Pediatric Rheumatology Interactive case series

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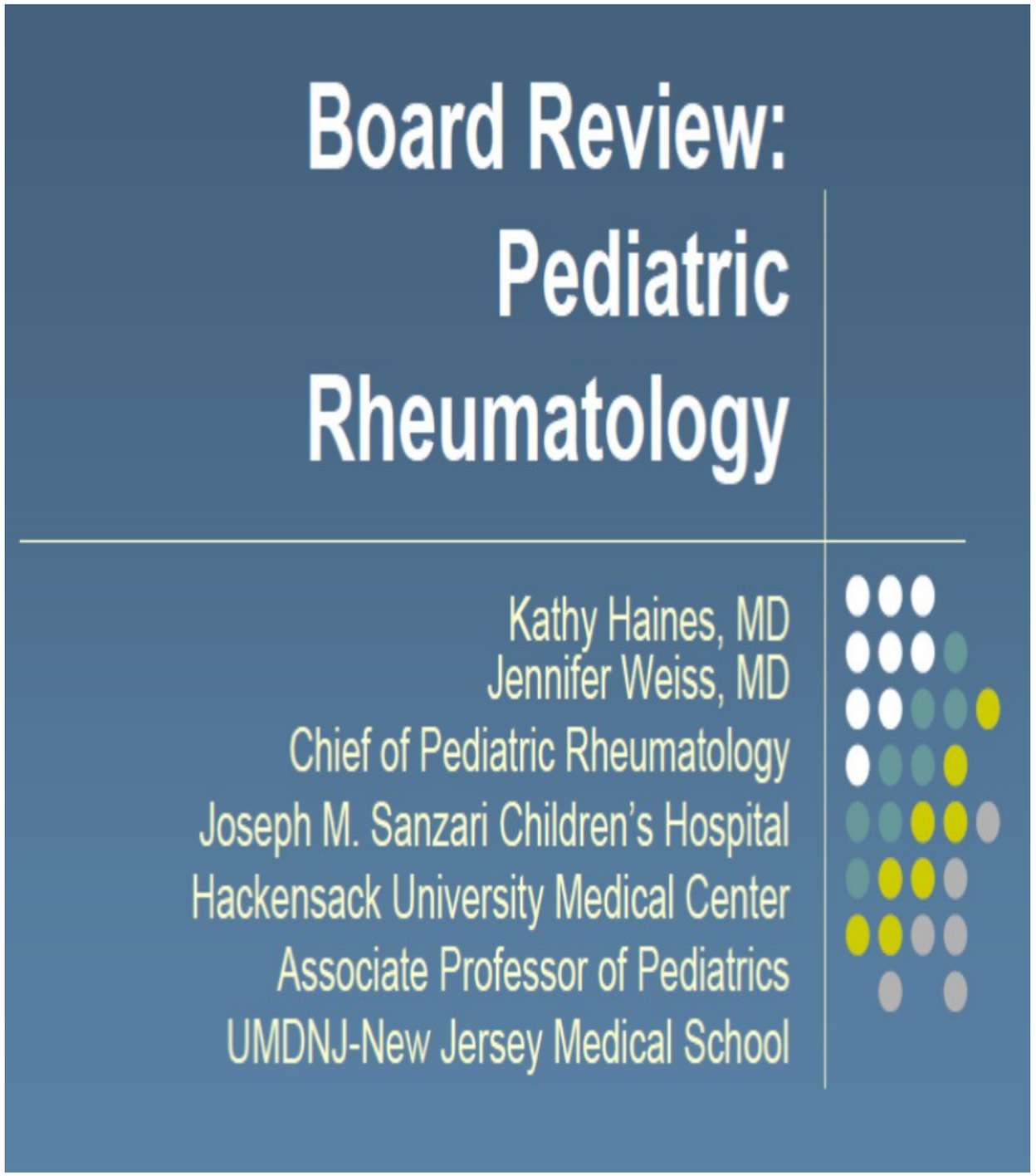
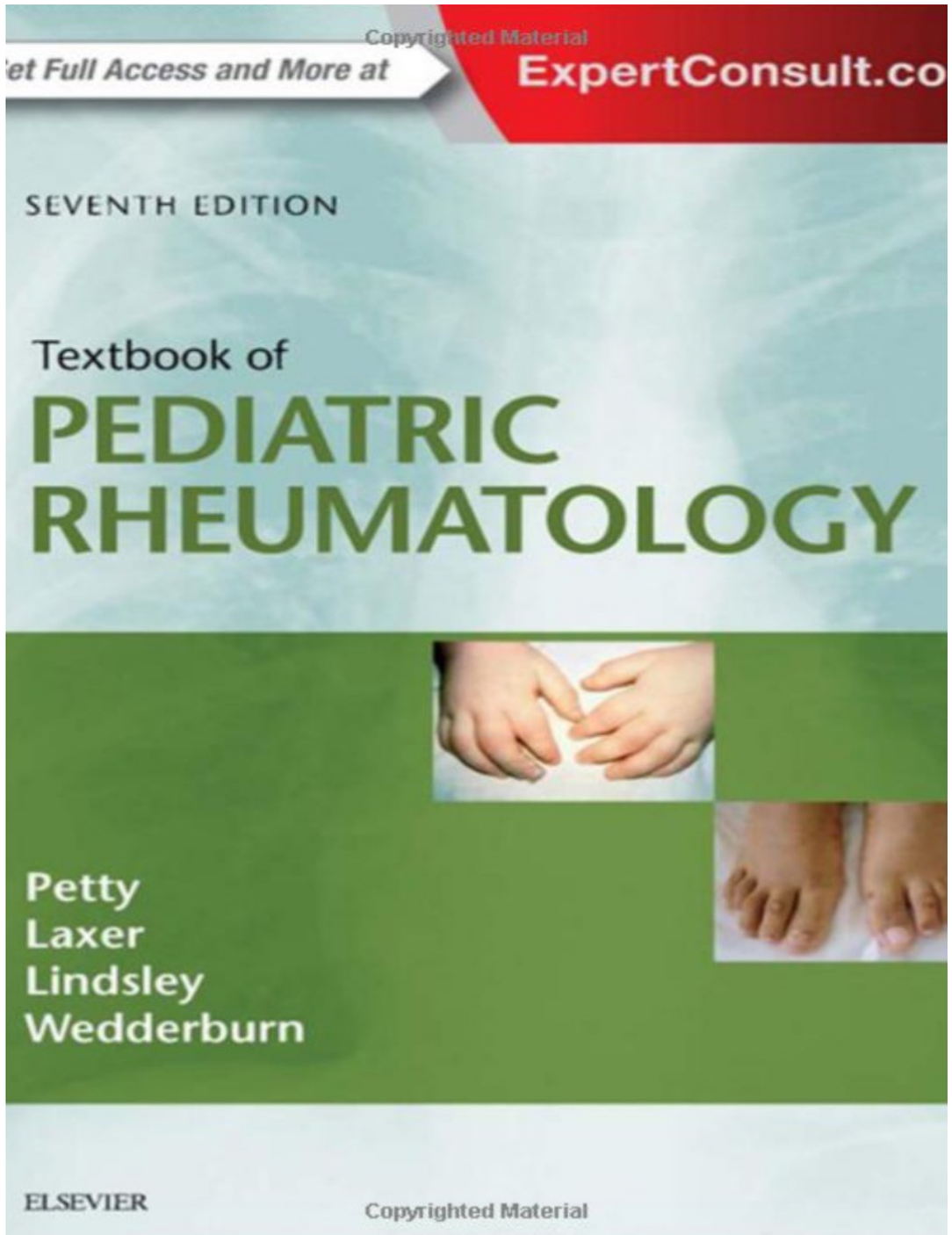
nmc specialty hospital
مستشفى ان ام سي التخصصي

Outline

- Introduction
- Chronic Arthritis case/Complication
- Acute arthritis case/2
- Connective tissue case/vasculitis
- Auto inflammatory case /infrequent complication

Major resources





Resources

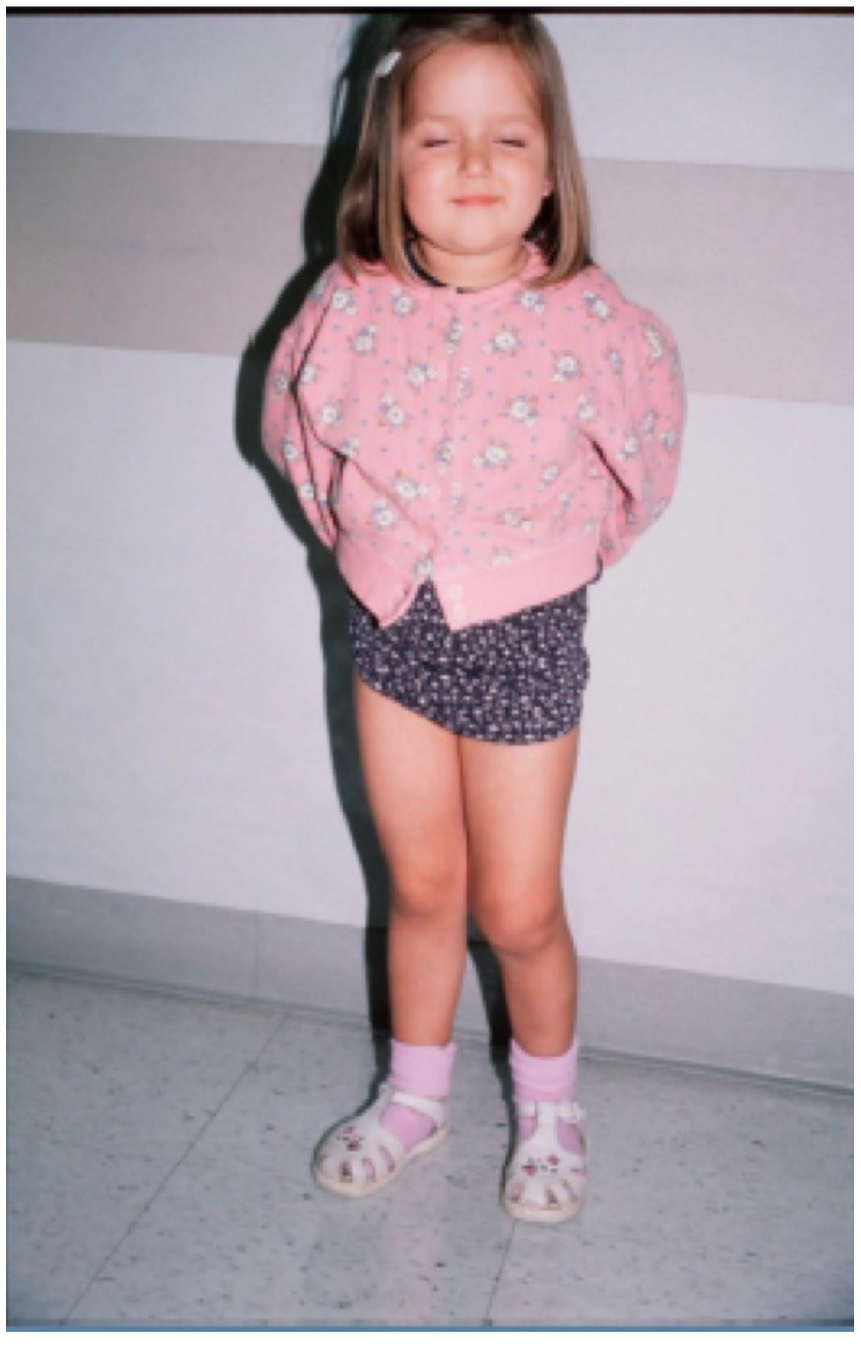
- Protocols for the initial treatment of moderately severe JDM, CARRA consensus, Arthritis care Res,2010,feb

