Systemic inflammatory diseases

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Primary Immunodeficiencies / Autoinflammatory Disorders
Autoimmune Diseases / Paediatric Rheumatic Diseases

Overview

- Juvenile idiopathic arthritis
- Systemic vasculitides
- Systemic lupus erythematosus
- Idiopathic inflammatory myopathies
- Scleroderma

Juvenile Idiopathic Arthritis

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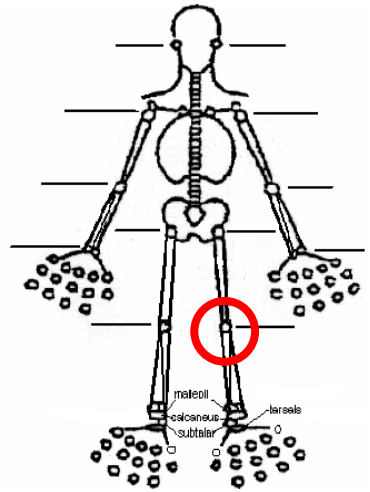
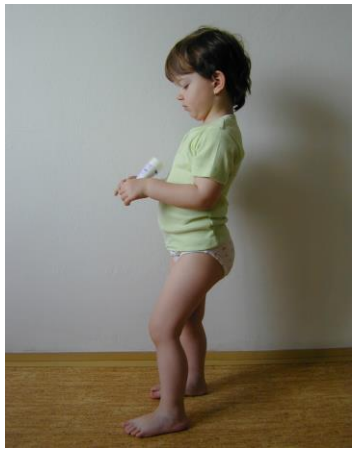
Kate‘s story

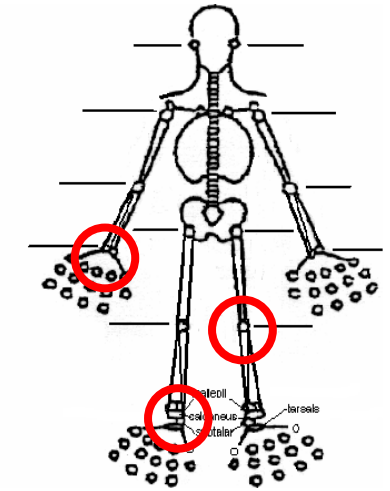
- 2 yrs healthy girl fell while running around
- Primary care physician – surgeon
  - L knee XR, basic bloods normal
  - Knee aspirate sterile, immobilisation with plaster splint
- 3 – 8 weeks later
  - Swelling worse, refuses weight-bear in the morning, negativistic
  - Knee MRI (general anaesthesia) – synovitis
  - Rheumatology referral

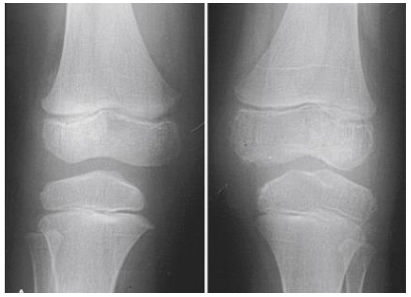


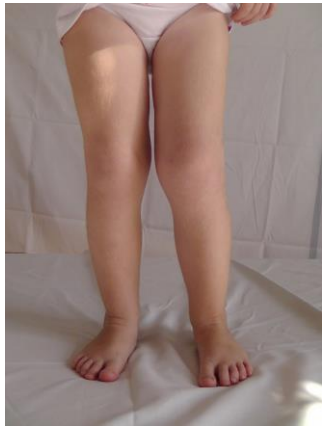


At paed rheum

- MSK exam (30 min)
  - 3 active joints
  - L leg muscle atrophy and overgrowth
- Chronic anterior uveitis on slit lamp exam
- Labs: normal, ANA+
- Dg: JIA (oligoarticular)







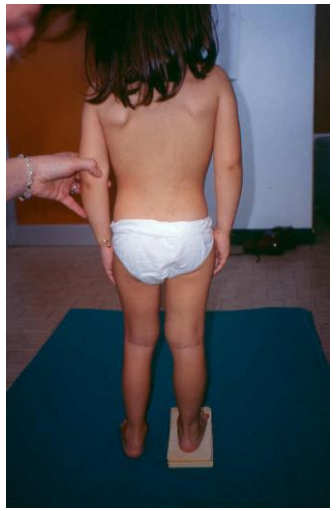
JIA - definition

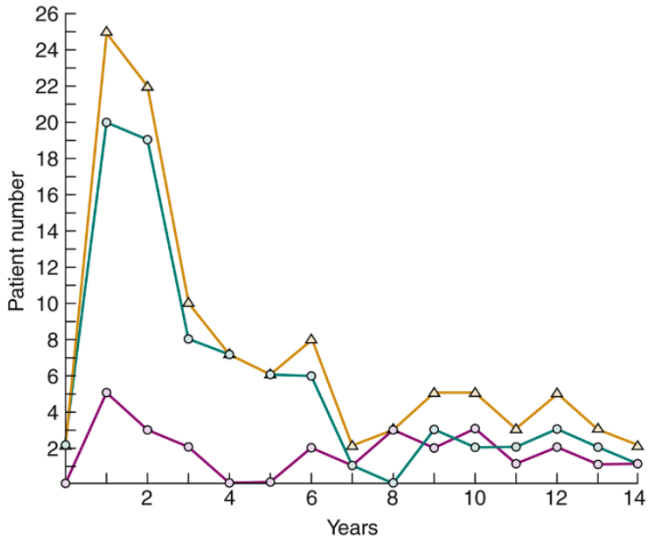
- Diagnosis of exclusion
- Childhood onset of synovitis continuously present in at least 1 joint
  - For A minimum of 6 wks
- Incidence
  - 1.6 - 23 / 100 000 children
  - Pooled incidence in Caucasians 8.3 (CI 8.1-8.7)/100 000
- Prevalence
  - 3.8 – 400 / 100 000 children
  - Pooled prevalence 32.6 (CI 31.3-33.9)/100 000
  - Girls 19.4, boys 11.0

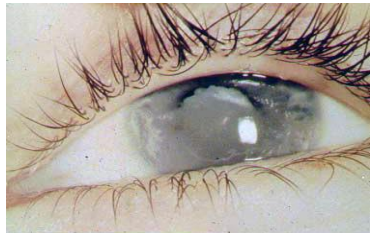
S. Thierry, B. Fautrel, L. Lemelle, F. Guillemin: Prevalence and incidence of juvenile idiopathic arthritis. A systematic review. *Joint Bone Spine.* 81:112-117 2014

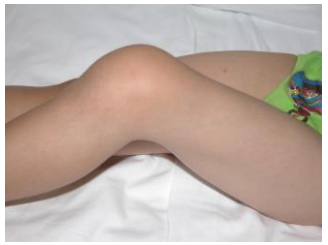
JIA subtypes: Oligoarthritis

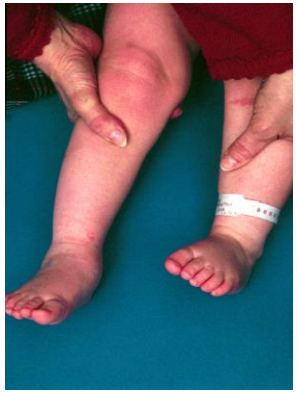
- Oligoarthritis – up to 4 joints
  - Persistent, extended
  - Most common – 40% of all JIA
  - Peak onset – toddlers
- Most commonly affected joints *Sharma S, Sherry DD 1999*
  - Knee 56%
  - Ankle 20%
  - Wrist 4 %
- Typical features
  - Absence of systemic inflammation
  - Often absence of pain
  - ANA – some prognostic value (uveitis)
  - Growth disturbances common
- **High UVEITIS risk (**30%) *Petty RE et al 2003*
  - Regular slit lamp exam







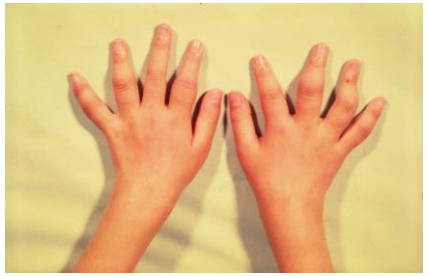


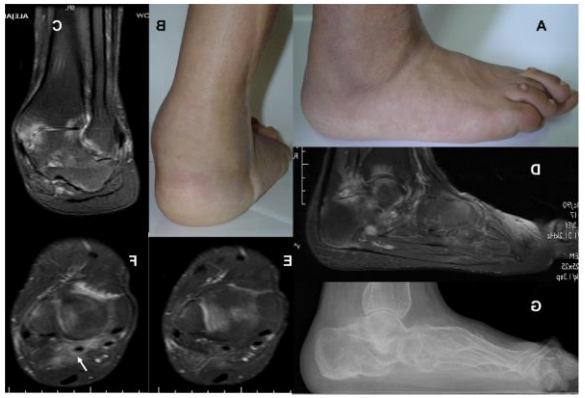


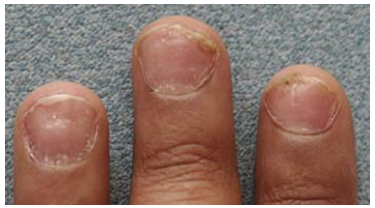
Sullivan DB, Cassidy JT, Petty RE: Pathogenic implications of age of onset in juvenile rheumatoid arthritis, *Arthritis Rheum* 18:251, 1975.

