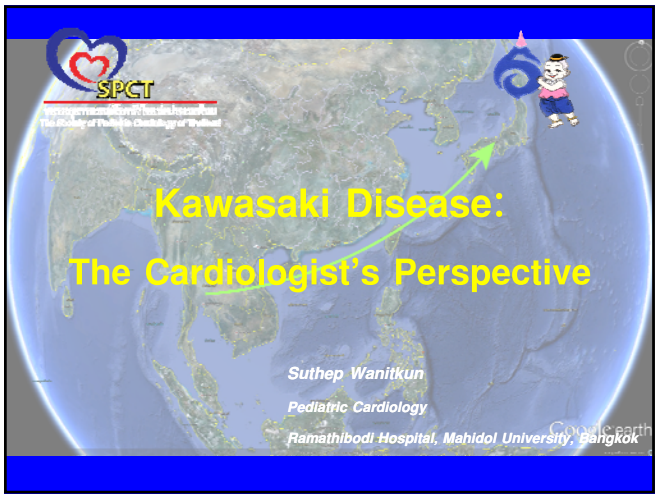


アレルギー, 16 (3)
178～222, 1967(昭42)

指趾の特異的落屑を伴う小児の急性熱性
皮膚粘膜淋巴腺症候群

(自験例50例の臨床的観察)

日本赤十字社中央病院小児科(部長:神前章雄博士)
川 崎 富 作

(受付:1月19日, 1967)

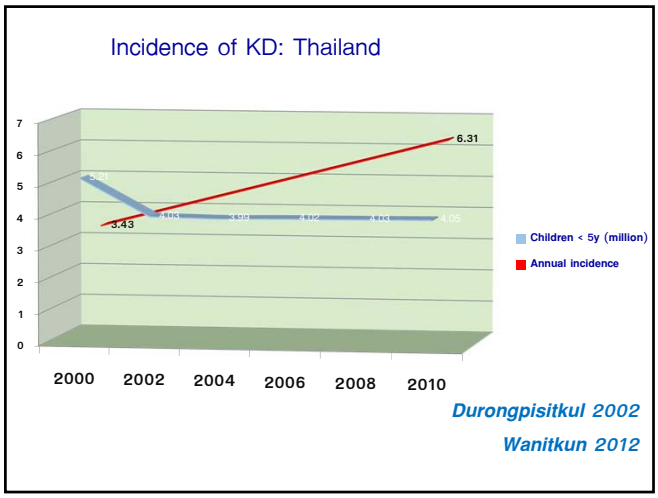
1. 緒 言

1876年 Fuchs[1] の発表した Herpes iris conjunctivae 以来, 多数の学者によつて, 眼, 皮膚, 粘膜を侵す一連の症候群に対して数多くの病名が与えられているが, 1939～1940年 Franceschetti et Valerio[2], 1945年 Proppe[3] 等により眼皮膚粘膜症候群に統一され, 多形滲出性紅斑の亜型と考えられるに至つた. 我が国に於ても, 1958年文部省綜合研究班[4]"はこの症候群を整理して,

1) 多形滲出性紅斑症候群
2) Behcet 氏症候群
3) Reiter 氏病

6) 両手, 両足が血管神経性浮腫状を呈する……22例 (44%)
7) 指趾先の爪皮膚移行部よりの膜様落屑が主として第2病週中に始まる……49例 (98%)
8) 過半数が2年以下である……27例 (54%)
9) 再発がみられない.
10) 自然治癒し, 後遺症をのこさいない.
11) 同胞感染がみられない.