- Revision of Jones criteria for the diagnosis of ARF in the era of Doppler echocardiography, AHA scientific statement, Circulation, 2015

- PSRA in children a distinct entity from ARF, Uzeil et al, Pediatric Rheumatology,2011

- Juvenile idiopathic arthritis, Seminar, Lancet, 2007

Arthritis/ 20-30٪ of pediatric ER, OPD

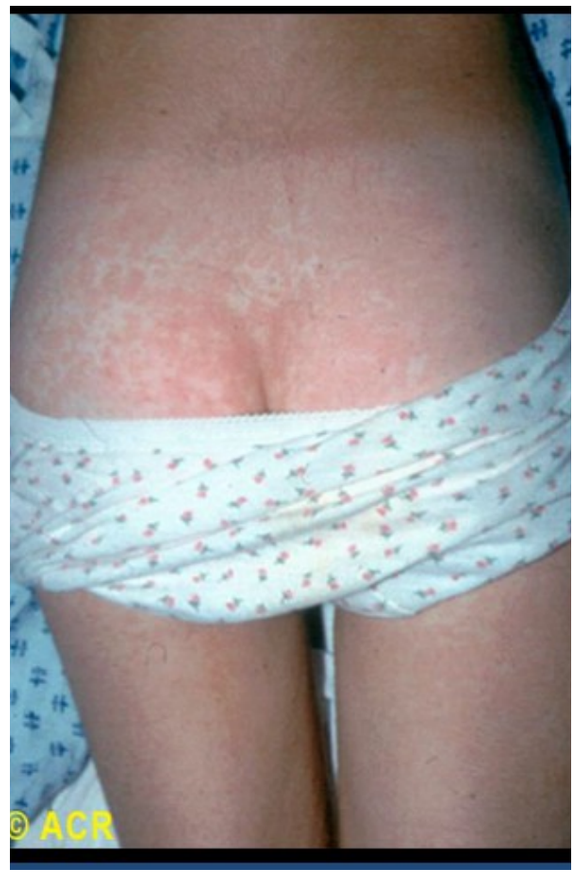


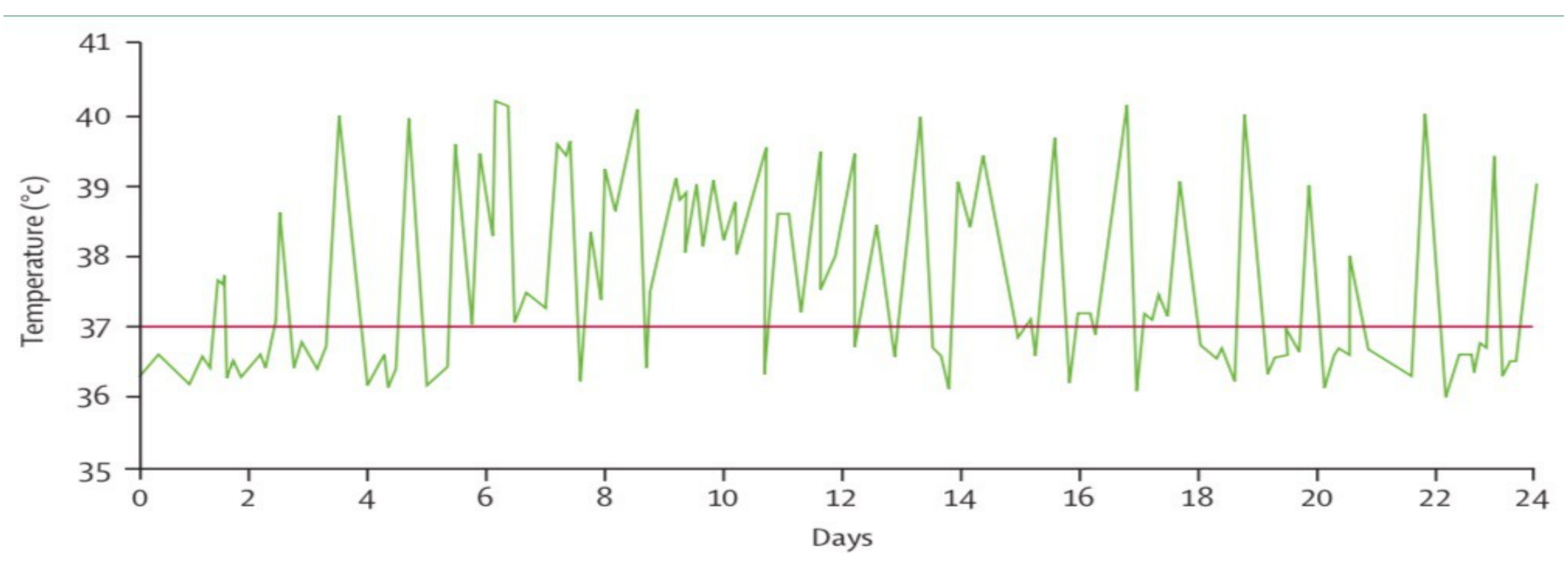
- JIA 10 times more common than ALL, Hemophilia, muscular dystrophy
- As frequent as juvenile DM
- 4 times more common than CF, Sickle cell anemia

Pediatrics in Review
April 2006, VOLUME 27 / ISSUE 4

Case 1

A 6 years girl with this fever/ 3 weeks,no arthritis detected,what is the pattern?, what physical signs to anticipate