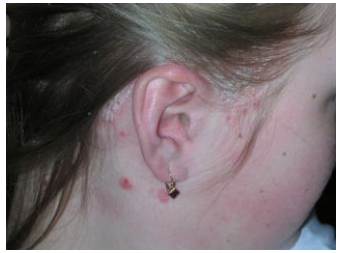
Other JIA subtypes

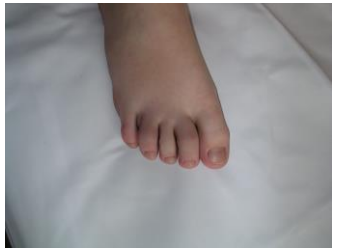
- **Polyarthritis**: 5+ joints affected, about 20%
  - Common involvement of TMJ, forefoot, wrist, hip, C-spine
  - Raised inflammatory markers non-specifically
  - RF IgM positivity rare (1-2%)
    - Adolescent girls, similar to RA
  - RF IgM negative polyJIA most common
- **Enthesitis-related arthritis/juvenile spondylarthritis**
  - Often with HLA B-27, lower extremity joints, SI, enthesitis
  - Acute uveitis
- **Psoriatic arthritis**
  - Dactylitis, nail pitting, family history







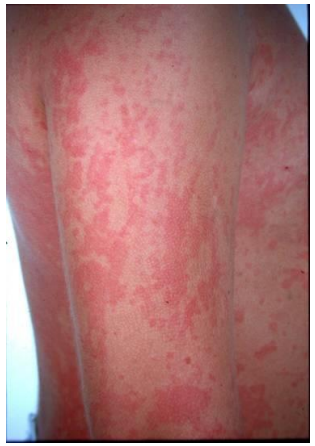


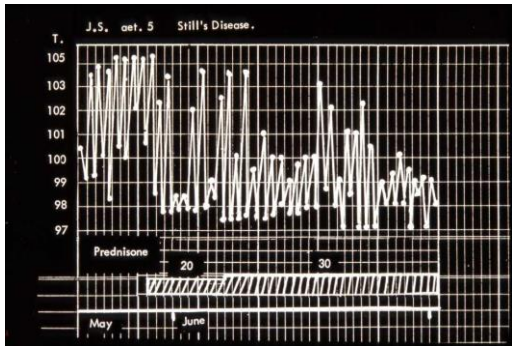


Stoll ML et al: Arthritis Rheum 2006,54:3564-72

JIA subtypes: Systemic (Still´s disease)

- Relatively rare subtype 10-15%
  - Peak onset toddlers
- **Arthritis** with or preceded by daily **fever** of at least 2 weeks' duration (documented as quotidian for minimum 3 days) accompanied with one or more of:
  - Evanescent, non-fixed erythematous **rash**
  - Generalised **LNpathy**
  - **Hepato or splenomegaly**
  - **Serositis**
- Heterogeneous phenotype
  - "autoinflammatory" type – systemic features predominate
  - Destructive polyarthritis



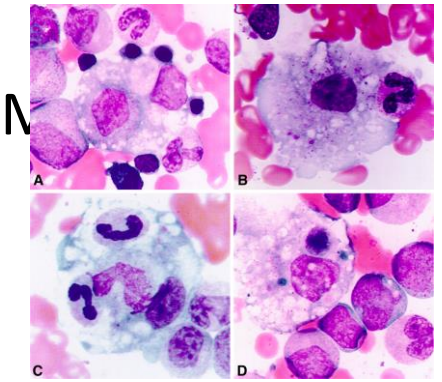


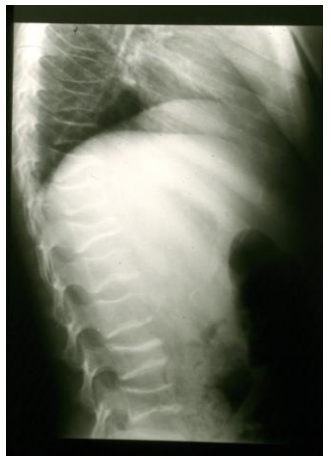
SJIA - presentation

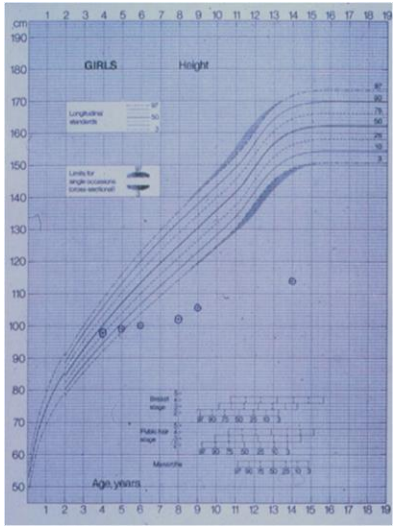
- **Fever may precede arthritis by months**
- Variable **arthritis and tenosynovitis,** may be absent
- Pericarditis = the most frequent **serositis**
- Prominent general deterioration during febrile intervals
- Persistent destructive arthritis (30%)
- Labs
  - Non-specific inflammatory response: High FW, CRP, WBC, PLT, anemia
  - Raised ferritin, endothelial activation (d-dim), high FBG

SJIA - Complications

- Acute life threatening complication: Macrophage Activation Syndrome (M HLH
  - Persistent **fever** and malaise, neurological abnormalities, rash
  - Acute **hepatopathy**, multi-organ failure
  - **Cytopenia** with haemophagocytosis in marrow aspirate
  - Consumptive **coagulopathy** with DIC → ↓fibrinogen and ESR, ↑d-dimer, FDP, APTT
  - **Drop in ESR** and fibrinogen
  - Raised **ferritin** and **IL-18**
- Long-term complications:
  - Growth delay
  - Osteoporosis and other glucocorticoid toxicity
- Outcome
  - About 80% children have intermittent or persistent disease
  - About 20% have treatment-refractory disease

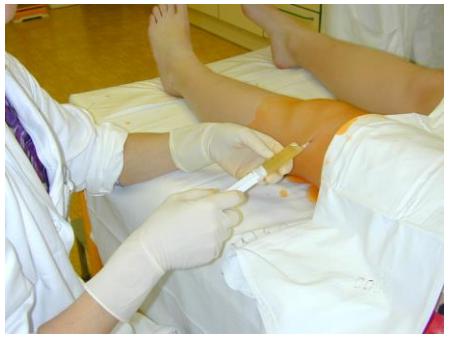






JIA therapy

- Intraarticular corticosteroids (triamcinolone hexacetonide)
- Methotrexate
  - Oral or s.c., low dose once weekly
- „Directed“ therapies
  - Biologics: Blockade of inflammatory cytokines (TNFa, IL6, IL-1, co-stimulation), B-cell depletion
  - Small molecules: JAK inhibitors



Vasculitis

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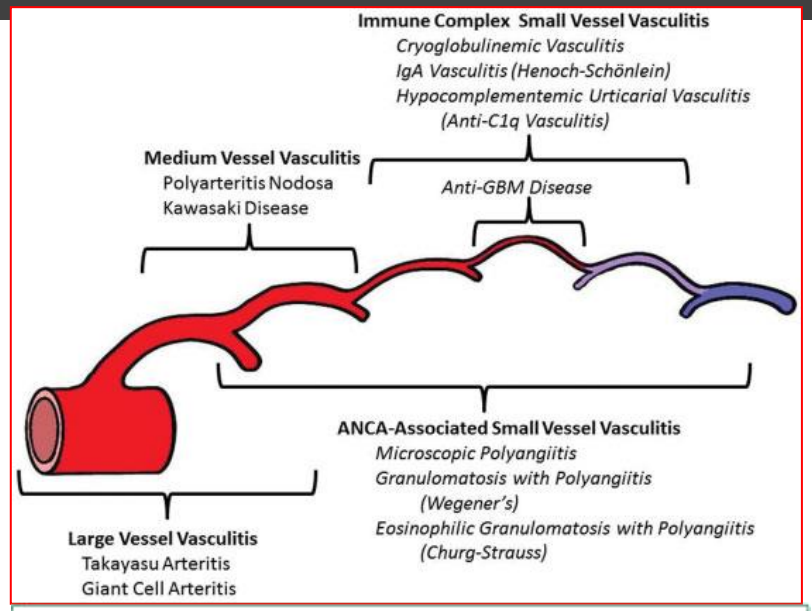
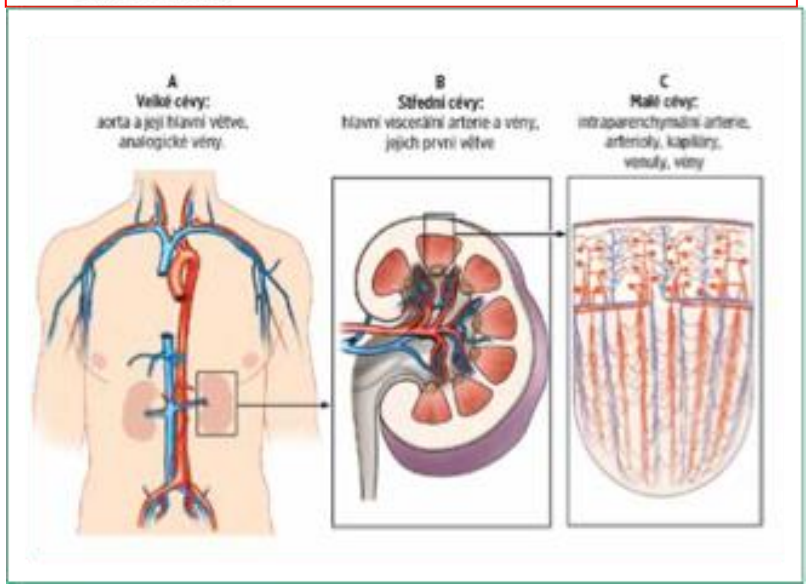
Primary vasculitis in children

- **More frequent entities:** typical childhood disease, acute conditions
  - IgA vaskulitis (incidence 20/100 000 children)
  - Kawasaki disease (3,1-111/100 000)
- **Rare conditions:** chronic vascilitis, incidence <1/100,000
  - Polyarteritis nodosa (PAN)
  - Ganulomatosis with polyangiitis (GPA)
  - Eosinofilic granulomatosis with polyangiis (EGPA)
  - Takayasu arteritis (TA)

Doležalová P et al. J Rheumatol. 2004 Nov;31(11):2295-9
Gardner-Medwin J et al. Lancet 2002;360(9341):1197-202