私ははじめ, この特徴的な落屑に注目し, 本症候群を猩紅熱に似て非なる落屑性疾患, 即ち "非猩紅熱性落屑症候群について" と題して, 昭和37年10月第61回千葉地



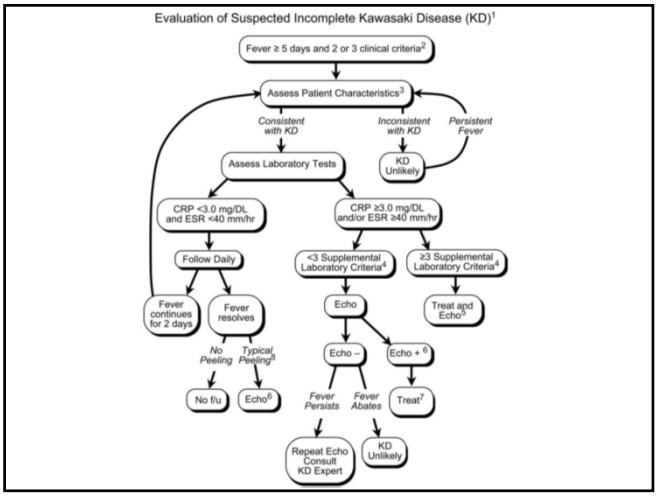
Epidemiology

- Incidence 10-223/100,000 (worldwide)
- Japan 223/100,000
- Hongkong 156/100,000
- Korea 117/100,000
- Taiwan 69/100,000
- China 60/100,000
- Singapore 32/100,000
- Thailand 10/100,000
- Malysia 84 cases/4 years
- The Philippines 1526 cases/5 years
- India 4.54/100,000
- Canada 25/100,000
- Europe 10/100,000
- Australia 3.7/100,000

Diagnostic Criteria

- Fever ≥ 5 days
- Presence of ≥ 4/5 features
  - -Bilat Conjunctival injection
  - -Changes in lips & oral cavity
  - -Cervical lymphadenopathy
  - -Polymorphous exanthem
  - -Changes in extremities
- Exclusion of other diseases with similar findings

Newburger et al. Circulation 2004;110:2747

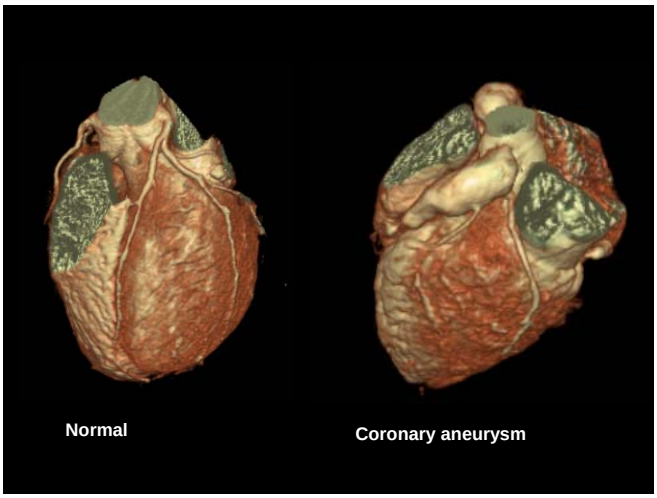


Supplemental lab

- Albumin ≤ 3 g/dL
- Anemia for age
- ↑ alanine aminotransferase
- Platelet after d7 ≥ 450,000/mm^3
- WBC ≥ 15,000/mm^3
- Urine ≥ 10 WBC/HPF

Positive echo

- Z-score LAD or RCA ≥2.5
- Aneurysm criteria
- ≥3 of
  - Perivascular echo brightness
  - Lack of tapering
  - ↓ LV function
  - Mitral regurgitation
  - Pericardial effusion
  - Z-score 2-2.5



Normal

Coronary aneurysm

Genetics: What we know?

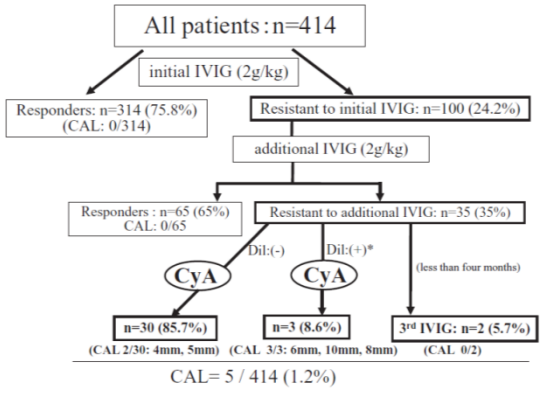
Population	FCGR2A	CASP3	HLA	BLK	ITPKC	CD40
	rs1801274	rs113420705	rs2857151	rs2254546	rs28493229	rs4813003
Japanese	0.79	0.37	0.75	0.71	0.16	0.67
Taiwanese	0.63	0.31	0.73	0.81	0.054	0.68
European	0.54	0.73	0.58	0.88	0.15	0.87

Learn background genetic risk polymorphism!

