III. PEDIATRICS

CLINICAL, DEVELOPING AND THERAPEUTIC STAGES IN A KAWASAKI'S DISEASE CASE REPORT

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Abstract

Kawasaki disease (Kawasaki syndrom-KS) is an acute self-limited vasculitis of childhood that is characterized by fever, bilateral nonexudative conjunctivitis, erythema of the lips and oral mucosa, changes in the extremities, rash and cervical lymphadenopathy(1,2). Coronary artery aneurysms or ectasia develop in 15% to 25% of untreated children and may lead to ischemic heart disease or sudden death.

We present a case of Kawasaki disease in a small child, using a modern algorithm of diagnosis. The patient received the classical therapy with Immunoglobulin and Aspirin. The repeated cardiac ultrasound made it possible to rule out the presence of the dreaded complication that is the coronary artery aneurysms disease.

Key words: Kawasaki disease, coronary artery aneurysms, child

Introduction

Kawasaki disease was first described in Japan in 1967 by Tomisaku Kawasaki. The disease is now known to occur in both endemic and community – wide epidemic forms in the Americas, Europe and Asia in children of all races(6). In the United States, Kawasaki disease has surpassed acute rheumatic fever as the leading cause of acquired heart disease in children. Treatment of Kawasaki disease in the acute phase is directed at reducing inflammation in the coronary artery wall and preventing coronary thrombosis, whereas long – term therapy in individuals who develop coronary aneurysms is aimed at preventing myocardial ischemia or infarction(3,4,5). Recommendations of initial evaluation, treatment in the acute phase and long – term management of patients with Kawasaki disease are intended to assist physicians in understanding the range of acceptable approaches for caring for patients with Kawasaki disease. Ultimately, management decisions must be individualized to a patient's specific circumstances(10,11,12).

Case report

The authors present the patient A.R., 2 years old male, hospitalized in the Bega 2nd Clinic of Pediatrics for: drowsiness alternating with irritability, inappetence, fever, paleness, oral enanthema, fingers presenting lamellar desquamation, nonexudative conjunctival congestion accompanied by pruritus, aching edema at superior and inferior limbs level.

History: the patient is the 2nd born child from normal pregnancy, normally delivered at full term, weigh at birth = 3500g, height at birth = 50cm, with no neonatal distress, breast fed from birth, current adequate vaccinations.

The patient came to our unit in its 8th day of illness, being hospitalized for erithemato - pultaceous tonsillitis accompanied by fever and for polymorphic erythema and previously treated with antibiotics (Ampicillin, Gentamicin, one day, and then Ceftriaxone 4 more days) and with HSH for 6 days. Under the treatment, the patient's condition did not improve, febrile peeks 2-3 times a day (over 39^0C), skin erythema gradually diminishing.

Physical examination:

- Bad general state, drowsiness, inappetence
- fever (39,50C)
- intense paleness, lamellar desquamation of the fingers in the superior limbs, red-carmine colored oral enanthema, strawberry, lucid appearance of the tongue, dry cracked lips (fig.1)

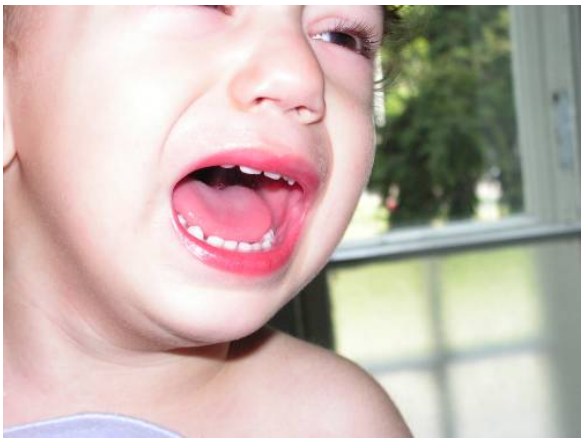

Fig. 1.