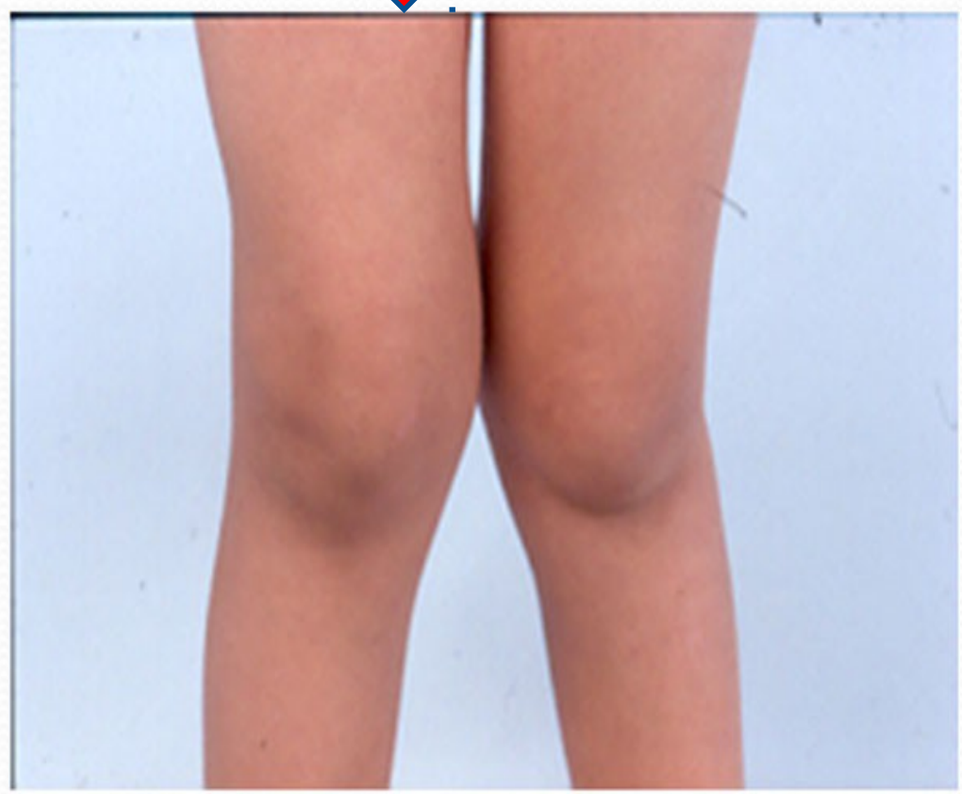


Case 1/ Findings

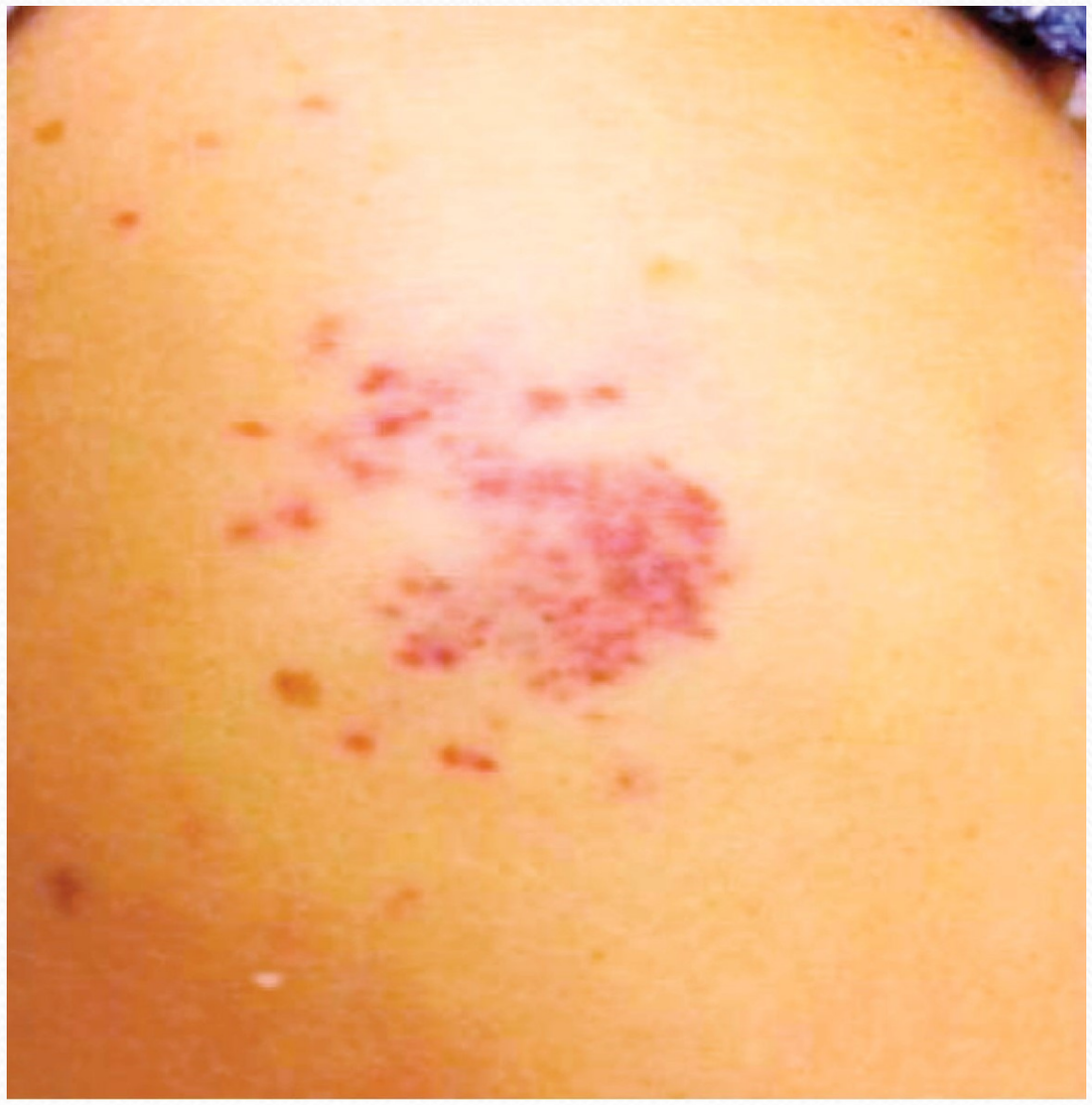
- Fever, quotidian pattern, ill during febrile episodes
- Rash occasional , evanescent, mild liver/spleen enlarg.

IV Methylprednisolone 2mg/kg

Findings	25/3/2017	27/3/2017
Fever	++	+
WBC'S Platelets	23.5 K 529 K	12.3 K 285 K
ESR CRP	105 96	65 64
SGPT/SGOT	135/95	83/76
Ferritin	1300	--

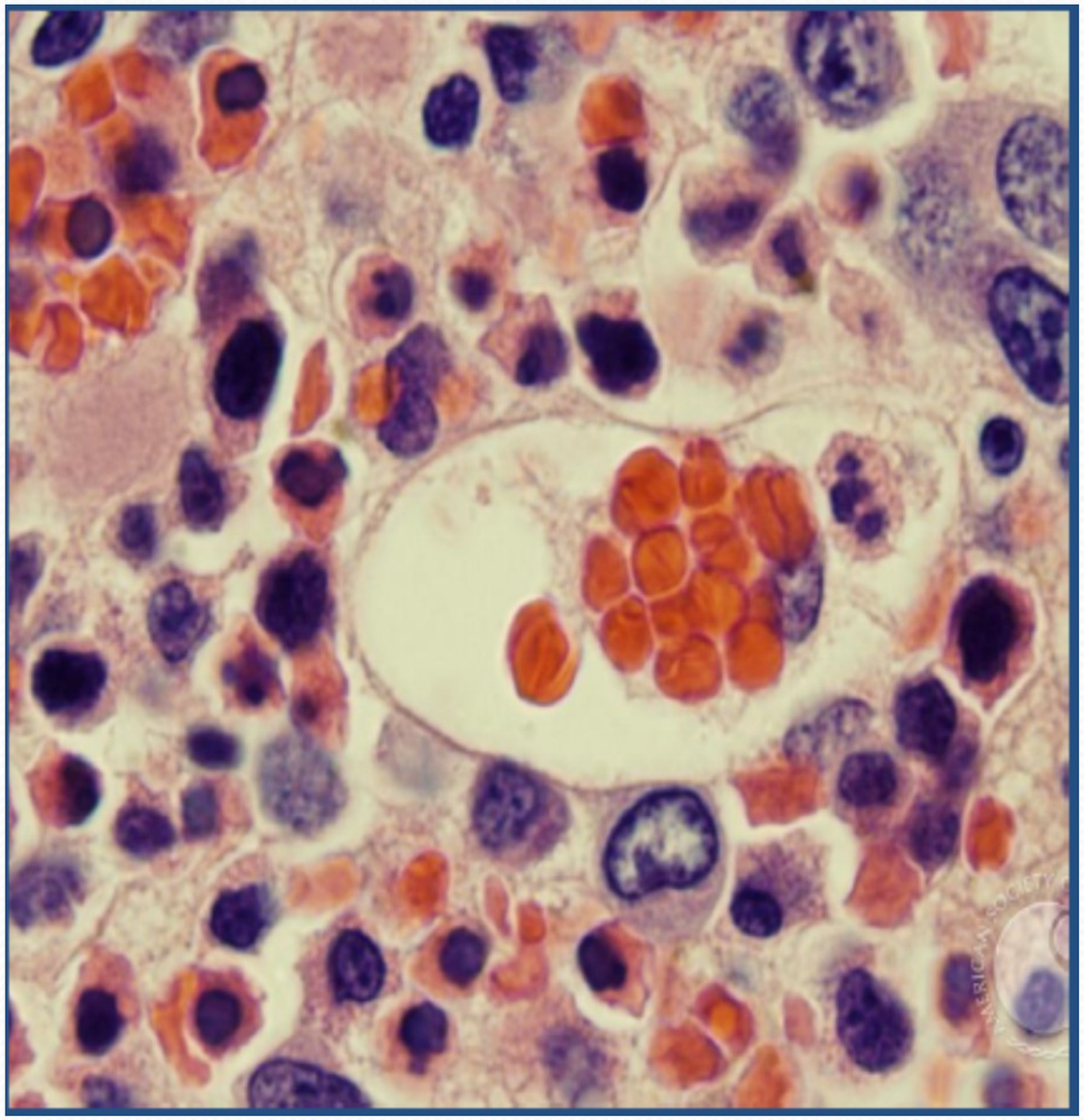


Something went wrong !?



Findings	25/3/2017	27/3/2017	30/3/2107
Fever	++	+	++++
WBC'S Platelets	23.5 K 529 K	12.3 K 285 K	3.4 K 115 K
ESR CRP	105 96	65 64	10 172
Fibrinogen PT/PTT	------- 16/33	------ ------	1.8 19/49
Triglyceride TG			269
Ferritin	1300	--	2800

A febrile patient with known or suspected systemic juvenile idiopathic arthritis is classified as having macrophage activation syndrome if the following criteria are met:



Variable	OR	P Value
Ferritin- **>684** ng/ml	>999.999	< 0.0001
Platelet count **< 181 × 10^9**/ L	237.0	< 0.0001
Triglycerides **> 156** Mg/dl	18.3	0.009
Fibrinogen **<360** Mg/dl	16.0	0.009
SGOT **>48** IU/L	10.0	0.029

EULAR/ACR CLASSIFICATION CRITERIA FOR MAS

ARTHRITIS & RHEUMATOLOGY
DOI 10.1002/ART.39332

RAVELLI ET AL

Management

- **Immunomodulatory dose / Pulse IVMP 30 mg/kg**
- **Cyclosporine A/ Parenteral 3-6 mg/kg IV**
- Anti IL 1
- Anti IL 6
- Anti CD20 /Rituximab
- Anti TNF Alpha/ Inflixibmab
- Intravenous Immunoglobulins 2 g/kg
- Etopside

Case 2

- An 8 year old boy, previously healthy, with:
- A three week history of right hip pain and one week history of pain in the right knee, no fever.
- Diagnosed with streptococcal tonsillitis a month ago.
- Rx: acetylsalicylic acid for 2 weeks/minimal improvement.
- Arthritis was found in both the Rt hip and the Rt knee.