Onouchi 2012

Application of genetics knowledge

- ITPKC pathway: cyclosporine suppress T-cell activation
- Identify risk allele for coronary aneurysm: additional treatment on top of standard IVIG
- Identify children at risk and attempt to capture microorganism at the onset
- Create animal model for pathogenesis and new treatment study



Suzuki 2012

Role of echocardiography

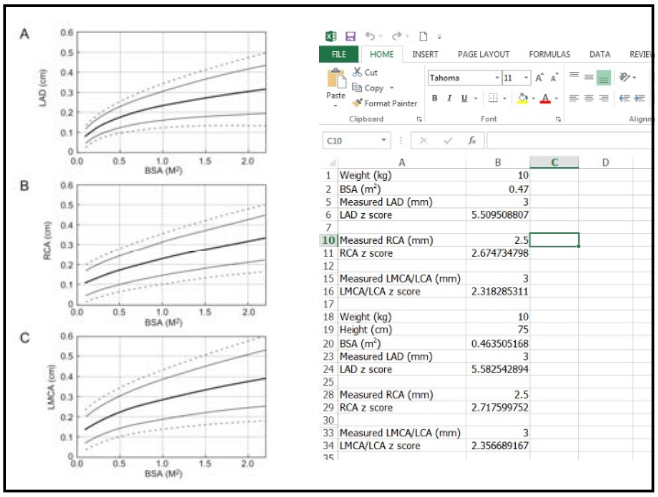
- Evaluate baseline coronary artery dimensions
- Helpful to establish Dx in incomplete KD
- Serial follow up:
  - At Dx
  - 2 wks
  - 2 mo.
  - 6–12 mo.

Coronary artery abnormalities

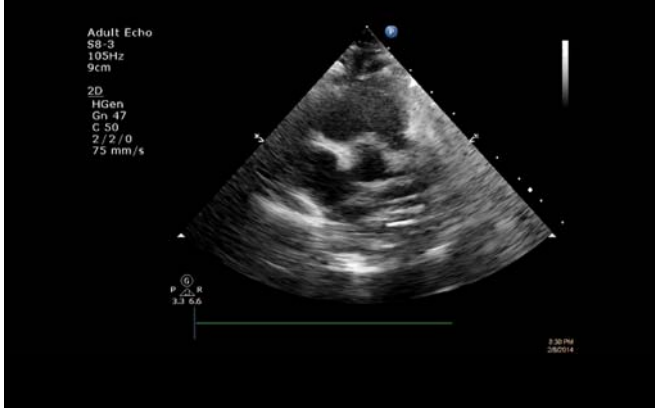
- Perivascular echo brightness
- Ectasia
- Aneurysm: saccular, fusiform
  - Small: < 5 mm
  - Medium: 5–8 mm
  - Giant: > 8 mm
- Coronary stenosis

Normal coronary arteries

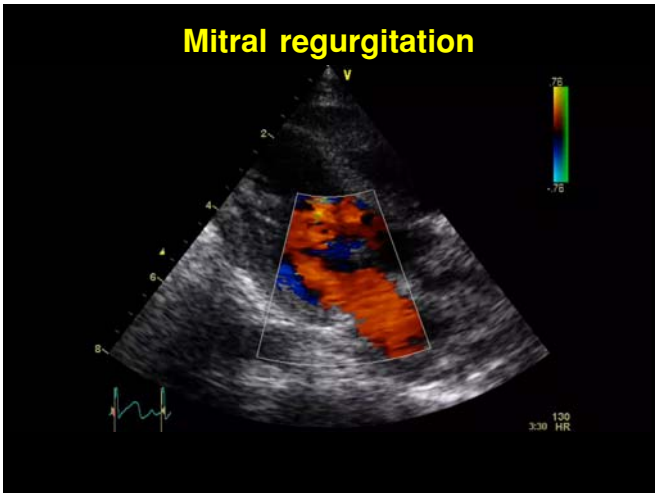
- Japanese Mnistry of Health & Welfare
  - <5 yr ⟶ < 3 mm
  - >5 yr ⟶ < 4 mm