Childhood Vasculitis classifiction





I Predominantly large vessel vasculitis

- Takayasu arteritis

II Predominantly medium sized vessel vasculitis

- Childhood polyarteritis nodosa
- Cutaneous polyarteritis
- Kawasaki disease

III Predominantly small vessels vasculitis

(A) GRANULOMATOUS

- Wegener's granulomatosis
- Churg-Strauss syndrome

(B) NON-GRANULOMATOUS

- Microscopic polyangiitis
- Henoch-Schönlein purpura
- Isolated cutaneous leucocytoclastic vasculitis
- Hypocomplementic urticarial vasculitis

IV Other vasculitides

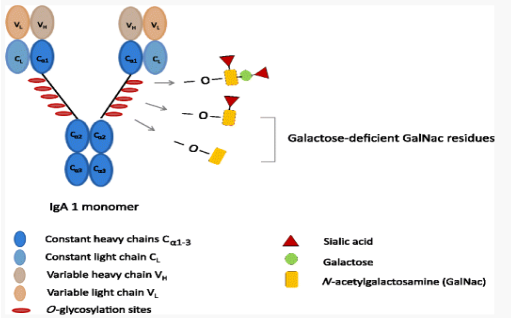
- Behçet disease
- Vasculitis secondary to infection (including hepatitis B associated polyarteritis nodosa), malignancies, and drugs, including hypersensitivity vasculitis
- Vasculitis associated with connective tissue diseases

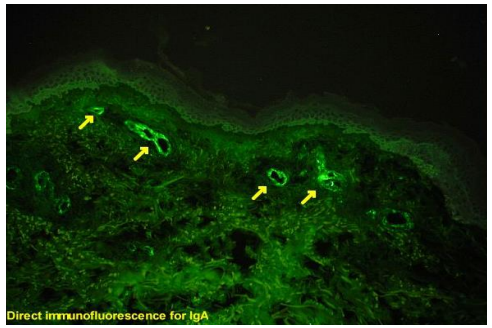
IgA vasculitis (IgAV, Henoch-Schönlein purpura)

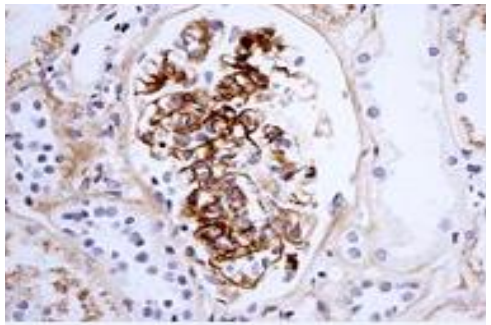
- Most common paediatric vasculitis

Definition :

- vasculitis with IgA1 dominant imune deposits affecting small blood vessels
- typically skin, GIT, joints, kidneys
- glomerulonephritis indistinguishable from IgA nephropathy







Jennette JC….:Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum.2012: 20143 (65):1-11

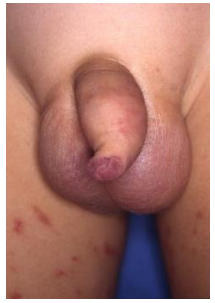
IgAV

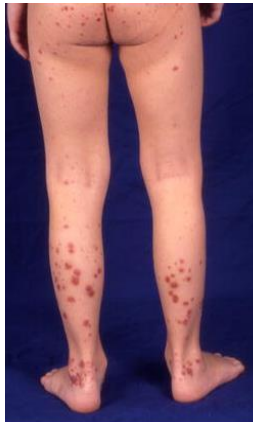
Classification criteria

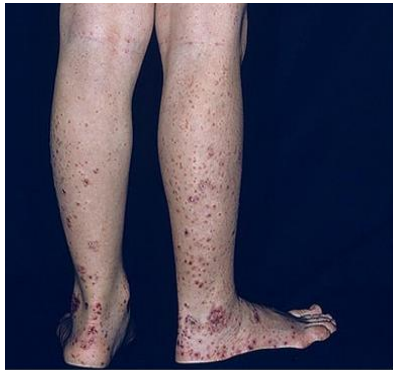
- palpable purpura with predominant low extremity distribution

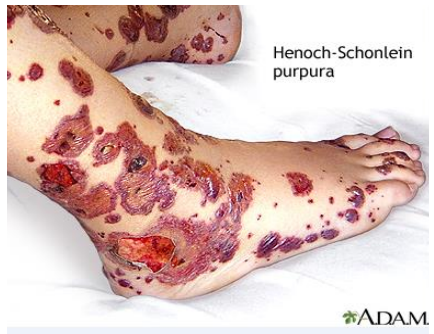
  + minimum of one out of:

  - abdominal pain
  - histopathology finding
  - arthritis and/or arthralgia
  - nephritis









Disease course and outcome

- Variable, often relapsing
  - 1/3 – 2 wks course
  - 1/3 – resolution up to 1 month
  - 1/3 – recurrent course for months
- IgAV nephritis (HSPN)
  - Most often benign
  - 1,6-3% příčin terminálního renálního selhání v UK
- Generally benign disease, more severe organ involvement very rare (gut, CNS, renal vasculitis)

Ozen S et al.: EULAR/PRINTO/PRES criteria for HSP, childhood PN, WG a TA: Ankara 2008: Part II: Final classification criteria. Ann Rheum Dis 2010: 69: 798-806

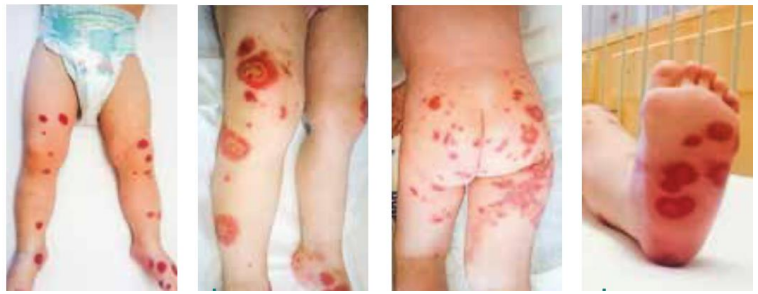
IgAV diagnosis

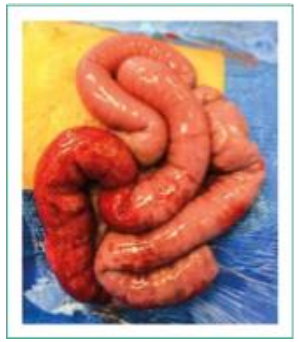
- EULAR/PRES/PRINTO criteria
- **Skin biopsy** rarely performed (atypical manifestations)
  - Absence of IgA deposits does not exclude IgAV
- **Kidney function** (eGFR, hematuria, proteinuria – UP:UC)
  - Most common: microhematuria
  - Paediatric nephrology
    - Significant proteinuria
    - Decreased GFR
  - **Renal biopsy**
    - proteinuria : UP/UC ratio > 250mg/mmol
    - Low GFR
- **Abdominal US**
  - To rule out intussusception

RHEUMATOLOGY
Original article
doi:10.1093/rheumatology/kez041

European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative

Seza Ozen[1], Stephen D. Marks[2], Paul Brogan[2], Noortje Groot[3,4,5], Nienke de Graeff[3], Tadej Avcin[6], Brigitte Bader-Meunier[7], Pavla Dolezalova[8], Brian M. Feldman[9], Isabelle Kone-Paut[10], Pekka Lahdenne[11], Liza McCann[5], Clarissa Pilkington[2], Angelo Ravelli[12], Annet van Royen[3], Yosef Uziel[13], Bas Vastert[3], Nico Wulffraat[3], Sylvia Kamphuis[4] and Michael W. Beresford[5,14]





IgAV - therapy

- **Analgesia**
  - Adequate pain relief for arthritis
  - NSA not contraindicated when renal function normal
  - Adekvátní analgesia also for abdominal pain
- **Corticosteroids**
  - Indicated in rare organ involvement: Orchitis, CNS vasculitis, pulmonary haemorrhage, other organ involvement
  - Considered when severe abdominal pain and/or enterorhagia
  - 1-2mg/kg/den
- **Nephritis**
  - Per paed nephrology advice and renal biopy result
  - When persistent proteinuria **ACE inhibitors**

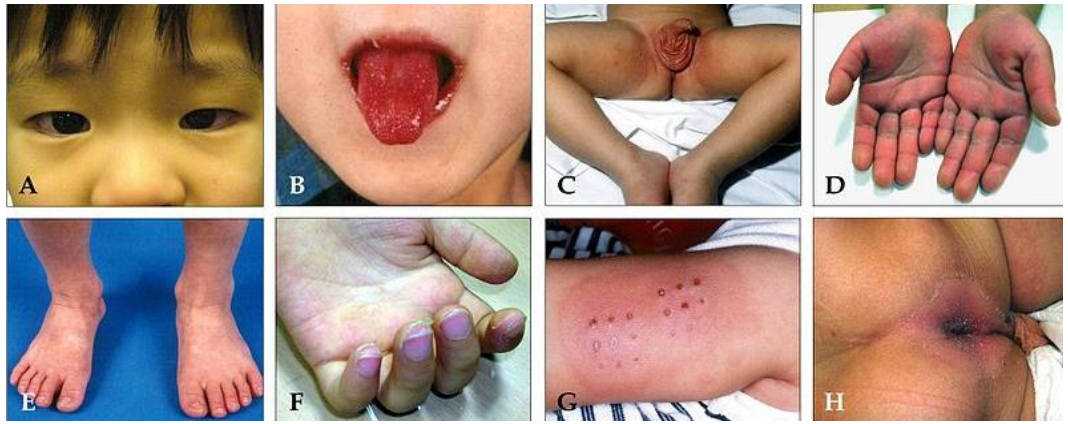
Kawasaki disease

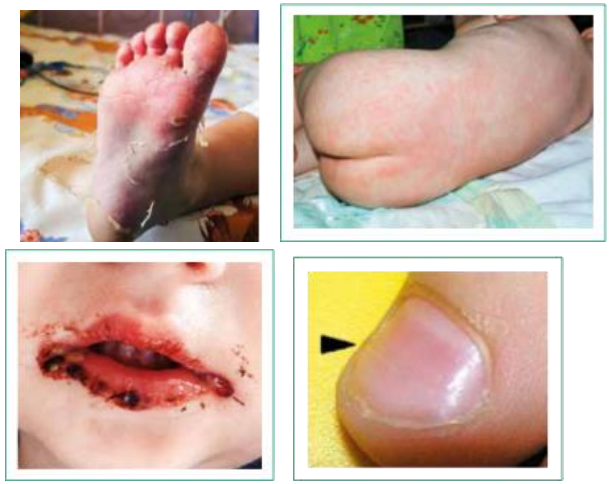
- 2nd most common primary paediatric vasculitis
- Asian ethnicity prevails
- Systemic vasculitis affecting medium-sized arteries
- 85% of patients are < 5 yrs (max. incidence 18-24 months)
- Most frequent cause of acquired heart disease in developed countries
- 15-25% untreated patients develop coronary aneurysms (CAA)
- 2-3% untreated patients die