Case 2

Labaratory

WBC'S	14.500 / Normal morphology
ESR	40 mm/hr
CRP	18 mg /l
ASOT	700 U/L
2D Echo	Normal

Diagnosis/ Treatment

- ✓ Additive arthritis, preceding GAS infection, clinical and serology.
- ✓ Not fulfilling Jones criteria
- ✓ Dx: PSRA
- ✓ Recommendations :

  Exclude carditis clinically and by echo

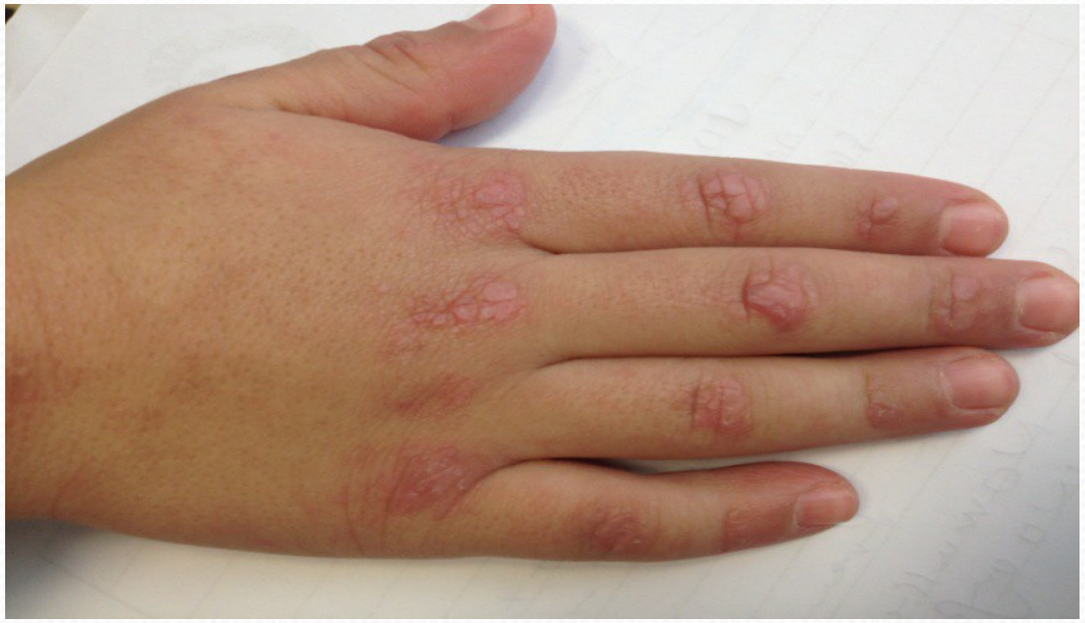
  Treat with prophylactic penicillin for 1 year

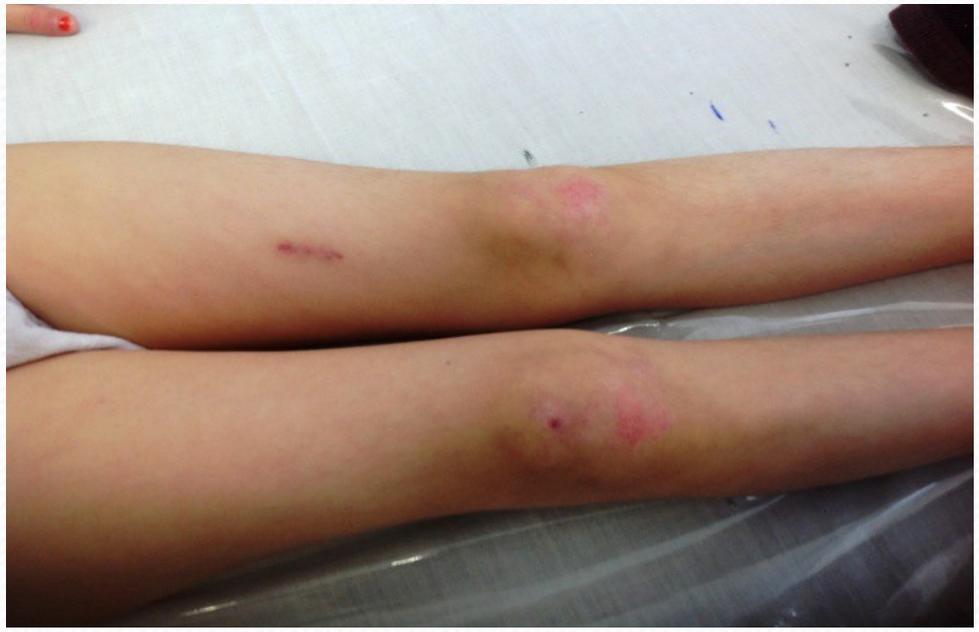
  Reevaluate with echo, if –ve stop Rx

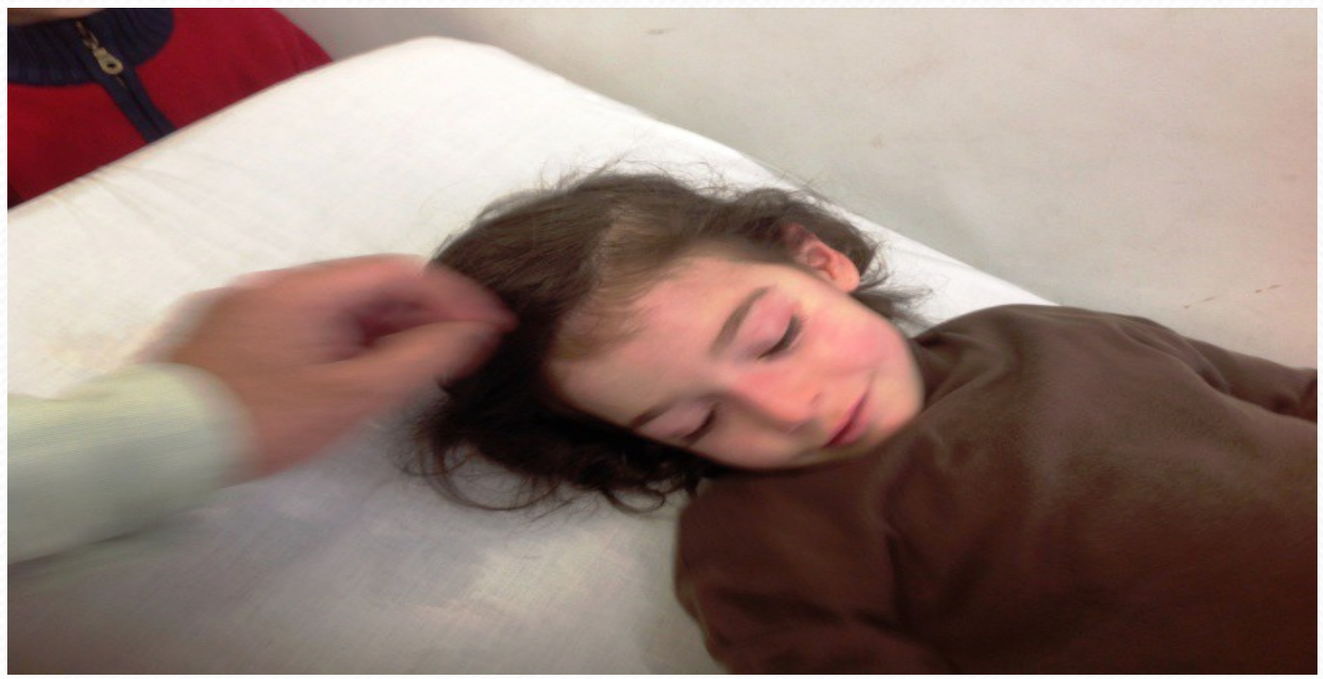
Case 3/ A girl with rash

- An 8 years old girl, with unremarkable previous medical history, was brought because of ***few weeks history of skin rash over cheeks and back of fingers***.
- Made worse by sun .
- She also complained of thigh and calf pain, and found difficulty set up from bed, and ***very slow in climbing stairs***
- Fatigue, appetite loss and some weight loss were also reported