- bilateral nonexudative conjunctival congestion accompanied by pruritus
- aching edema at superior and inferior limbs level (fist joint, tibio-tarsal joint – fig.2,3)
- left subangulo-mandibular adenopathy, 2cm in diameter, mobile, slightly sensible at palpation
- rhythmical cardiac sounds, tachycardia, HR=200b/min

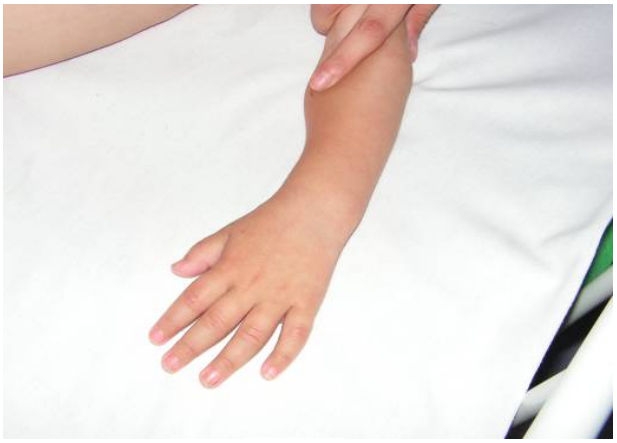

Fig.2.

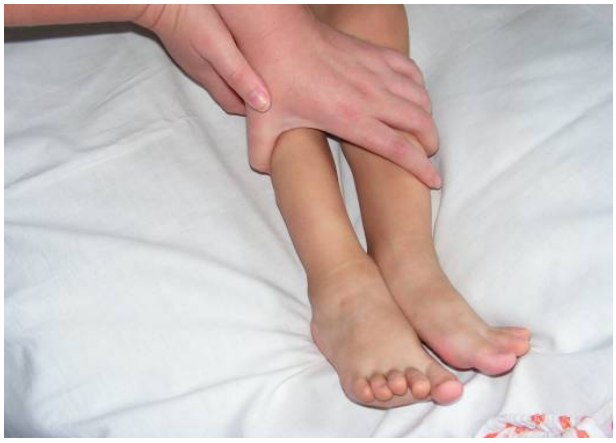

Fig.3.

Biological tests:

At admittance	
Red cells count /mm^3	3.800.000 ↓
Leucocytes /mm^3	25.900 ↑
Hb g%	10,6 ↓
Ht %	33 ↓
Thrombocytes /mm^3	500.000 ↑
Ly %	25,5
Mo %	3,5
Gr %	70,3 ↑
Eo %	0,7
ESR/mm	83 ↑
Seric proteins g%	5,3 ↓
Elfo: A g%	3,19 ↓
α1 %	3,2
α2 %	7,6
β %	10,8
γ %	18,3

At admittance	
Urine test	Normal
ALT ui	33
AST ui	37
CRP mg%	97 ↑
Fibrinogen g/l	6,8 ↑
ASLO UI	< 200
IgA g/l	2,3
IgM g/l	2,9
IgG g/l	15
IgE total UI/ml	80
Seric urea mg%	23
Seric creatinine mg%	0,5
Nasopharyngeal culture	Sterile
Stool culture	Sterile
Blood culture	Sterile

ECG (at admittance): sinusal tachycardia, HR=207 b/min, ax QRS intermediary, microvoltated, PQ=0.1 sec, stretched ST, flat T in DIII, V1. Myocarditis is suspected (fig.4).

Ecocardiography (at admittance): Ao=14mm, VS=18/24mm, VD=10/17mm, valves with normal ecostructure, thin blade of pericardic liquid (1mm). Exudative pericarditis (fig.5).

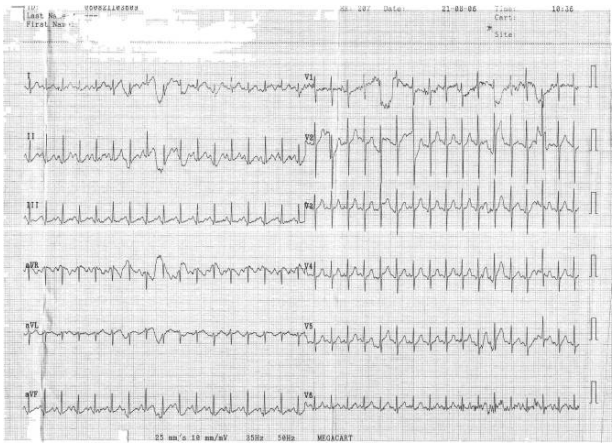

Fig.4.

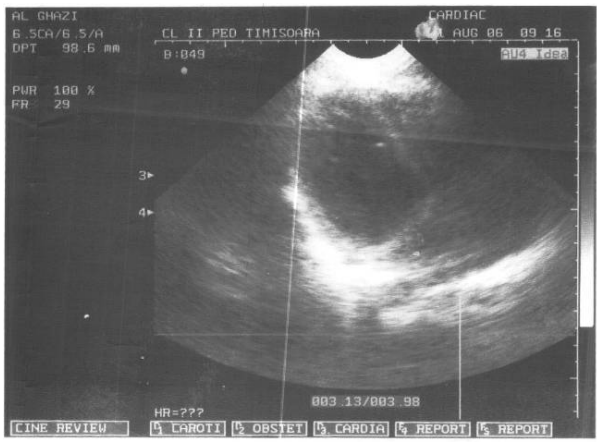

Fig.5.