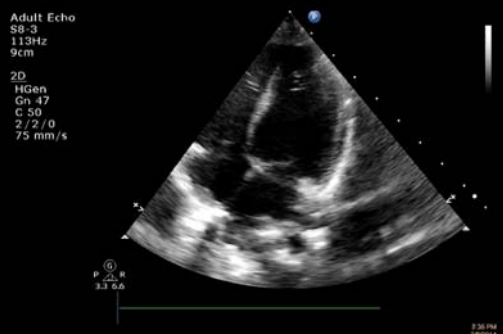
Perivascular echo brightness (PEB)



Mitral regurgitation



Pericardial effusion



Giant coronary aneurysm

Coronary artery thrombosis

Complete KD/ incomplete KD

- IVIG 2 g/kg infusion in 12 hr(within 10 d)
  - Chlorpheniramine 0.1 mg/kg IV
  - Start 0.6 mL/kg/hr, double rate q 15–30 min, max 4.8 mL/kg/hr
  - Record V/S, BP

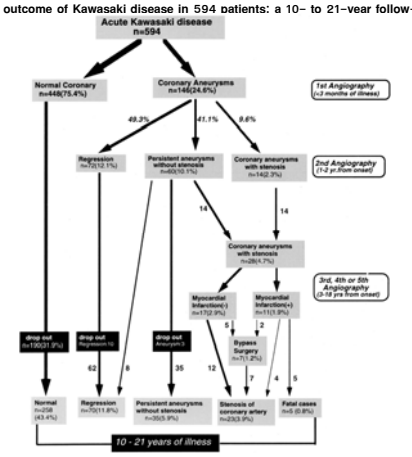
Complete KD/ incomplete KD

- Aspirin 80–100 mg/kg/day QID until afebrile or for 2 wks (baby ASA)

  then

  Aspirin 3–5 mg/kg/day QD for 6–8 wks if no CAL., continue indefinitely if CAL+
- Avoid ibuprofen
- Postpone live vaccine for 11 m (MMR, varicella, JE)

Long-term outcome of Kawasaki disease in 594 patients: a 10- to 21-year follow-up study.



Kato H et al. *Circulation.* 1996;94:1379-1385

Coronary revascularization

- Percutaneous transluminal coronary angioplasty (PTCA)
- Rotational atherectomy
- Stent
- Caronary artery bypass graft

Risk level	Pharmaco	Follow up
I (normal coronary)	ASA 8 wks	CVS risk q 5 y
II (transient ectasia)	ASA 8 wks	CVS risk q 3–5 y
III (small–medium aneurysm)	ASA until normal coro	Echo+ECG q 1 y Exercise test q 2 y
IV (giant aneurysm)	ASA + warfarin	Echo+ECG q 6 m Exercise test q 1 y Coronary angiogram at first 6–12 m of illness
V (coronary obstruction)	ASA + warfarin Beta blocker	Echo+ECG q 6 m Exercise test q 1 y Coronary angiogram as clinical indicated

Strategies to improve outcome of KD

- Enhance education for early recognition and early treatment
- Adequate and accessible effective treatment
- Research and implement genetics knowledge to identify high risk patients
- Develop new treatment based on discoveries in basic science of KD
- Attempt to identify etiologic microbial agent(s)

Strategies to improve outcome of KD

- Encourage heart healthy life style

Opportunity for collaboration

- Kawasaki disease registry
- Search for etiologic agent
- Genetics study

Conclusions

- **Majority of KD can be diagnosed clinically**
- **Cardiovascular complications of Kawasaki disease are serious long term issue**
- **Echocardiography plays supporting role**
- **Heart healthy life style should be encouraged in all KD patients**