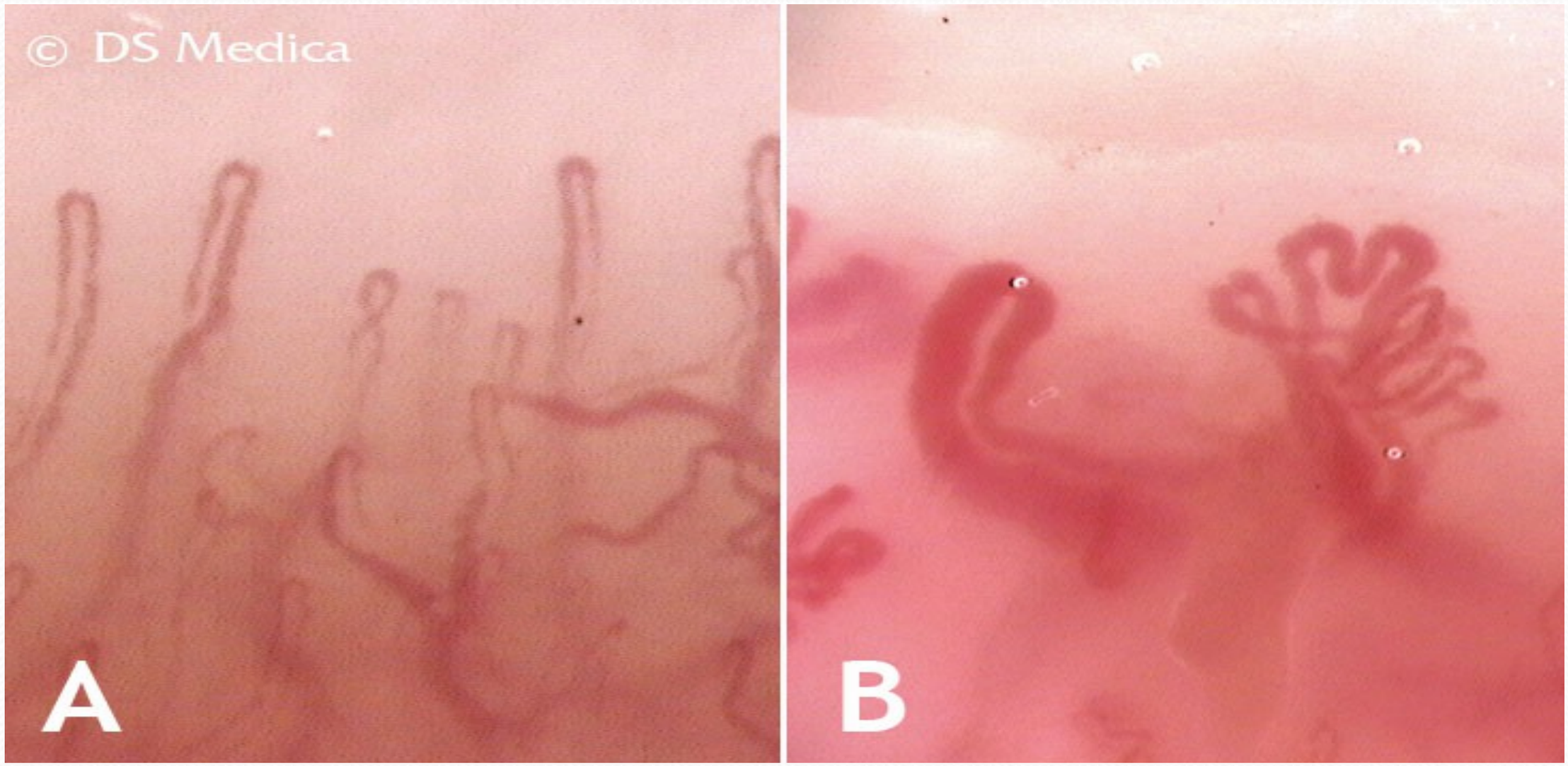
Physical findings







What is this sign? Significance



Case 3

Clinical

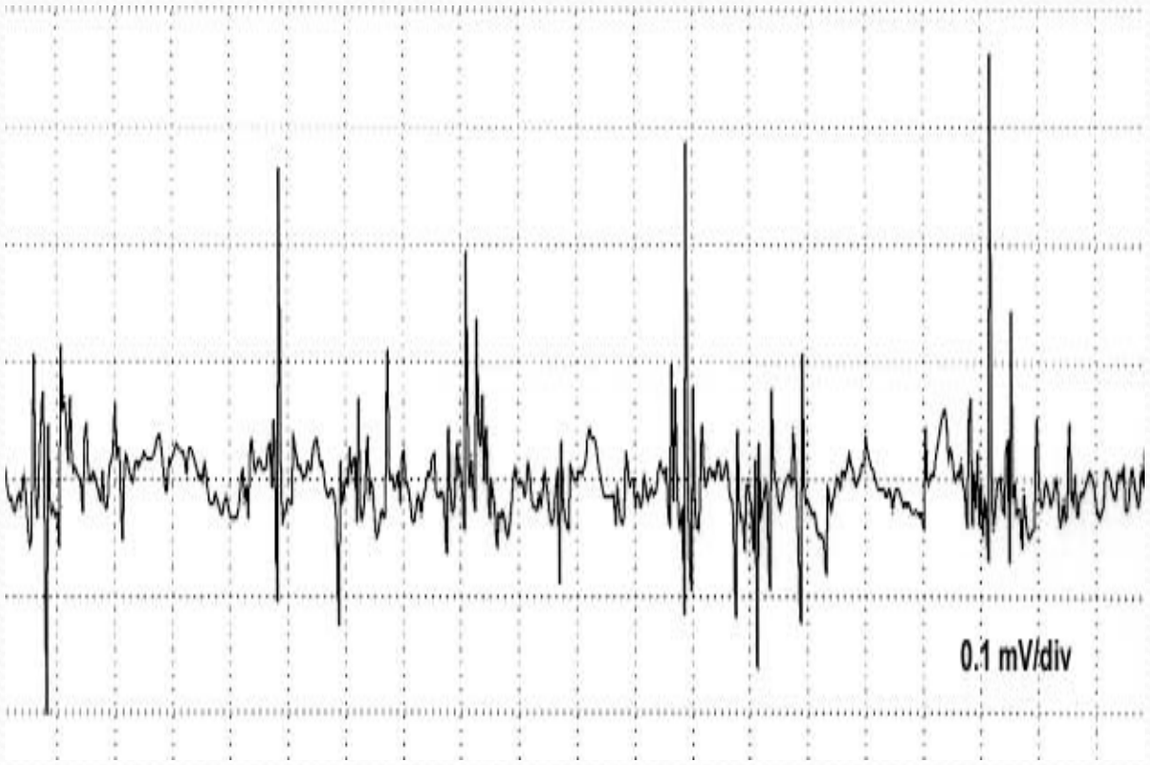
- In addition to skin findings, the girl showed
  - Symmetrical Hip girdle **weakness** , power 2/5
  - Neck flexor **weakness**, power 2/5
  - **Positive Gower's sign**
  - **Tender** calf and thighs, normal hand grip and distal power, normal joints

Labaratory

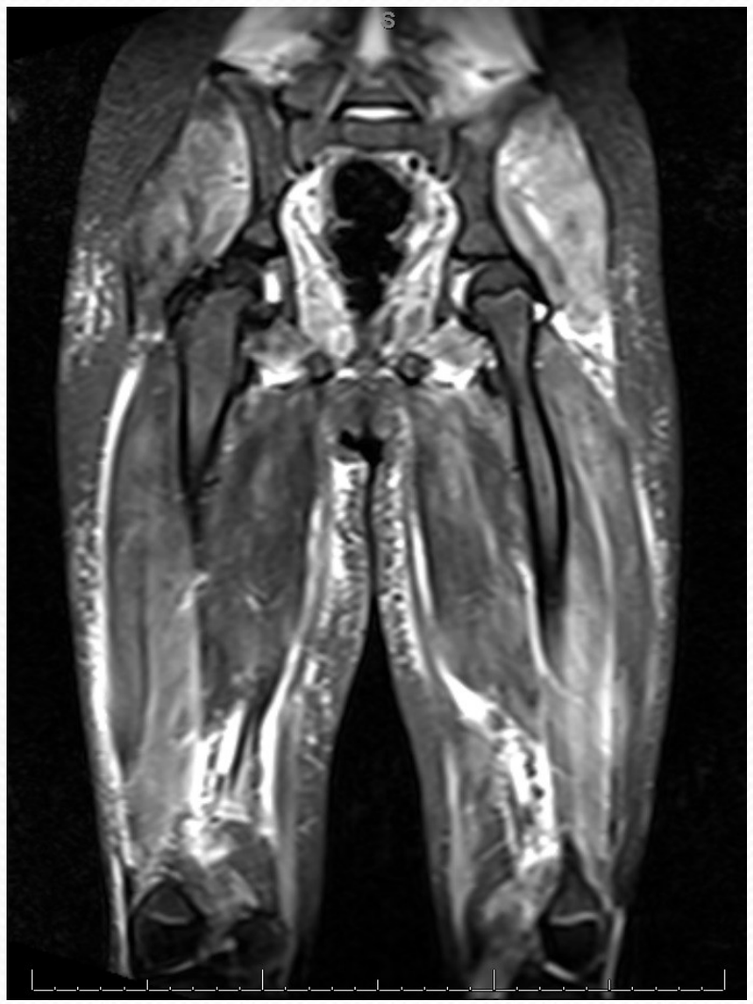
WBC'S	12300
Platelets	659 k
CRP	64 mg/l
ESR	70 mm/hr
ALT/AST	132/185
CK	925
LDH	587
ANA	1/320

EMG/Muscle MRI

Myopathic EMG: Small amplitude, brief, polyphasic action potentials



Muscle MRI, Fluid signal



Straightforward Dx of JDM/Definite, do we need Biopsy ?

Bohan and Peter criteria for diagnosis of dermatomyositis

Symmetric weakness of the limb-girdle muscles and neck flexors

Muscle-biopsy evidence of necrosis, phagocytosis, regeneration, perifascicular atrophy, fiber size variation, perivascular inflammation

Elevation of serum muscle enzymes

Electromyography showing short, small, polyphasic motor units, fibrillations, positive sharp waves and insertional irritability, and bizarre, high-frequency, repetitive discharges

Typical cutaneous features—heliotrope rash, Gottron papules/sign

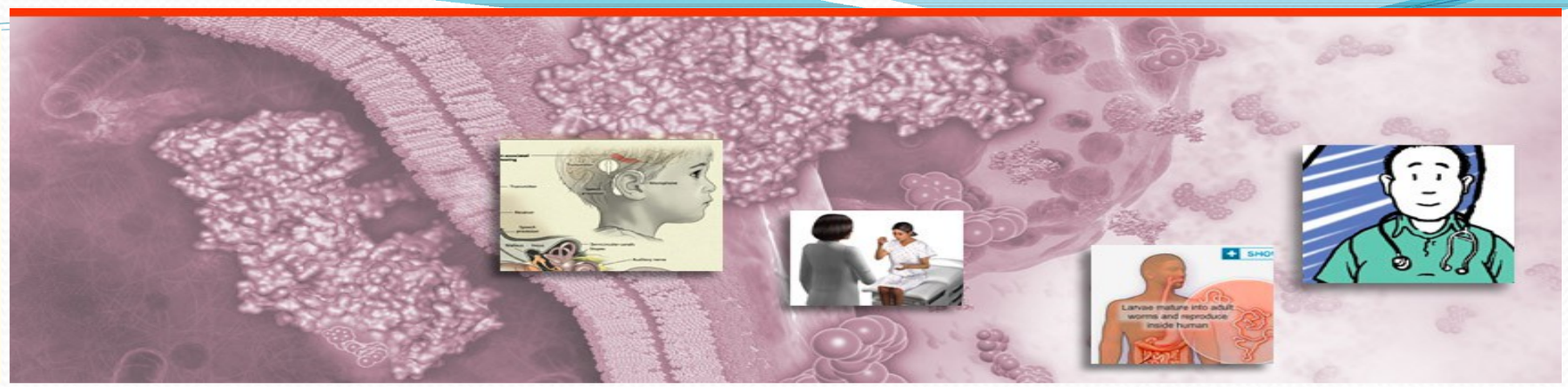
Patients are said to have "definite" JDM if they have rash + 3 other criteria

Patients are said to have "probable" JDM if they have rash + 2 other criteria

Patients are said to have "possible" JDM if they have rash + 1 other criteria

Data from Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med 1975;292(7):344–7.

Anthony Bohan, M.D., and James B. Peter, M.D., Ph.D.
N Engl J Med 1975; 292:403-407



According to the authors of the latest Case Record of the Massachusetts General Hospital, which one of the following findings is considered to be pathognomonic for dermatomyositis?