Cardio-pulmonary radiography: heart, lung within normal limits (fig.6).

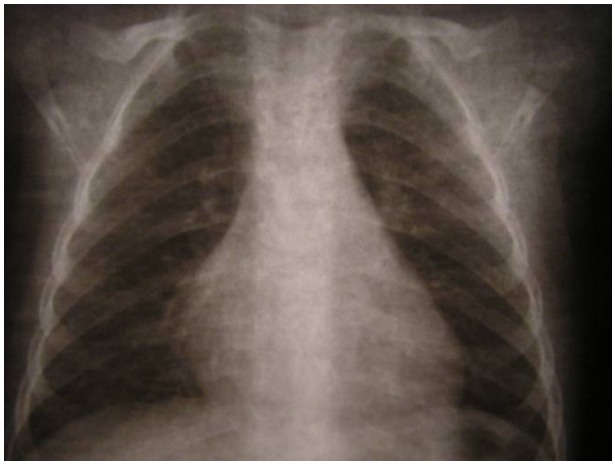

Fig.6.

The **positive diagnosis** of the Kawasaki disease was established on the basis of AHA Guidelines:

Clinical:

1. high fever, for more then 5 days, not responsive to antimicrobial and antipyretic agents
2. polymorphic erythema in the inferior half of the body
3. bilateral nonexudative conjunctivitis
4. aching edema at limbs level, lamellar desquamation of the fingers in the superior limbs
5. red-carmine colored oral enanthema, strawberry, lucid appearance of the tongue, dry cracked lips
6. left subangulo-mandibular adenopathy

The presence of 4 out of 5 clinical criteria plus fever more then 3 days certifies the diagnosis of Kawasaki's disease.

Biological tests:

1. leukocytosis with neutrophilia
2. acute – phase reactants: ESR, CRP, fibrinogen
3. normocytic normochromic anemia
4. hypoalbuminemia
5. thrombocytosis
6. cardiac ultrasounds: exudative pericarditis

Differential diagnosis:

1. **Eruptive infections:**

A. **Measles**: Important differences between measles and KS include the presence of exudative conjunctivitis, Koplik spots and severe cough in patients with measles. The rash in measles generally starts on the face, behind the ears, whereas the rash in KS is generally most prominent on the trunk and extremities. The rash in measles generally becomes confluent as it fades and leaves a distinctive brownish hue to the skin, whereas the rash in KS generally fades abruptly without residua out.

B. **EBV infection**: Similarities with KS: high, continuous fever (39^{o}C), erithematous angina, maculopapular eruption, cervical adenopathy; differences: in the EBV infection laboratory tests show leukocytosis with lympho – monocytosis, IgM anti-EBV, IgG anti-EBV, general adenopathy and hepatosplenomegaly are also present.

C. **Enteroviral eruptions** (e.g. Echo, Coksackie) : fever, polymorphic erythema are present in both illnesses, yet in enteroviral diseases there is naso-pharyngeal purring thrill, leukocytosis with eosinophilia.

2. **Bacterial infections:**

A. **Scarlet fever** should be easily diagnosed by the presence of exudative pharyngitis with group A streptococci isolated by throat culture. Elevations in the leukocyte count and sedimentation rate may be seen both in KS and in streptococcal infections. Because patients with scarlet fever have a rapid clinical response to Penicillin therapy, treatment with Penicillin for 24 to 48h, with clinical reassessment at that time, generally clarifies the diagnosis.

B. **Staphylococcic toxic shock syndrome** can be differentiated from KS on the basis of a number of clinical features. First is the presence of hypotension in toxic shock syndrome, which is not seen in KS in the absence of overwhelming cardiogenic shock. In addition, renal involvement, elevation of the creatinine phosphokinase level in serum and a focus of staphylococcal infection are all characteristic of toxic shock syndrome but not of KS.