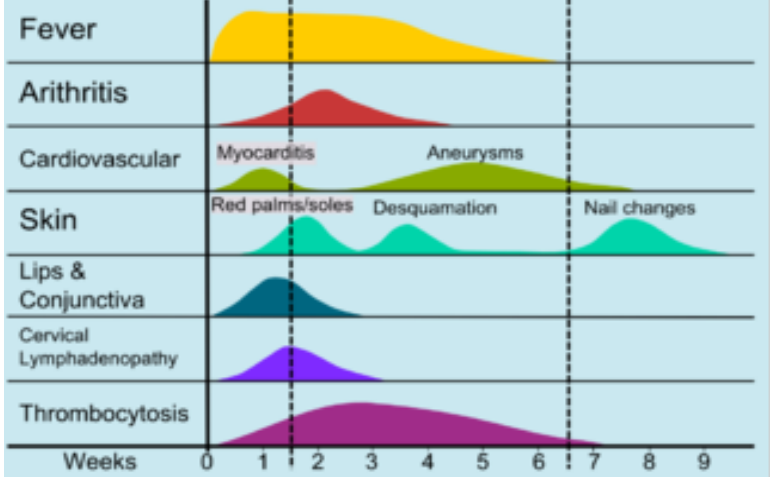
KD diagnosis

Fever at least 5 days + at least 4 of :

1. erythema and induration of palms and soles→ desquamation during convalescent phase
2. rash - polymorphous
3. conjunctivitis
4. mucous membrane changes
5. cervical lymphadenopathy often asymetrical >1,5 cm

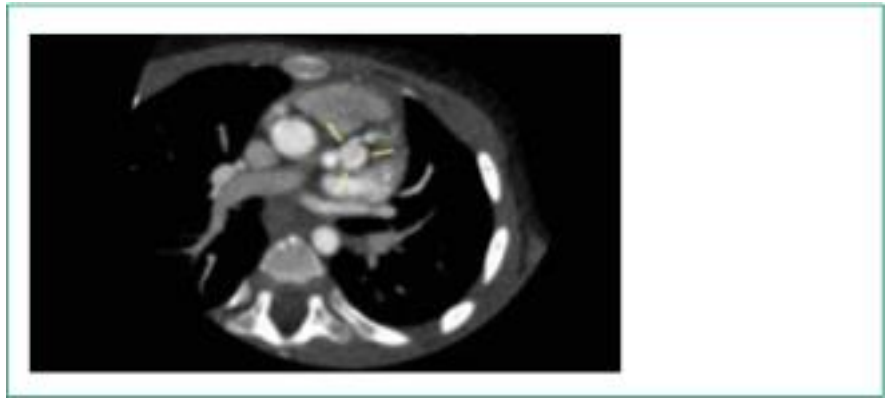






- Diagnosis based on combination of clinical criteria and lab results
- Presence of coronary artery aneurysms in febrile child less than 4 critera possible
- Incomplete KD: patient with high degree of suspicion, but only 2-3 criteria (mainly infants)

KD clinical presentation



- **Typical presentation**
  - irritability (aseptic meningitis),
  - Erythema and induration at BCG vaccination site
- **Cardiovascular involvement**
  - Acute phase – carditis (peri-, myo-, endo-, pancardits),
  - Convalescent phase (2.–3. wk) – CA vasculitis with dilatations and aneurysm formation
    - CAA develop in 15–25 % untreated and 2–8 % treated children
- ***Other presentations***
  - artralgia, arthritis, uveitis, urethritis, aseptic meningoencefalitis…
  - GI involvement: gastroenteritis, abd pain, hepatopathy, gall bladder hydrops, pancreatitis

KD investigations

- **Inflammation, FBC, biochemistry**
  - ESR (↑), CRP (↑, prognostic factor), albumin (↓, prognostic fcktor).
  - Leucocytosis, prominent thrombocytosis (from week od 2.–3.)
- **Mikrobiology, urine, CSF**
  - Cultures, infectious serology
- **ECG, echocardiography**
  - Paediatric cardiologist, CA detection and size measurment (age- and weight- related, Z-score) necessary
- **When cardiology normal**
  - Repat in 10-14 days and 6–8 wks from onset
  - When inflammatory aktivity persists, remeat 2-weekly until normalisation
- **When CA affected**
  - Weekly re-evaluation until resolved or remain stable
  - When CAA persist – individual frequency and long-term F/U (life-long)

KD therapy

•Start as soon as possible

IVIG

•IVIG 2 g/kg

ASA

•30-50 mg/kg/day until

- •Afebrile for 48h
- •Clinically improving
- •Dropping CRP

•Reduction to 3-5 mg/kg o.d.

•When CAA

- •longterm

- **Risk factors of IVIG resistence (tzv. Kobayashi Risk Score):**
  - age ≤ 12 months (1),
  - Disease duration before therapy ≤ 4 days (2),
  - elevated CRP ≥ 100mg/l (1),
  - elevated AST ≥ 100 IU/l (2),
  - PLŤ ≤ 300×10 /9/l (1),
  - neutrofilia ≥ 80 % (2),
  - hyponatremia ≤ 133 mmol/l (2).
- score 4 and higher = risky
  - Korticosteroids
  - Biologics –IL-1, TNF blockade

KD corticosteroids

- Indications:
  - IVIG Resistence
  - Kobayashi score ≥5 [*Sleeper et al.*]
  - Secondary HLH
  - Kawasaki Shock Syndrome
- Consider to add to IVIG immediately:
  - Infants
  - Aneurysms identified at onset

RHEUMATOLOGY

Original article

doi:10.1093/rheumatology/key344

European consensus-based recommendations for the diagnosis and treatment of Kawasaki disease – the SHARE initiative

Nienke de Graeff[1,*], Noortje Groot[1,2,3,*], Seza Ozen[4], Despina Eleftheriou[5], Tadej Avcin[6], Brigitte Bader-Meunier[7], Pavla Dolezalova[8], Brian M. Feldman[9], Isabelle Kone-Paut[10], Pekka Lahdenne[11], Liza McCann[3], Clarissa Pilkington[5], Angelo Ravelli[12], Annet van Royen-Kerkhof[1], Yosef Uziel[13], Bas Vastert[1], Nico Wulffraat[1], Sylvia Kamphuis[2], Paul Brogan[5,†] and Michael W. Beresford[3,14,†]

KD immunisations

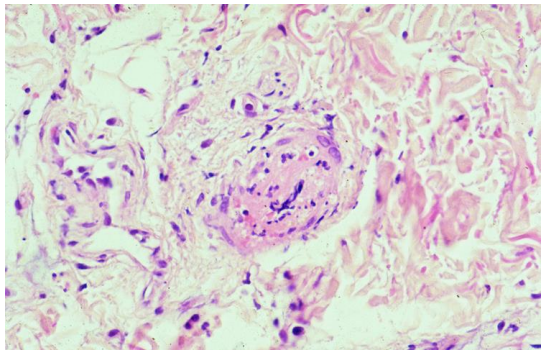
- Delay any vaccination for 6 months
- Delay live vaccines for 12 months

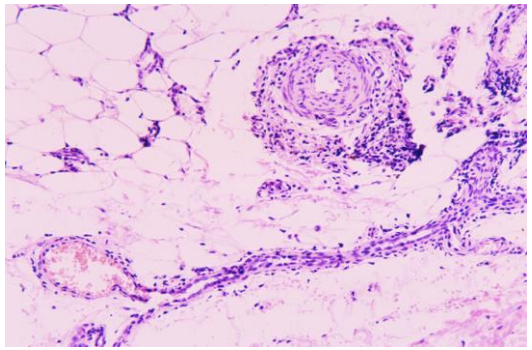
Rare primary systemic vasculitis

- **General non-specific presentations:**
  - fatigue, weight loss, fever, arthralgia/myalgia
- **Specific presentations:**
  - Related to the location, vessel size, type of involvement
  - Stenosis vs occlusion, ischaemia vs bleeding,
  - Severity - brain vs skin
- **Suspicious presentations**
  - ***Vasculitis = dif dg of any unclear systemic inflammatory condition***
  - FUO
  - Vaculitic skin rash
  - Nervous systém involvement
  - Unexplained musculoskeletal symptoms
  - Other unexplained manifestations (pulmonary, GIT, cardiovascular, renal)