A. Gottron's papules.
B. Heliotrope rash.
C. Malar rash.
D. Periungual erythema and edema.

Protocols for initial treatment of moderately severe JDM

Arthritis Care & Research
Vol. 62, No. 2, February 2010, pp 219–225
DOI 10.1002/acr.20071

Protocol A
- IVMP
  - 30 mg/kg/day (maximum 1 gm) for 3 days
  - Continue once/week, optional
- MTX
  - Subcutaneous unless only oral possible
  - Lesser of 15 mg/m^2 or 1 mg/kg (maximum 40 mg) once/week
- Prednisone
  - 2 mg/kg/day (maximum 60 mg) once/day for 4 weeks, then decrease by 20%†

Protocol B
- IVMP
  - 30 mg/kg/day (maximum 1 gm) for 3 days
  - Continue once/week, optional
- MTX
  - Subcutaneous unless only oral possible
  - Lesser of 15 mg/m^2 or 1 mg/kg (maximum 40 mg) once/week
- Prednisone
  - 2 mg/kg/day (maximum 60 mg) once/day for 4 weeks, then decrease by 20%†
- IVIG
  - 2 gm/kg (maximum 70 gm) every 2 weeks for 3 weeks, then monthly
- IVMP once with each dose, optional

Protocol C
- MTX
  - Subcutaneous unless only oral possible
  - Lesser of 15 mg/m^2 or 1 mg/kg (maximum 40 mg) once/week
- Prednisone
  - 2 mg/kg/day (maximum 60 mg) divided twice/day for 4 weeks, then consolidate to once/day†

Case 4

- A 5 and ½ years old female from West Bank.
- Generalized edema over the preceding 2 weeks.
- General weakness , started earlier 5 mo. Ago
- History of febrile convulsions, intermittent chronic diarrhea
- **Remarkable past hx. of RAP, fever and arthralgias**
- Underwent appendictomy at age of 3 years
- Result of consanguineous marriage, healthy parents and one brother
- **Maternal aunt with CRF secondary to amylodosis and FMF**

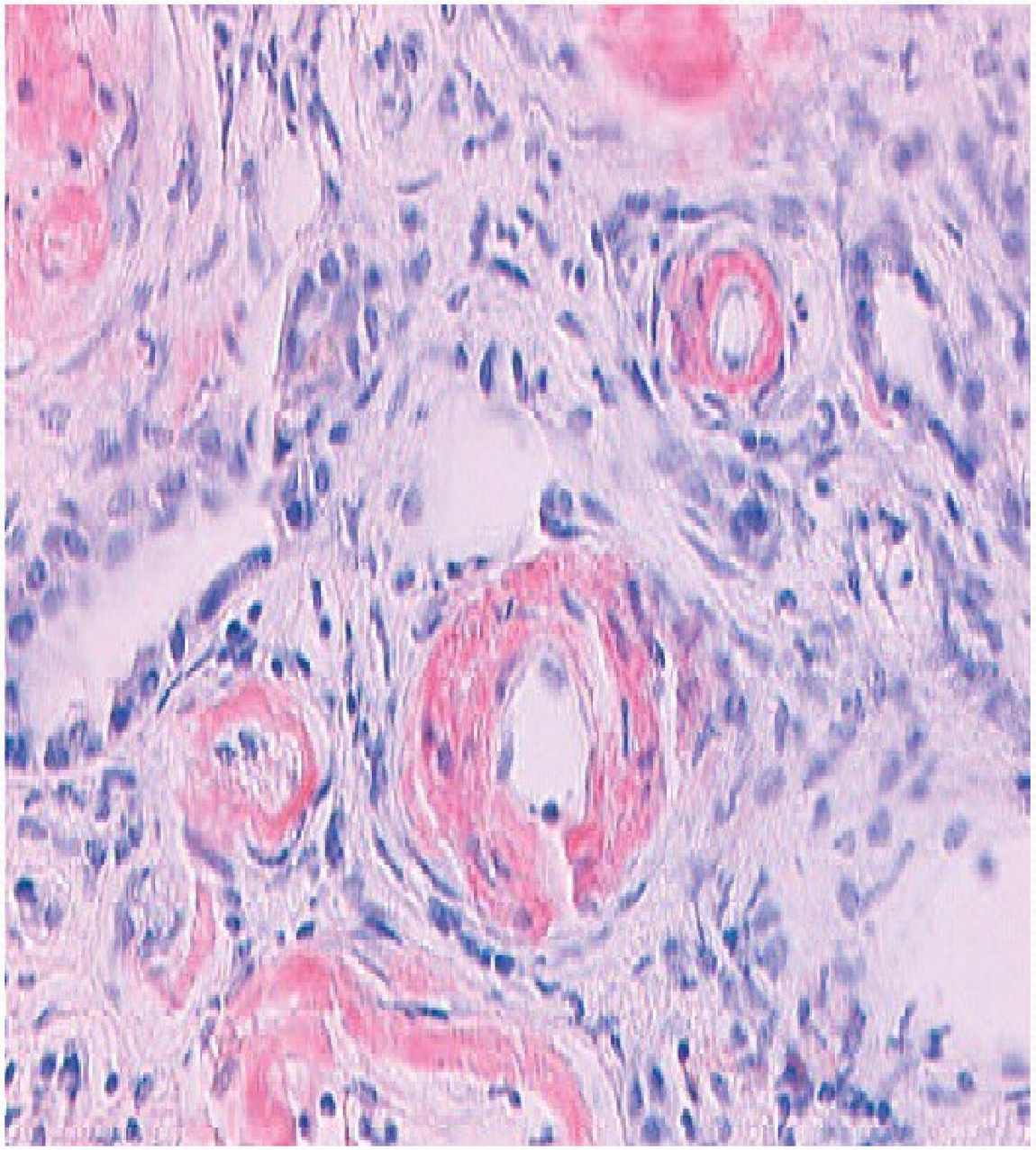
Case 4 findings

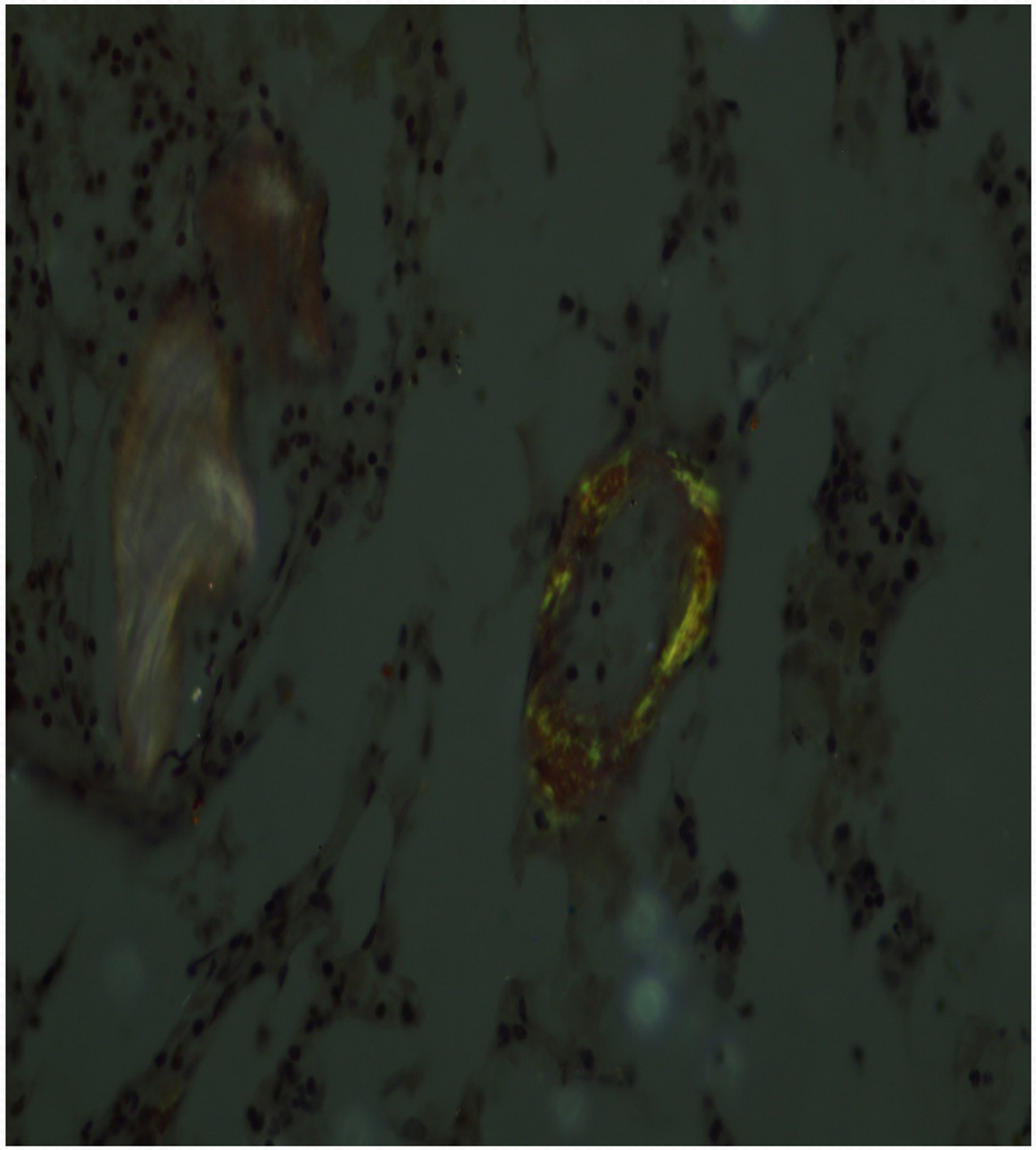
- Pale, asthenic patient, dehydrated, normal low BP- 10%-25%, Normal weight and height for age
- RIF surgical scar, LL edema +2
- Elevated WBC'S, PMN'S, and normal low Hct.
- Platelets initially normal then low normal.
- KFT, Liver enzymes: N, LDH elevated, ESR 40-50
- CRP: Negative/ Ca, K and Na : Low,
- ***Profoundly low albumin : ≤ 15-20, urine protein +3***
- ***Protein/creatinine : > 20***
- ***M694V homoaygous FMF genotype***

Laboratory & Imaging

- Normal heart by echocardiography
- U/S ;Enlarged echogenic both kidneys ,loss CM differentiation.
- CXR Normal
- ***Markedly elevated TG and cholestrol***
- ***TSH high, T_4 low***
- ***SAA wasn't measured***

Kidney Biopsy





Working Diagnosis

- Reactive (AA) Amylodosis, complicating FMF, M694 V (+/+)
- Evidence of Renal, GI, Thyroid involvement
- Inadequately treated or Rx intolerance with colchicine, since 2 years
- Aggressive inflammation is running behind.

Management /Discharge Plan

- Intravascular volume expansion with IV fluids, initially daily Albumin infusion then 2-3 times/wk
- Colchicine 2 mg/day PO divided
- IV solumedrol 2 mg /kg , then PO pred tapering dose
- Azathioprine 2.5 mg/kg
- L-thyroxine 50 mic/day
- Captopril 1 mg/kg, spironolactone 2 mg/kg
- ***Feb,23,2013***

Discharged in relatively acceptable condition , no marked edema, urine protein +2, albumin of 2.2

1 Week later/February,28,2013

- **Re admitted**, frequent emesis, diarrhea, BP 80/45 (<5 %), pale, cold edematous extremities, (Intravascular depletion state) and Ascitis.
- Hemoconcentration (Hb 12.5), High WBC'S , PMN and platelets
- Albumin 0.9, urine +4 albumin, N KFT and GFR of 198 ml/min (age N 80-170). Hypokalemia(k=2.2).

