrs)	N(6mos)	N(6wks)	N(6mos)	N
Note: CAA: coronary artery abnormality, CRP: C-reactive protein, IVIG: intravenous immunoglobulin, ESR: Erythrocyte sedimentation rate, PR: present report, UR: tricuspid regurgitation, AR: aortic regurgitation, IKD: Incomplete Kawasaki disease, CKD: complete Kawasaki disease, 1) oral changes (lips red/cleft or straw application, 5) bilateral coronary artery aneurysms										

Due to the lack of characteristic laboratory indicators, the diagnosis of KD is mainly dependent on clinical manifestations. Neonatal immune system development is not perfect, clinical symptoms are not typical with low incidence, so it is not easy to be noticed. Okazaki et al. [6] reported that 1 case of NKD without fever was a premature infant, with a rash as the first manifestation, accompanied by red lips, conjunctival congestion and acral edema, and IVIG was effective for treatment. In another case, coronary artery dilatation occurred on the first day after birth without other KD features, after excluding other diseases that could cause coronary artery dilatation, pericardial effusion, decreased PLT and hyperbilirubinemia [36], and IKD was diagnosed retrospectively. In addition to fever, the most common clinical manifestation was acral extremity change. Among the 19 cases, there were 13 cases of acral extremity edema in the early stage, and 4 cases of peeling after IVIG treatment without acral extremity edema in the stage (patient 4, 7, 13, 19). Other clinical manifestations, in descending order of frequency, were skin rash, oral mucosal changes, conjunctival congestion, and cervical lymph node enlargement. Because oral mucosa changes and conjunctival congestion are transient, if there are any omissions in the medical history or physical examination, it is easy to misdiagnose. Neck lymph node enlargement accounts for only 16%, which is consistent with the literature conclusion of Manhiot et al [37]. CRP was normal in 6 (33%) of the 19 NKD cases (with 1 unreported CRP value). In our case, CRP was normal in the acute phase and began to rise after 4 days of illness. Elevated infection-related indicators are more common in older children, making the diagnosis of NKD particularly difficult in infants and young children.

The 19 cases of NKD were mostly late neonates, and only 2 (10.6%) of them were early neonates, which may be related to the immunity of the infant.

Echocardiography was performed in 19 cases with KD, and 10 of them had coronary changes (53%), which was much higher than that in older children, and also higher than Hangai et al (20%) [5]. If the children had coronary changes, KD was easier to be diagnosed with other signs and symptoms, while those without coronary changes were more likely to be missed.

The treatment for KD is the same as that for IKD, the preferred scheme is the combination of immunoglobulin and aspirin, which can rapidly reduce fever and improve clinical symptoms while reducing the incidence of coronary artery disease. But approximately 20–30% of KD patients had no response to IVIG [29–30]. Currently, prednisolone (PSL) is used for the treatment of IVIG-resistant KD. A pilot study (RAISE study) showed the efficacy of first dose IVIG plus PSL in reducing inflammation in severe KD, compared with IVIG alone [38]. The infliximab may be considered as an alternative to a second infusion of IVIG or

corticosteroids for IVIG-resistant patients. The cyclosporine may be considered in patients with refractory KD in whom a second IVIG infusion, infliximab, or a course of steroids has failed. The immunomodulatory monoclonal antibody therapy, cytotoxic agents, or plasma exchange may be considered in highly refractory patients who have failed to respond to a second infusion of IVIG, an extended course of steroids, or infliximab [2].

In conclusion, neonatal febrile diseases are easily misdiagnosed as sepsis, viral infection or immune diseases. If NKD loses the best time for IVIG treatment, aggravating the body's immune response and eventually developing into coronary artery damage. It is essential to maintain a high index of suspicion for NKD in febrile neonates which fail to respond to antibiotics, and attention should be paid to the observation of skin rash, changes in oral and lip mucosa, changes in acral extremity edema, and timely complete the Echocardiography examination, early detection, early intervention may appear coronary artery damage and long-term damage. The low incidence of NKD may be related to passive immunity from maternal antibodies [39]. Besides, NKD is more manifested as an incomplete type, which may be related to the immature immunity of neonates.

Strengths and limitations

·The clinical characteristics, laboratory examination, treatment and follow-up of one case of NKD were retrospectively analyzed.

·Our literature review encompassed a thorough search of the electronic databases of PubMed and Chinese databases for KD presenting in the neonatal period from January 2000 to December 2019.

·A detailed qualitative approach was used, English and Chinese articles were reviewed.