3. **Systemic – onset JRA** may resemble KS. The presence of lymphadenopathy and hepatosplenomegaly suggests JRA as the diagnosis, as does the presence of an evanescent, salmon – colored rash. Rarely, a patient with systemic – onset JRA may be treated for KS, with the diagnosis becoming apparent over time as symptoms persist or relapse.
4. **Leptospirosis** is considered from the point of view of fever presence, conjunctivitis, maculo-erythematous eruption, adenopathy, leukocytosis with granulocytosis, nonspecific inflammatory syndrome.
5. **Allergic reaction to drugs** (Ampicillin): experienced clinicians can often distinguish drug reactions from KS based upon the nature of the rash and other features of illness such as periorbital edema, which is often present in drug allergy but not in KS. In difficult cases, obtaining a sedimentation rate may be useful, since it is generally less elevated in patients with drug reactions and very high in those with KS.

Treatment

A. Medical therapy:
   1. Pathogenic :
   - Intravenous immunoglobulin (IVIG) 1g/kgc/day, every 2 days, 2 doses (Octagam)
   - Aspirin 80mg/kgc/day, 4 times /day, 2 weeks, then 5mg/kgc/day, 4 times/zi, 6 more weeks
   - Pentoxifilin 10mg/kgc/day, 2 times/day

   2. Symptomatic :
   - Gastric antisecretory (Arnetin) 3mg/kgc/day inj i.v. slowly, diluted with SF, 4 doses/day, 2 weeks.
   - Antipyretic (Paracetamol, Algocalmin)

B. Hygienic treatment:
   - Obligatory rest
   - Hydro-electrolytic balance

Complications:

1. of the illness:
   - Coronary artery aneurysms (5% in treated patients)
   - Thrombosis of the aneurismal coronary artery
   - Myocardium infarction
   - Cardiomegaly
   - Arrhythmia
   - Late coronary atherosclerosis
   - Sudden death (4%)
2. of the therapy:
   - Reye Syndrome (following Aspirin)

Monitoring showed a decrease of the inflammatory syndrome, with the thrombocytes value going back to normal, hemoleukogram and electrophoresis normalization, remission of pericarditis, lack of cardiac complications.

The tables below presents the most significant biological events during hospitalization:

	After IVIG	4 weeks after the onset	8 weeks after the onset
Red cells count	3.100.000/mm3	4.340.000/mm3	4.500.000/mm3
Leukocytes	8.800/mm3	9.400/mm3	8.200/mm3
Hb	9,4g%	11,3g%	11,9g%
Hat	28%	32,9%	34%
Trombocytes	540.000/mm3	500.000/mm3	430.000/mm3
FL: Ly	43,6%	47,29%	56,72%
Mo	5,8%	13,39%	12,02%
Gr	50,6%	36,03%	28,61%
Eo	0,7%	2,22%	2,65%
ESR	120 mm	53 mm	10mm
CRP	18mg%	6mg%	1mg%
Fibrinogen	5,85g/l	4,37g/l	3,31g/l
ASLO	-	73ui	< 200ui

	After IVIG	4 weeks after the onset	8 weeks after the onset
Urine tests	normal	normal	normal
ALT	26ui	28ui	31ui
AST	21ui	22ui	7ui
Seric proteins	5,6g%	6,23g%	6,5g%
Elfo: A	3,23g%	4,03g%	4,05g%
$\alpha 1$	3,4%	3,4%	3%
$\alpha 2$	7,8%	6,5%	7,2%
β	10.86%	10,1%	0,8%
γ	17%	15,3%	17%
Seric urea	21mg%	28mg%	21mg%
Seric creatinine	0,7mg%	0,42mg%	0,4mg%
Nasopharyngeal culture	sterile	sterile	sterile
Stool culture	Sterile	-	-

ECG (4 weeks after the onset): sinusal tachycardia, HR=135b/min, ax QRS intermediary (fig.7).

Ecocardiography (4 weeks after the onset): SIV=0,5/0,8cm, DTD=3cm, DTS=1,9cm, FE=0,69, FS=38%, Ao=1,6cm, AS=1,9cm, vmaxAo=0,93m/sec, pmaxAo=3,5mmHg, AP=1,5cm, vmaxAP=0,96m/sec, pmaxAP=3,7mmHg, left coronary artery=2mm, right coronary artery=1,8mm, integer septum, thin blade of pericardic liquid (1mm) (fig.8).