Evidence of intense inflammation; 3/3/2013

SAA was 209 mg/L

What is next ?

To: ped-rhe-list@mailman1.cis.McMaster.CA Hide

Bcc: Adel Wahadneh

From: Zeyad Habahbeh

Amylodosis case

March 1, 2013, 10:36 AM

Dear colleagues:
I would like to share you with the challenge managing a 6 years old girl , referred to our facility couple of months ago, with :

1. Oedema, high grade proteinuria/albuminuria(nephrotic range) and kidney Bx consistent with AA amylodosis.
2. She has clinical background of recurrent abdominal pain and strongly positive FHx of FMF and homozygous M694V mutation, for which she was on colchicine over the last year or two , but suboptimal dose and sometimes without complete adherence.
3. Patient had also protracted chronic diarrhea for around 2-3 months/year in the last 2 years that get worse with colchicine, but showing normal growth indices and chronic anemia, GI Bx wasn't done so far
4. She has also intermittent fever, apathy, anorexia and nervousness
5. Her kidney function is normal, inflammatory markers are modestly elevated, thyroid function is depressed.
6. Patient persisted to have diarrhea and recurrent vomiting so that we couldn't go up to optimal colchicine dose, and her GI disturbance is constantly troublesome.

Besides supportive Rx , repeated albumin infusions, fluid and electrolytes corrections , colchicine oral divided to reach 1mg/day now , l-thyroxine replacement, steroids reducing course after 2mg/kg /day for two weeks, antibiotics to decontaminate the gut, we added azathioprine since 2 **weeks and patient is still having refractory GI disease profoundly hypoalbuminemic and oedematous with high grade prteinuria**

We are planning to add biological treatment,Anakinra or Infliximab, have any one tried that?
We want to tap your collective wisdom and experience in the best next option for this girl?
Does any one has a similar experience and what is your preferred choice?
Your input is highly needed and appreciated

Regards
Zeyad Habahbeh MD
Pediatric rheumatology, immunology and allergy
King Hussein Medical center
Amman,Jordan

“One of the youngest patients, I have ever heard to develop amyloidosis “

From: "Hawkins, Philip" <p.hawkins@ucl.ac.uk>
Date: March 1, 2013, 12:46:19 PM GMT+03:00
To: "'ped-rhe-list@mailman1.cis.McMaster.CA'" <ped-rhe-list@mailman1.cis.McMaster.CA>
Cc: "Woo, Patricia" <patricia.woo@ucl.ac.uk>, "Lachmann, Helen" <h.lachmann@ucl.ac.uk>
Subject: [ped-rhe] (no subject)
Reply-To: ped-rhe-list@mailman1.cis.McMaster.CA

Dear Zeyad

Pat Woo forwarded me your email about this unfortunate young girl with AA amyloidosis complicating FMF. I would strongly support her receiving anakinra ~2mg/kg/day. We have documented a number of excellent responses to anakinra in patients with FMF who cannot be controlled by colchicine alone.

Do you have access to measuring the plasma SAA concentration? There may be a window of opportunity to save her kidney function if her inflammatory disease can be completely suppressed with urgency. We would recommend measurement of her SAA 2 weekly during the first 2 months of anakinra therapy, and then monthly thereafter.

If you cannot get the SAA measured locally, we'd be happy to do this for you in our lab, requiring one ml of serum that can be transported at room temperature over 2-3 days. CRP measurements are a reasonable surrogate in this situation, but it is vital to measure SAA as well, at least initially.

Kind regards

Philip Hawkins

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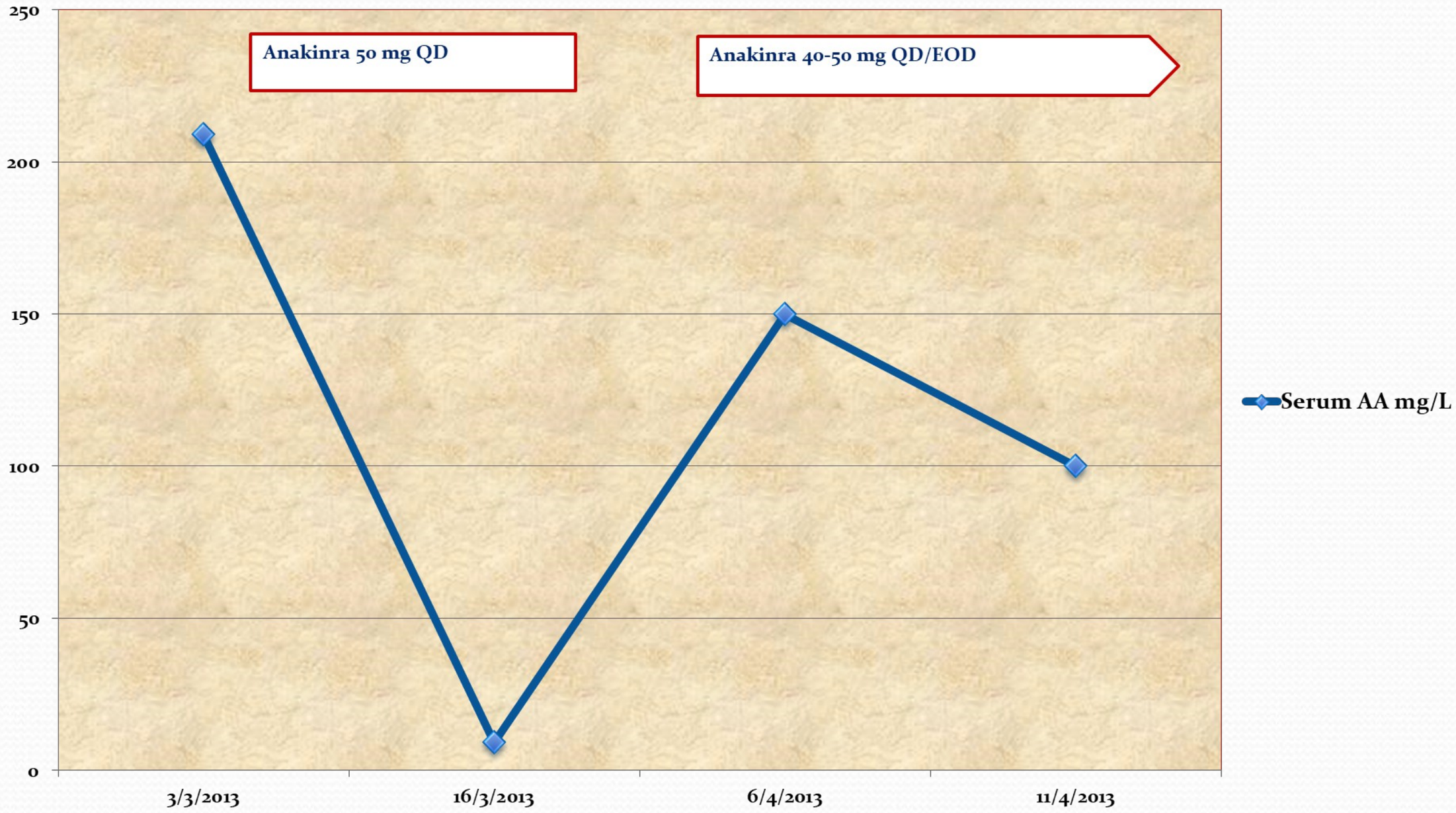
Anakinra successfully suppress inflammation



≥2 Major or 1 major and 2 minor

Table 1. Tel-Hashomer diagnosis criteria

Major criteria	Minor criteria
Recurrent febrile episodes with serositis (peritonitis, synovitis or pleuritis)	Recurrent febrile episodes
Amyloidosis of AA type without a predisposing disease	Erysipelas-like erythema
Favorable response to regular colchicine treatment	FMF in a first-degree relative

FMF Diagnosis/Livneh criteria

- ≥ 1 major criteria, or ≥2 minor criteria, or ≥1 minor criterion plus ≥5 supportive criteria,.
- Typical attacks are defined as recurrent (≥3 of the same type), febrile (rectal temperature of 38°C or higher, and short (lasting between 12 hours and 3 days)
- Incomplete attacks : 1) Temperature
  2) Duration
  3) no signs of peritonitis
  4) localized
  5) The arthritis

Table 2A. Livneh criteria set for the diagnosis of familial Mediterranean fever*

Major criteria
Typical attacks of:
1. Peritonitis (generalized)
2. Pleuritis (unilateral) or pericarditis
3. Monoarthritis (hip, knee, ankle)
4. Fever alone
Minor criteria
1-3. Incomplete attacks involving 1 or more of the following sites:
1. Abdomen
2. Chest
3. Joint
4. Exertional leg pain
5. Favorable response to colchicine

Supportive criteria
1. Family history of FMF
2. Appropriate ethnic origin
3. Age ≤20 years at disease onset
4-7. Features of attacks
4. Severe, requiring bed rest
5. Spontaneous remission
6. Symptom-free interval
7. Transient inflammatory response, with one or more test result(s) for white blood cell count, erythrocyte sedimentation rate, serum amyloid A, and/or fibrinogen
8. Episodic proteinuria/hematuria
9. Unproductive laporatomy or removal of white appendix
10. Consanguinity of parents