·the shortcoming of this paper is that the number of cases studied is too small, and we need more case studies to be more convincing.

Abbreviations

CAA: coronary artery abnormality

CRP: C-reactive protein

IVIG: intravenous immunoglobulin

ESR: Erythrocyte sedimentation rate

KD: Kawasaki disease

IKD: Incomplete Kawasaki disease

CKD: complete Kawasaki disease

NKD: Neonatal Kawasaki disease

Declarations

Patient and public involvement

The child was a newborn, and we did not study the diagnosis and treatment of the child until we obtained the informed consent of the family. During the whole study, children were only subjects, there was no public involved, and all the data were collected clinically by researchers.

Ethics approval and consent to participate

This study was reviewed and approved by the Ethics Committee of the Children's Hospital of Soochow University (Suzhou, Jiangsu, China)

Consent for publication

Written informed consent for publication was obtained from all participants

Availability of data and materials

All data are fully available without restriction

Competing interests

No financial or nonfinancial benefits have been received or will be received from any party related directly or indirectly to the subject of this article

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Authors' contributions

CL, YD participated in the study design and writing of the manuscript. HW participated in clinical data collection. GW carried out the interpretation of data. XZ participated in data analysis, interpretation of data and writing of the manuscript. All authors read and approved the final manuscript.

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References

- [1] Shulman ST. IVGG therapy in Kawasaki disease: mechanism(s) of action. *Clin Immunol Immunopathol*. 1989;53:S141-S146.
- [2] McCrindle BW, Rowley AH, Newburger JW et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. 2017;135(17):e927-e999.
- [3] Ohmoto-Sekine Y, Ishihara M, Hsieh SD et al. Giant coronary artery aneurysms associated with Kawasaki disease detected on whole-heart magnetic resonance coronary angiographic screening. *Intern Med* 2013;52:977-80.
- [4] Samada K, Shiraishi H, Sato A et al. Grown-up Kawasaki disease patients who have giant coronary aneurysms. *World J Pediatr*. 2010;6:38-42.
- [5] Hangai M, Kubota Y, Kagawa J et al. Neonatal Kawasaki disease: case report and data from nationwide survey in Japan. *Eur J Pediatr*, 2014,173(11):1533-1536.
- [6] Okazaki K, Matsui K, Takahashi N et al. Kawasaki disease in a preterm neonate: Case report and cytokine profile. *Pediatr Int*. 2018;60(11):1037-1039.
- [7] Altammar F, Lang B. Kawasaki Disease in the neonate: case report and literature review. *Pediatr Rheumatol Online J*, 2018,16(1):43.
- [8] Parashar R, Lysecki PJ, Mondal T. Diffuse coronary artery dilatation in a neonate: a case report. *J Neonatal Perinatal Med*. 2013;6(3):263-266.
- [9] Nasir A, Al Tatari H, Hamdan MA. Very high serum ferritin levels in three newborns with Kawasaki-like illness. *Paediatr Child Health*. 2012;17(4):201-204.
- [10] Sarah Mitchell, Joshua Francis, Burgner D. Kawasaki Disease in the neonate period. *City: Journal of Pediatric Infectious Disease*. 2011:265-267.
- [11] Karia VR, Hescocock GC, Gedalia A et al. Successful emergent coronary thrombolysis in a neonate with Kawasaki's disease. *Pediatr Cardiol*. 2010;31(8):1239-1242.
- [12] Nakagawa N, Yoshida M, Narahara K et al. Kawasaki disease in an 8-day-old neonate. *Pediatr Cardiol*, 2009;30(4):527-529.
- [13] Thapa R, Pramanik S, Dhar S et al. Neonatal Kawasaki disease with multiple coronary aneurysms and thrombocytopenia. *Pediatric Dermatol*. 2007;24(6):662-663.
- [14] Bhatt M, Anil SR, Sivakumar K et al. Neonatal Kawasaki disease. *Indian J Pediatr*. 2004;71(4):353-354.
- [15] Stanley TV, Grimwood K. Classical Kawasaki disease in a neonate. *Arch Dis Child Fetal Neonatal Ed*. 2002;86(2): F135-136.
- [16] Sun Zhengyun, Wei Chaoxia. A case with neonatal Kawasaki disease J]. *Chin J Pediatr*, 2003; 41(12): 960-960. (in Chinese)
- [17] Yu Qingfeng. Incomplete kawasaki disease in a neonate. *China Prac Med*. 2012;7(33): 168-168. (in Chinese)
- [18] Du Cengqing. Incomplete kawasaki disease complicated with Aseptic Meningitis in a neonate J]. *Chin J Pediatr*. 2014;52(1): 63-64. (in Chinese)
- [19] Xiong Peng, Liu Tonlin, Chen Yu et al. Misdiagnosis of incomplete Kawasaki disease in neonate: a case report and literature review J]. *J Clin Pediatr*. 2017;35(3): 176-178. (in Chinese with English abstract)
- [20] Chang RK. The incidence of Kawasaki disease in the United States did not increase between 1988d and 1997. *Pediatrics*. 2003;111(5 Pt 1):1124-1125.
- [21] Holman RC, Curns AT, Belay ED et al. Kawasaki syndrome hospitalizations in the United States, 1997 and 2000. *Pediatrics*. 2003;112(3 Pt 1):495-501.
- [22] Maddox RA, Holman RC, Uehara R et al. Recurrent Kawasaki disease: USA and Japan. *Pediatr Int*. 2015;57: 1116-1120. doi:10.1111/ped.12733.