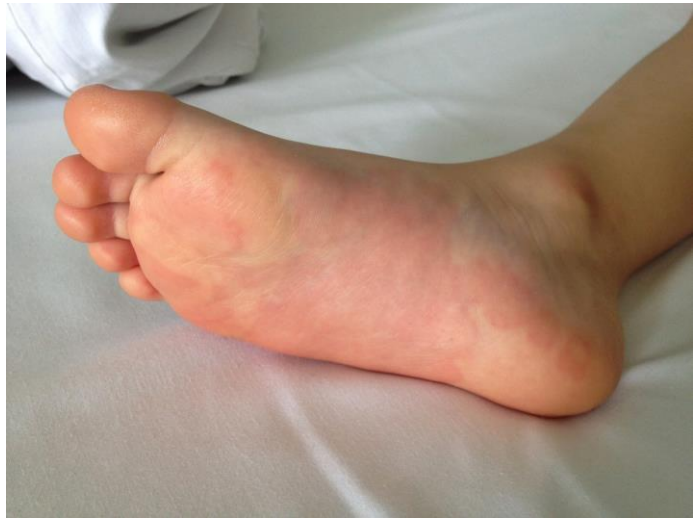
Childhood polyarteritis nodosa (cPAN)

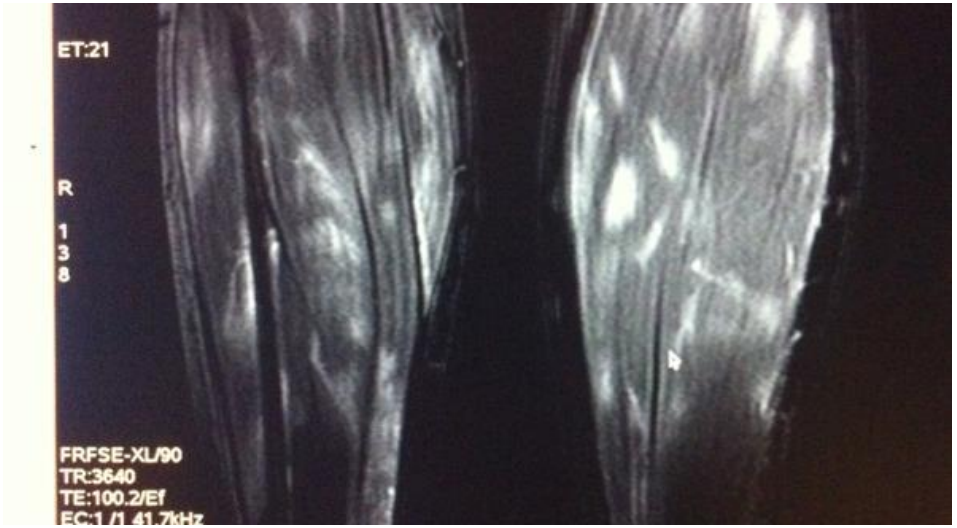
- **Necrotising inflammation** of medium and/or small arteries
- **Epidemiology**
  - worldwide, rare
  - equal sex distribution
  - peak age at onset 10 years
- **Histopathology**
  - fibrinoid necrosis
  - pleiomorphic infiltration
  - disarranged wall architecture
  - healing with fibrosis.

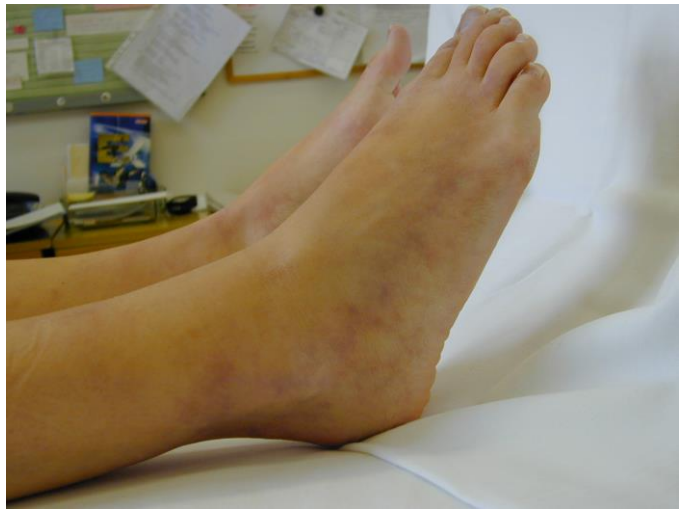


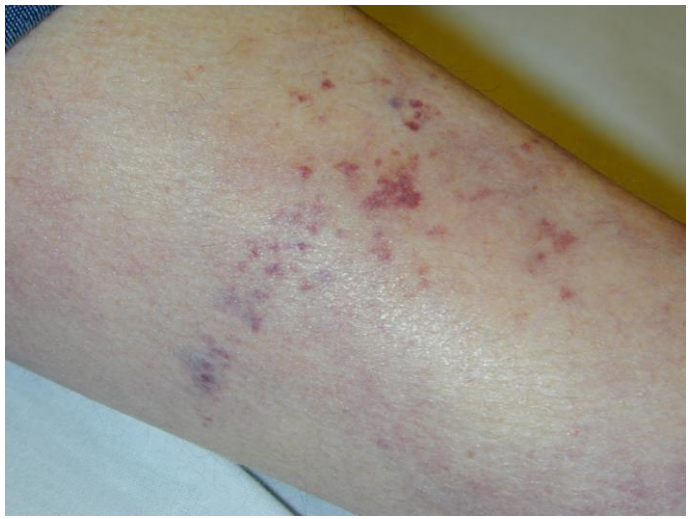


cPAN









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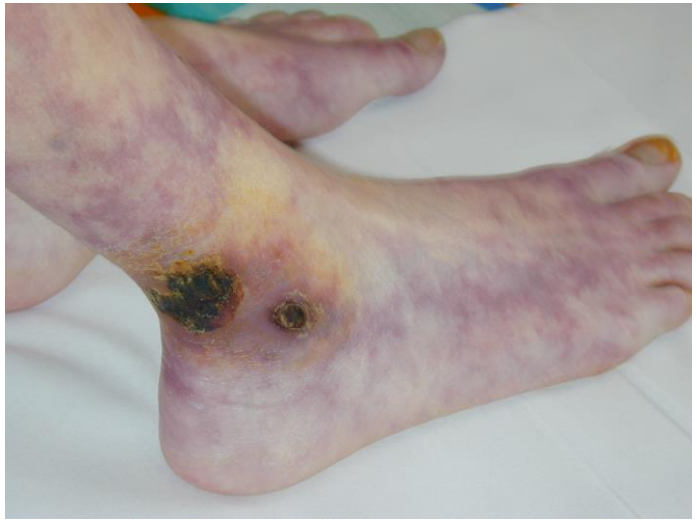

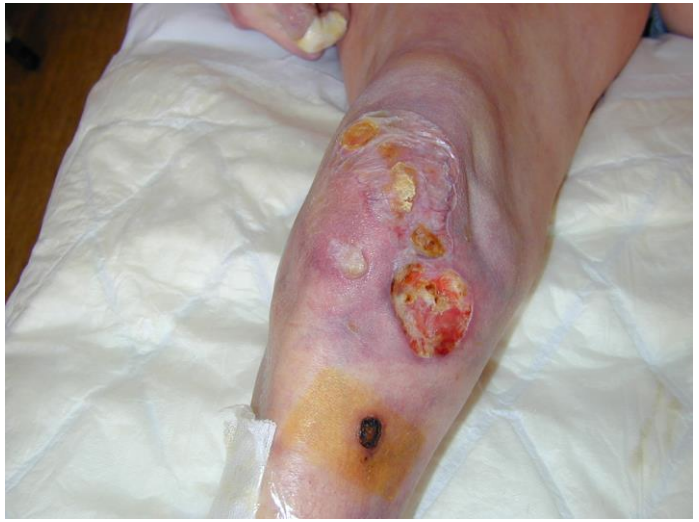

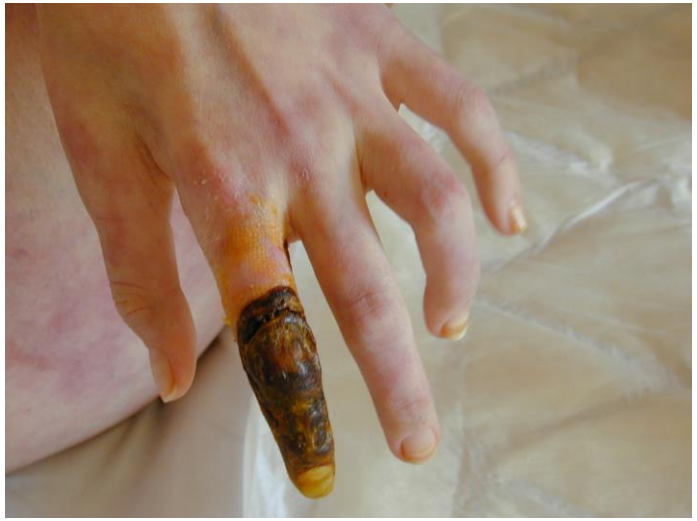

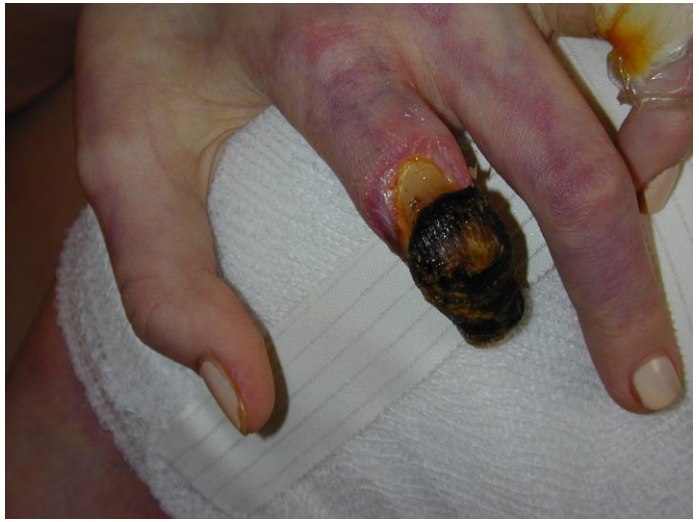

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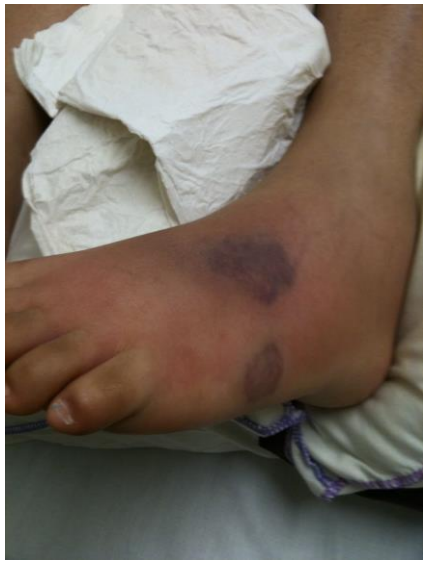