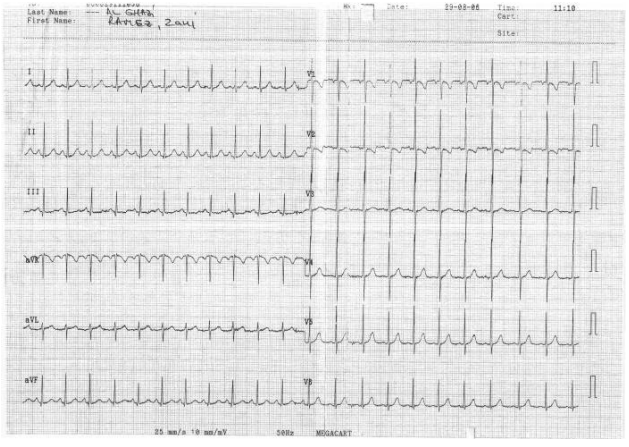

Fig.7.

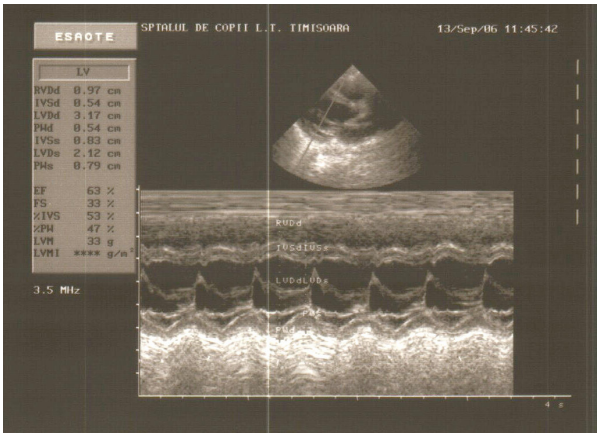

Fig.8.

Ecocardiography (8 weeks after the onset): integer SIA, SIV. FE=75%, valves with normal ecostructure. No coronary artery aneurysms detected (fig.9).

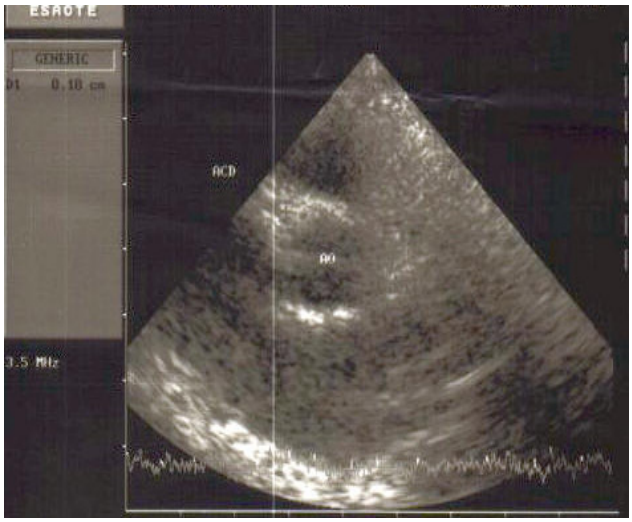

Fig.9.

Prognosis:

Immediate: favorable, considering the patient's outcome. To support the above statements we also underline the fact that the cardiologic investigations (ECG, cardiac ultrasound), repeated over a period of 2 months from the disease's first episode normalized and stayed within normal limits.

Long term: good, but cardiac monitoring is mandatory.

Follow up:

- Physical effort must be avoided for 2 months;
- Vaccination is contraindicated for 12 months;
- Immediate vaccination of the patient is recommended in case of known contact with other patients diagnosed with infectious-contagious illnesses (measles, smallpox);
- Periodical examination (ECG, cardiac ultrasounds): 6 month, 12 month, then every year for at lest 5 years.

Discussions

The clinical diagnosis of Kawasaki disease is possible with a good history and physical exam and the laboratory tests are usually consistent. Etiology still not identified. No diagnostic test available. As new agents are identified and new molecular biologic techniques developed, the etiology may become clear. A highly effective therapy is available:
IVIG and Aspirin, with an overall treatment failure rated of 2,8%. Persistent or recrudescent fever following IVIG administration is associated with the development of coronary artery aneurysms(7,8,9).

The patient became afebrile after beginning the treatment with IVIG. The clinical state improved visibly, appetite reappeared progressively, conjunctivitis ameliorated, edema remitted step by step, subangulo-mandibular adenopathy became smaller, still oral enanthema persist.

There is a favorable evolution in the treatment with Aspirin (large doses for 2 weeks – until patient is afebrile, then small doses up to 8 weeks), presenting complete and total remission of all clinical symptoms.

Conclusions

1. Kawasaki syndrome is not a rare disease and the clinicians should be aware of its signs.
2. Usually no diagnosis is suspected at admittance and just the effectiveness of IVIG can establish it.
3. Even if the short term outcome is good, the cardiac follow up of the patient is mandatory.

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