- [23] Chang FY, Hwang B, Chen SJ et al. Characteristics of Kawasaki disease in infants younger than six months of age. *Pediatr Infect Dis J*,2006;25(3):241-244.
- [24] Manlhiot C, Yeung RS, Clarizia NA et al. Kawasaki disease at the extremes of the age spectrum. *Pediatrics*, 2009;124(3): e410-415.
- [25] Newbyrger JW, Takahashi M, Gerber MA et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation*.2004;110:2747-2771.
- [26] Grun S, Backes M, Schumm J et al. Long-term impact of undetected Kawasaki syndrome on coronary morphology and physiology. *Circulation*, 2012;125: e640-644.
- [27] McCrindle BW. Kawasaki disease: a childhood disease with important consequences into adulthood. *Circulation*, 2009;120:6-8.
- [28] Senzaki H: Long-term outcome of Kawasaki disease. *Circulation*2008;118: 2763-2772.
- [29] Tremoulet AH, Best BM, Song S et al. Resistance to intravenous immunoglobulin in children with Kawasaki disease. *J Pediatr* 2008; 153:117-121.
- [30] Hwang JY, Lee KY, Rhim JW et al. Assessment of intravenous immunoglobulin nonresponders in Kawasaki disease. *Arch Dis Child* 2011;96:1088-1090.
- [31] Nakamura Y, Yashiro M, Uehara R et al. Epidemiologic features of Kawasaki disease in Japan: Results from the nationwide survey in 2007-2008. *J Epidemiol*, 2010;20(4): 302-307.
- [32] Fujita Y, Nakamura Y, Sakata K et al. Kawasaki disease in families. *Pediatrics*.1989;84:666-669.
- [33] Uehara R, Yashiro M, Nakamura Y et al. Kawasaki disease in parents and children. *Acta Paediatr*.2003;92:694-697.
- [34] Nakamura Y, Yashiro M, Uehara R et al. Epidemiologic features of Kawasaki disease in Japan: Results of the 2009-2010 nationwide survey. *J. Epidemiol*. 2012;22:216-221.
- [35] Park YW, Han JW, Hong YM et al. Epidemiological features of Kawasaki disease in Korea,2006-2008. *Pediatric.Int*.2011;53:36-39.
- [36] Krapf R, Zimmermann A, Stocker F. Lethal vasculitis of coronary arteries in a neonate and two infants: possible neonatal variant of the MLNS/IPN complex? *Helv Paediatr Acta*. 1981;36(6):589-598.
- [37] Lee KY, Hong JH, Han JW et al. Features of Kawasaki disease at the extremes of age. *J Paediatr Child Health*. 2006;42(7-8)423-427.
- [38] Kobayashi T, Saji T, Otani T et al. Efficacy of immunoglobulin plus prednisolone for prevention of coronary artery abnormalities in severe Kawasaki disease (RAISE study): A randomised, open-label, blinded-endpoints trial. *Lancet* 2012; 379:1613-1620.
- [39] Rowley AH, Baker SC, Shulman ST et al. Detection of antigen in bronchial epithelium and macrophages in acute Kawasaki disease by use of synthetic antibody. *J Infect Dis*. 2004;190(4):856-865.

Figures

Figure 1

Clinical manifestations of our case. Figure 1A: card around scar; Figure 1B: Systemic congestive rash; Figure 1C: Cracked lips; Figure 1D/E: distal extremity desquamation