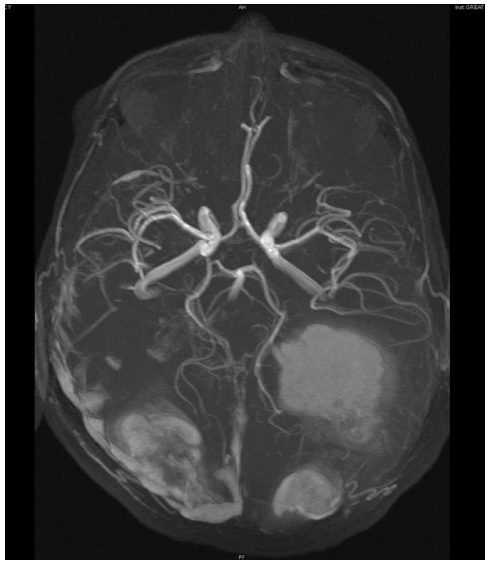

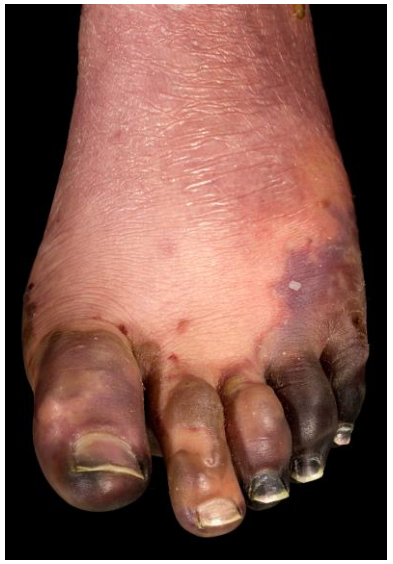

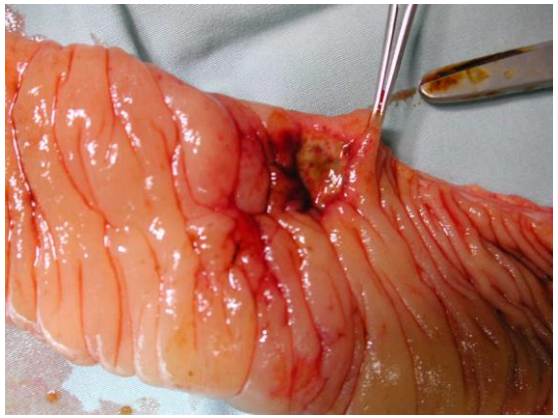

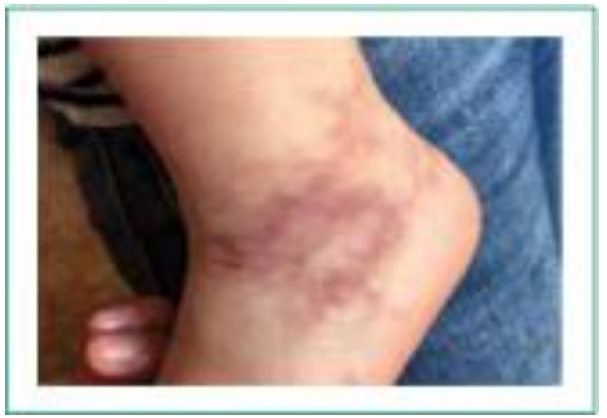

Takayasu arteritis

RHEUMATOLOGY

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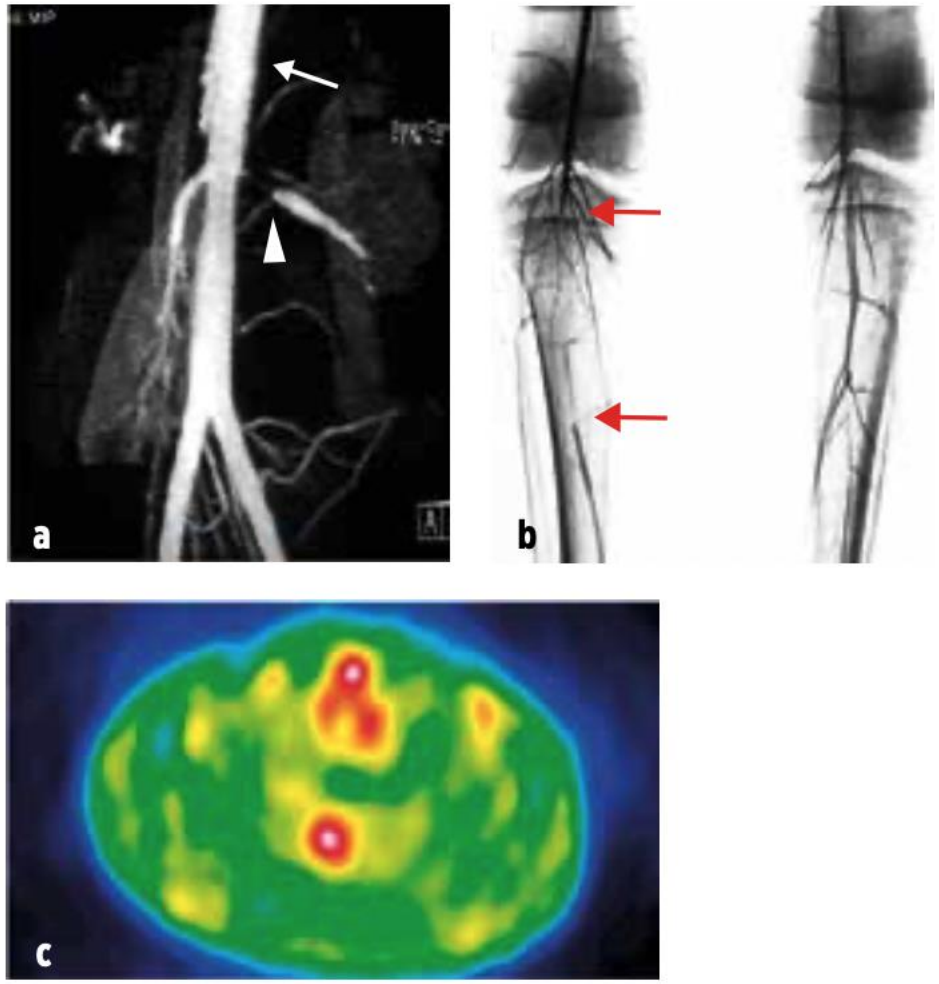
Original article

European consensus-based recommendations for the diagnosis and treatment of rare paediatric vasculitides – the SHARE initiative

Nienke de Graeff[1,*], Noortje Groot [1,2,3,*], Paul Brogan[4], Seza Ozen[5], Tadej Avcin[6], Brigitte Bader-Meunier[7], Pavla Dolezalova[8], Brian M. Feldman[9], Isabelle Kone-Paut[10], Pekka Lahdenne[11], Stephen D. Marks[4], Liza McCann[3], Clarissa Pilkington[4], Angelo Ravelli[12], Annet van Royen[1], Yosef Uziel[13], Bas Vastert[1], Nico Wulffraat[1], Sylvia Kamphuis[2] and Michael W. Beresford [3,14]

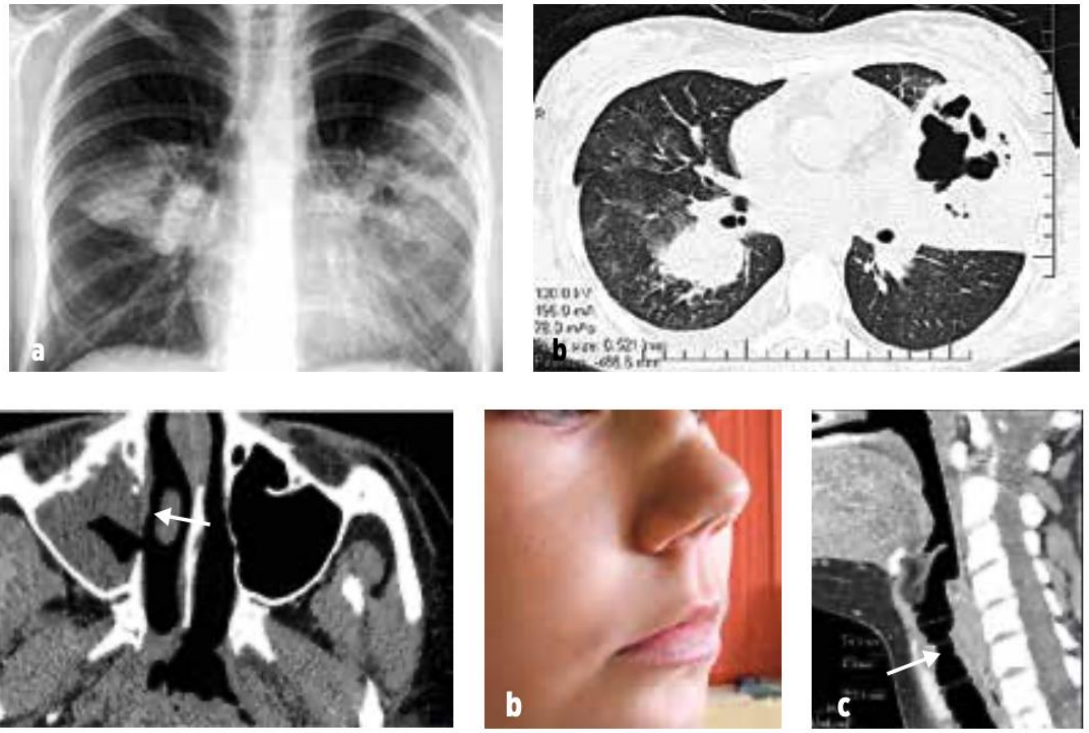


Takayasu arteritis

- Segmental arteritis causing stenoses of large muscular arteries, prediminantly aorta and its main branches
- Abdominal aorta more often involved in children, often systemic hypertension
- Non-specific symptoms common
  - Fevers, elevation of ESR/CRP, malaise, weight loss, palpitations, headaches
  - Vascular bruits, pulse and BP assymetry
  - Laboratory: Non-specific inflammation