Anti IL1 indications in FMF

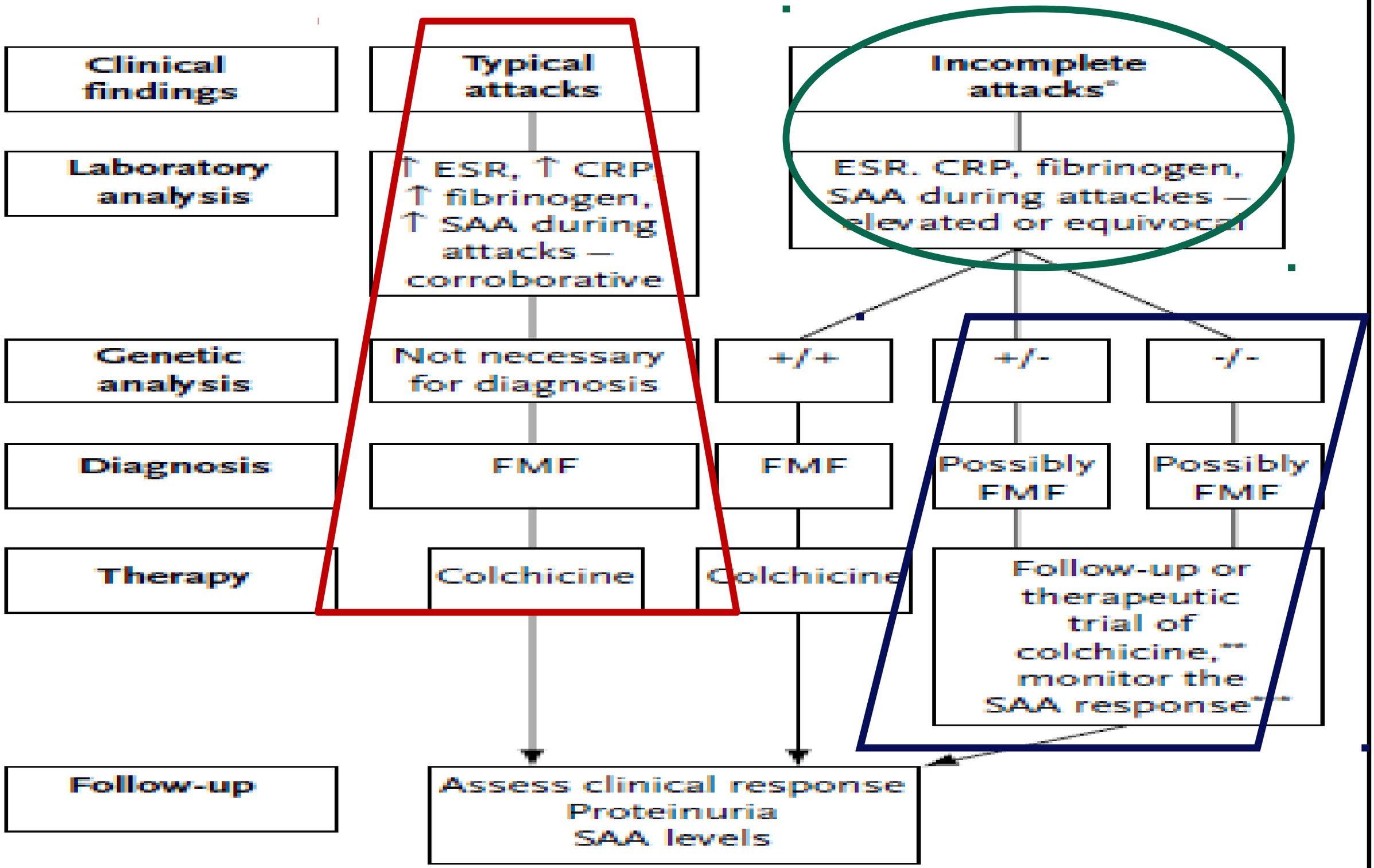
Despite adequate and optimal colchicine

- Incomplete control of disease activity .
- Failure to suppress SAA
- FMF associated Vasculitis
- Severe side effects or intolerance to colchicine
- Amylodosis

Interleukin-1 Targeting Drugs in Familial Mediterranean Fever: A Case Series and a Review of the Literature

Ulrich Meinzer, MD, PhD,* Pierre Quartier, MD, PhD,†

Figure 1. *Diagnostic algorithm*



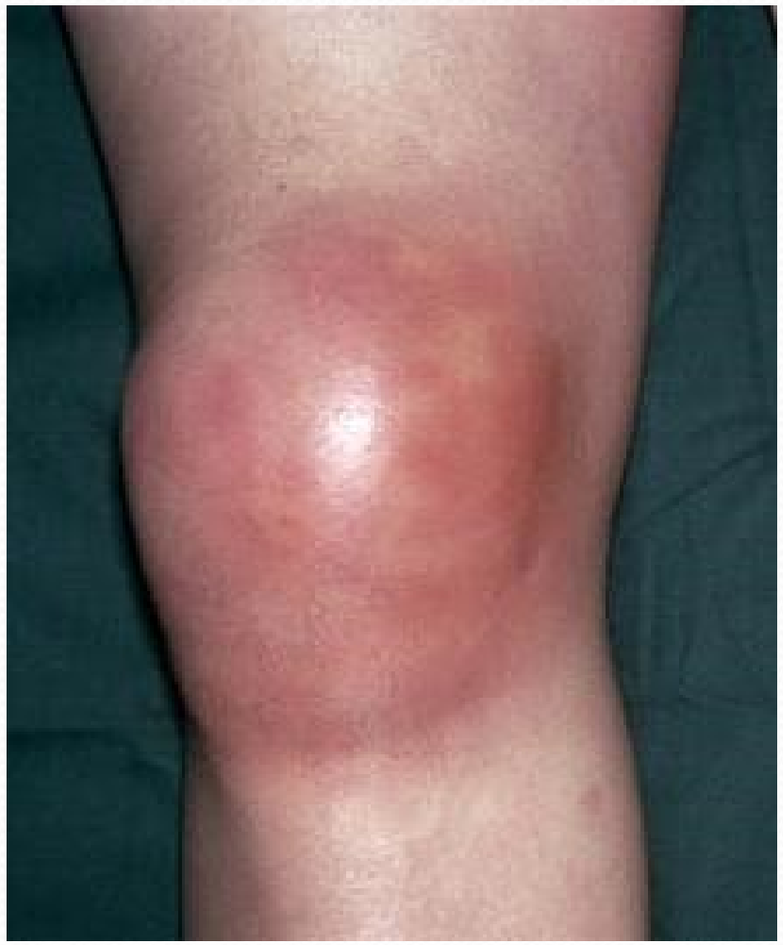
Case 5

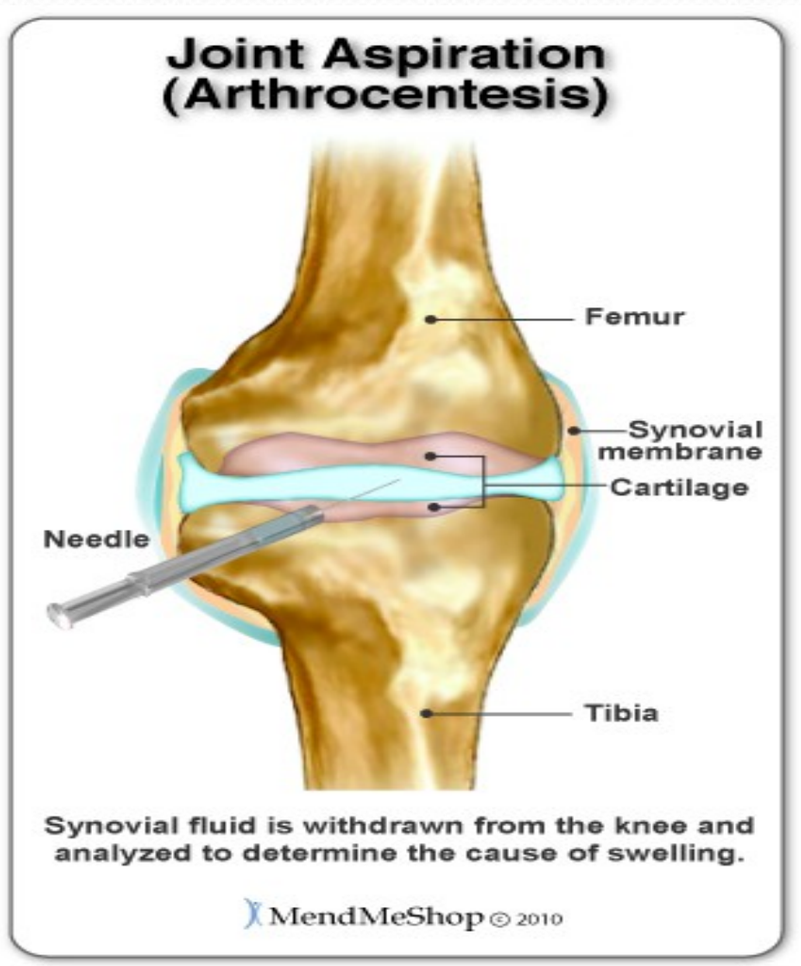
- An 8 years old girl presented to the ER with 2 days of left knee pain and fever; admitted to the pediatric ward; Pyrexia ,Lt knee arthritis.
- Ill looking, febrile , very tender , swollen joint
- Streptococcal tonsillitis one month ago.
- CBC was normal, the ESR was 90 mm/hr and the ASLO was 800 IU/mL.

What is the diagnosis

? What to do next? What is your treatment

WBC’S 50,000/PMN’S 70 %





Case 5/ 3rd in hospital

- Left Knee arthritis disappeared
- Right hip started to show LOM
- US showed effusion in the hip
- Echocardiography is normal
- So fleeting or migratory arthritis +

  Fever, and GAS infection evidence

Case 5 summary: **RF**

- ✓ Fever and monoarthritis, aspirate joint and treat as septic knee
- ✓ Once arthritis became fleeting, with serological dx of GAS

  then she is fulfilling Jones criteria(One major and 2 minor)
- ✓ The girl should start long-term secondary antibiotic prophylaxis.

Revised Jones Criteria 2015

A. For all patient populations with evidence of preceding GAS infection	
Diagnosis: initial ARF	2 Major manifestations or 1 major plus 2 minor manifestations
Diagnosis: recurrent ARF	2 Major or 1 major and 2 minor or 3 minor
B. Major criteria	
Low-risk populations*	Moderate- and high-risk populations
Carditis†	Carditis
• Clinical and/or subclinical	• Clinical and/or subclinical
Arthritis	Arthritis
• Polyarthritis only	• Monoarthritis or polyarthritis • Polyarthralgia‡
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
C. Minor criteria	
Low-risk populations*	Moderate- and high-risk populations
Polyarthralgia	Monoarthralgia
Fever (≥38.5°C)	Fever (≥38°C)
ESR ≥60 mm in the first hour and/or CRP ≥3.0 mg/dL§	ESR ≥30 mm/h and/or CRP ≥3.0 mg/dL§
Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)	Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)

(*Circulation*. 2015;131:000-000. DOI: 10.1161/CIR.0000000000000205.)

Thank you for your attenti on