Granulomatosis with polyangiitis

- Granulomatous inflammation of small vessels and tissues
- Predilection towards upper and lower airways and kidneys
- Typically
  - subglottic stenosis,
  - nasal bleeds/crusting, sinusitis
  - nasal septum perforation,
  - retroorbital mass
  - Lung infiltrates / cavities
- PR3 ANCA od C-ANCA stain



Systemic lupus erythematosus

- ..."episodic, multisystemic autoimmune disease characterised by vessel and connective tissue inflammation and presence of antinuclear antibodies…."

- Patogenesis and general mechanisms common with adult disease
- More severe phenotype in children
- Annual incidence 0,3-0,9/100 000 children
  - Predominantly adolescent girls, prevalence higher in other than Caucasian ethnicities
  - If in younger children, monogenic disease to be considered (complement deficiencies)

SLE - manifestations

- **Clinical course** - variable, unpredictable, potentiall life- or organ-threatening
- **Presenting symptoms**
  - Often non-specific – fevers, fatigue, weight loss, arthralgia, various skin manifestations often photosensitive
- Most severe organ manifestations
  - Nephritis
  - Neurolupus
  - Pulmonary haemorhage

SLE - diagnosis

- Combination of clinical and lab features
- Main presentations covered by SLICC classification criteria **SLICC (Systemic Lupus International Collaborating Clinics) 2012**
  - CAVE – classification vs diagnosis

RheumTutor.com

SLICC† Classification Criteria for Systemic Lupus Erythematosus

Requirements: ≥ 4 criteria (at least 1 clinical and 1 laboratory criteria)
OR biopsy-proven lupus nephritis with positive ANA or Anti-DNA

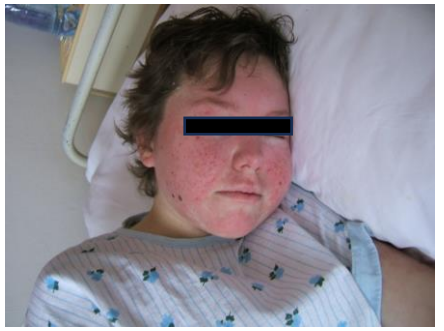
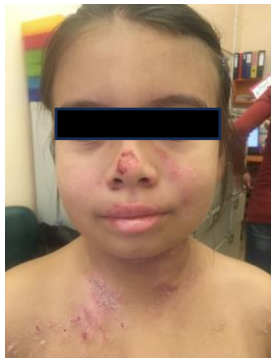
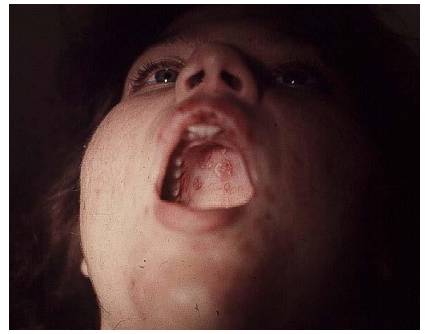
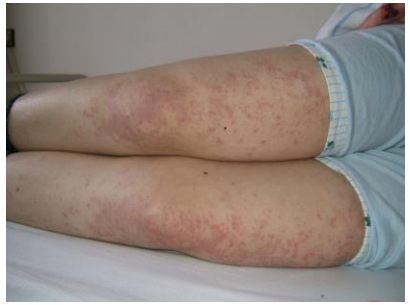
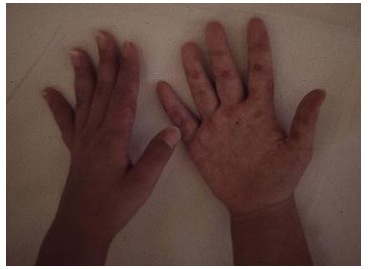
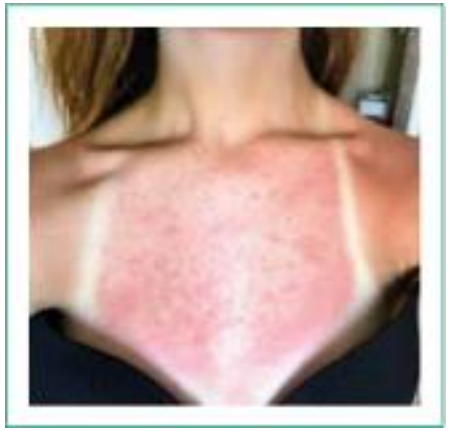
Clinical Criteria	Immunologic Criteria
1. Acute Cutaneous Lupus*	1. ANA
2. Chronic Cutaneous Lupus*	2. Anti-DNA
3. Oral or nasal ulcers *	3. Anti-Sm
4. Non-scarring alopecia	4. Antiphospholipid Ab *
5. Arthritis *	5. Low complement (C3, C4, CH50)
6. Serositis *	6. Direct Coombs' test (do not count in the presence of hemolytic anemia)
7. Renal *	
8. Neurologic *	
9. Hemolytic anemia	
10. Leukopenia *	
11. Thrombocytopenia (<100,000/mm^3)	

†SLICC: Systemic Lupus International Collaborating Clinics
* See notes for criteria details

Petri M, et al. Arthritis and Rheumatism. Aug 2012

SLE skin manifestations

- Acute skin manifestations
  - Malar rash, subacute skin lupus
- Chronic manifestations
  - Classical discoid lupus, lupus panniculitis (lupus profundus), mucosal involvement …
- Oral / nasal ulcerations
  - Palate, buccal, tongue, nasal
- Non-scarring alopecia

SLE – therapy and prognosis

- Treatment individually tailored
  - Immunosuppressive/antiinflammatory pharmacotherapy
    - Systemic corticosteroids, antimalarials
    - Azathioprine, methotrexate, mycophenolate mofetil
    - Cytotoxic therapy - cyclophosphamide
    - B-cell number or function affecting therapies – rituximab, belimumab
  - Other thgerapies
    - E.g. Anticoagulation in APLS
- Psychological care and support
- Long-term/lifelong disease with remissions and exacerbations, mortality 15%
  - Sepsis, renal failure

Neonatal lupus

- Maternal autoAbs (ENA - anti-Ro) from gestational week 12.-16. enter fetal circulation
  - Bind to fetal myocardial and other (skin) structures
- Clinically
  - A-V heart block – may require pacemaker
  - erythema annulare, discoid lupus, cytopenia – benign, self-limiting

Idiopathic inflammatory myopathies

For the diagnosis of juvenile dermatomyositis, the following findings should be present prior to age 18 years:

- Typical skin finding (heliotrope and/or Gottron-sign/–papules)

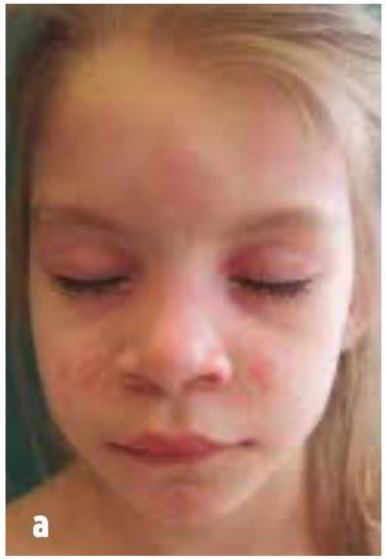
Additional criteria:

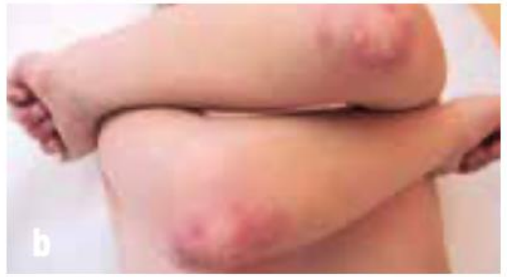
- Symmetric proximal muscle weakness and/or myalgia
- Increased muscle-related enzymes (creatine kinase, glutamate oxaloacetate transaminase, lactate dehydrogenase and/or aldolase)
- Typical findings on muscle biopsy
- Typical findings on magnetic resonance imaging

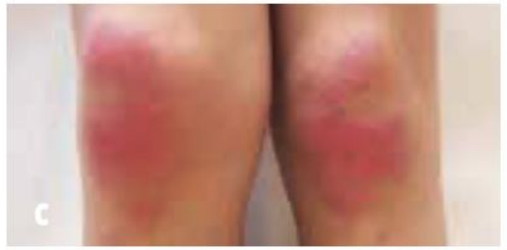
Other possible etiologies should be excluded.

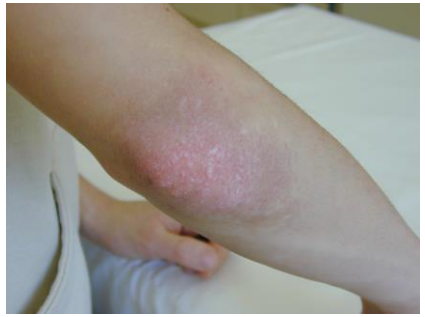
Probable JDM: Skin findings and at least 2 additional criteria

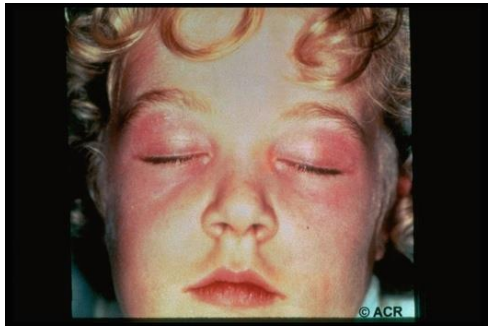
Definite JDM: Skin findings and at least 3 additional criteria











Early signs of JDM

- **Most common:** Muscle weakness + characteristic skin rash (100%,Pachman, J Rheumatol. 1998)
- **Less common**: Myopathic syndrome plus other vasculitis or „dermatomyositis sine myositis“
- **Warning signs**: dyslalia, voice change, dysphagia, fluid regurge

JDM investigations

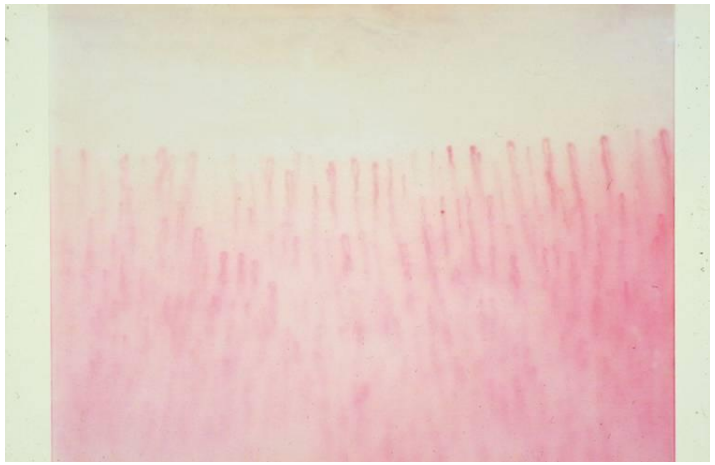
Labs

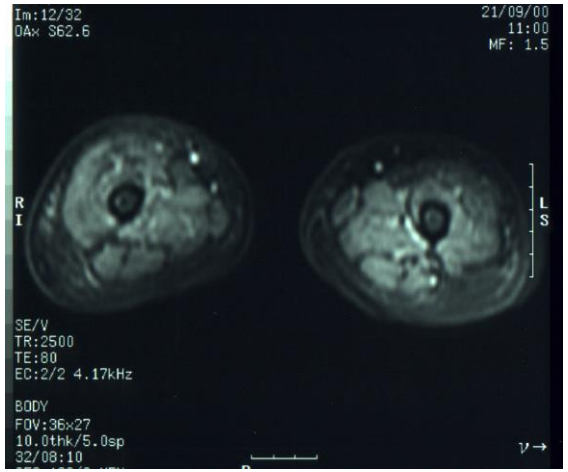
- ***Inflammatory markers***
- ***Muscle enzymes (all)***
- ***Immunology***: Ig,C, **ANA,** ENA, immunoblot (MAS, **MSA**) **B-ly** (CD 19), CD3+CD8+ T-ly
- ***Endothelial damage*** (***vWF***, neopterin, adhesion molecules)
- ***Metabolic screening***

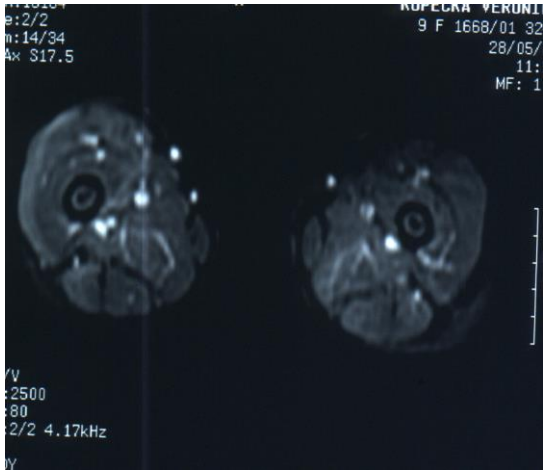
Imaging and other

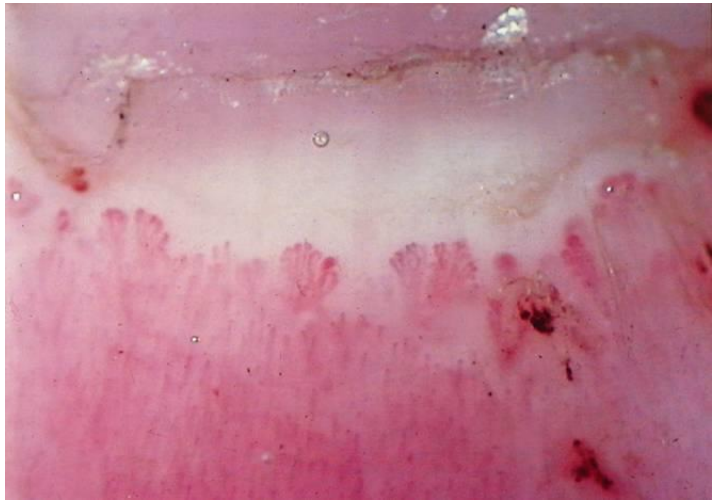
- ***Muscle MRI***
- ***EMG, muscle biopsy*** (both MRI/CT directed)

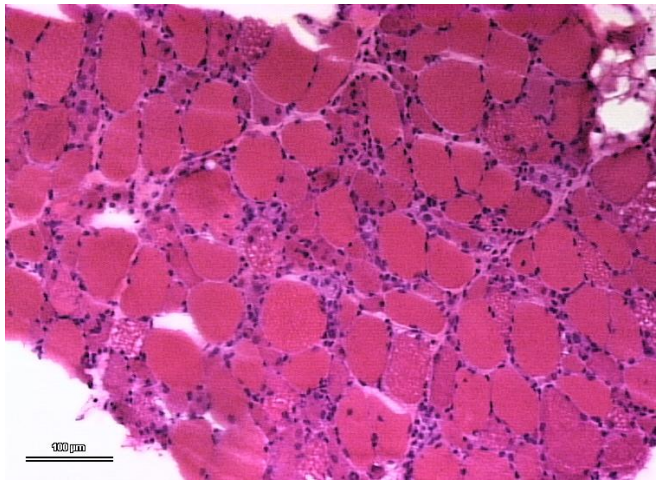
Nailfold capillaroscopy, muscle MRI, muscle biopsy











JDM/JPM differential

- ***Postinfectious myositis*** (influenza A,B, coxackievirus B, toxoplasmsis, trichinosis, staph pyomyositis)
- ***Neuromuscular disorders*** (spinal atrophy, myastenia)
- ***Metabolic and heritable myopathies*** (glykogen storage dis, lipidoses, carnitin def, β-oxidation disorders, dystrophinopathies…)
- ***Secondary myopathies*** (endocrinopthies, steroid induced)
- ***Other CTD*** (MCTD, SLE, vasculitis..)

JDM therapy and prognosis

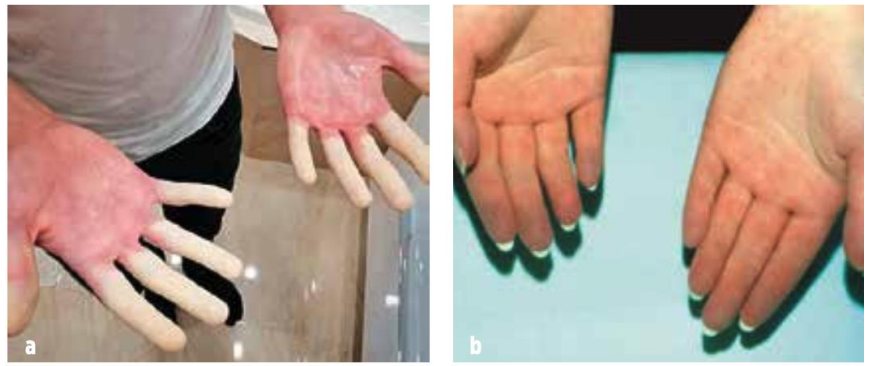
- ***Drug treatment:***
  - **CS** (+ osteoporosis prevention, K suppl)
  - **immunosuppressive / antiinflammatory**
    - hydroxychloroquine, MTX, CyA, IVIG, CFM,
    - Biologics – TNFi, rituximab
    - Small molecules – JAK inhibition
- ***Multi-discipliplinary***:
  - PT/OT, supportive, alimentation, hydration (myoglobinuria)

Disease course:

- **monocyclic** : limited, steroid responsive (27%)
- **persistent** (chronic ulcerative (33%)
- **polycyclic** (chronic nonulcerative): (40%)

Childhood scleroderma - systemic

- **Systemic sclerosis**:
  - ***diffuse*** (proximal skin, multiorgan involvement),
  - ***limited*** (CREST: Calsinosis, RS, Esophageal dysmotility, Sclerodaktyly, Teleangiectasia)
- **Clinical features**:
  - oedema-induration-sclerosis-skin atrophy,
  - calcinosis, RS (90%), ischemic fingertip ***ulceration***, contractures, weakness, arthralgia,
  - abd pain, GI dysmotility and malabsorption, dysphagia, pericarditis,
  - pulmonary fibrosis, PAH,
  - renal vasculitis with hypertension



Childhood scleroderma - localised

- **Localised**:

  - ***morphea***-oval shaped, circumscripted induration variable in size, depth and number

  - ***linear scleroderma***-often deep tissues involved incl muscle and bone, epilepsy, organ involvement

- **Eosinophilic fasciitis**:
  - skin induration with flexion contractures, eosinophilia, hypergamaglobulinemia, usually no organ involvement