A RARE CAUSE OF FEVER

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CASE SCENARIO

1 ½ year old girl c/o

* Prolonged fever – 20 days
* Puffiness of face and legs – 20 days
* Rash in the lower limbs – 20 days

Child was suspected to have angioneurotic edema outside

Rx with antibiotics & steroids for 10 days – not resolving
• Febrile
• Vitals – stable
• desquamation of oral mucosa +
• Periorbital edema and pedal edema +
• Papular rash + over trunk and limbs

No bleeding manifestation / lymphadenopathy/ icterus
Systemic Examination

* P/A : Liver +

* Joints – normal

* CNS : Conscious, resents examination with crying spells, always seen in mother’s lap, moving all 4 limbs in lying position. Not observed to stand or walk.

(Pitfalls - difficulty in assessing muscle strength in a crying infant)

Later – Child reassessed, hypotonia +, power – 2/5, reflexes - N

* CVS , RS : Normal
* CBC, CRP - N
* Albumin – 3.8
* Urine Routine, RFT, LFT – N
* Vasculitis workup - ASO, RA, ANA, ANCA – N
* ECHO – N
Fever of 1 month

- Inadequately treated infection
  - Enteric
  - Malaria
  - Leptospirosis
  - UTI
  - Scrub typhus

- Malignancy

- Connective tissue disorders
  - SLE
  - Kawasaki disease
  - SOJIA
  - Dermatomyositis

- HLH
Infections

- CBC, CRP – N
- Blood and urine c/s – negative
- CXR and USG abdomen - normal
- Treated for possible infections

Malignancy

- Peripheral smear & BMA – ruled out
## POSSIBLE DIAGNOSIS

<table>
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<th>DIAGNOSIS</th>
<th>POSITIVE</th>
<th>NEGATIVE</th>
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<td>Collagen vascular disease</td>
<td>• Female child&lt;br&gt;• Muscle tenderness, weakness&lt;br&gt;• Oral ulcer+&lt;br&gt;• Skin rash +&lt;br&gt;• ESR - high</td>
<td>• No arthritis&lt;br&gt;• No organomegaly&lt;br&gt;• CBC,CRP - N&lt;br&gt;• Vasculitic workup - N</td>
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Connective Tissue Disorders

Lead points - not able to roll over, inability to sit, wanting to be carried, crying when touched anywhere, change of voice, coughing during feeding, weak cough

- CPK - 14,632
- LDH – 1606
- Ferritin – 328.3
- Fluroscopy – Pharyngeal incoordination
TREATMENT

* Antipyretics
* NG tube feeds
* IV Methyl Prednisolone
* SC Methotrexate
* Folic Acid
* most common inflammatory myopathy with
* characteristic rash
* proximal, symmetric muscle weakness
* often responsive to the immunosuppressive therapy.
**INTRODUCTION**

- Incidence - 2 to 3/million children/year
- More common in girls - ratio 2.3 : 1
- Mean age of onset - 7 years
- 25% present - < 4yrs of age
- 2\textsuperscript{nd} peak : 45-65 yrs

• Genetic predisposition - Chromosome 6 - DQA1*0501, DRA1*301 and DRB1*0301 and HLA B8
• Immunologic factors: Increased mast cells, Antibodies – ANA, myositis specific antibody, maternal microchimerism
• Coxsackie virus B and group A streptococcus infections
• Excessive sun exposure
DIAGNOSTIC CRITERIA

• Characteristic rash – Heliotrope rash, Gottron papules

Plus 3 of the following

• Proximal Symmetric muscle weakness

• = 1 muscle enzyme elevation – CK, AST, LDH, Aldolase

• EMG – myopathy, denervation False negative

• Muscle biopsy – necrosis, inflammation patchy disease

AMYOPATHIC JDM:

- variant of JDM
- classic rash
- no apparent muscle weakness or inflammation
- Progresses to severe muscle involvement
**Symptoms**

- Weakness - 92/102
- Gottrons papules - 92
- Heliotrope rash - 77
- Ulcerative lesions - 18
- Abnormal nailfold capillaries - 76%
- Myalgia - 73%
- Pyrexia - 65%
- Irritability - 51%
- Arthritis - 35%

Less common symptoms -
- Generalised edema - 30%
- Dysphonia, dysphagia - 15 - 20%

Pachman et al - 1998 (79 pts)
A. V. Ramanan et al 2002 (102 pts)
Fever with myalgia

Less than one week
- Dengue
- Leptospirosis
- Viral myositis
- GBS (afebrile)

More than 1-2 weeks
- Malignancy
- Dermatomyositis
RASH:

*GOTTRON PAPULES (92%):* erythematous, papulosquamous eruption over the dorsal surfaces of the PIP & DIP, extensor aspect of knees, elbows, small joints of the toes, ankle malleoli.

*Facial rash (42%) – crossing the nasolabial folds (D/D SLE)*
*HELIOTROPE RASH (77%) of the eyelids

*blue violet discoloration may associated with periorbital edema.
*NAIL FOLD CAPILLARY PATTERN : (80%)

dropout of capillary loops, resulting in a wide band of avascularity. Dilated, tortuous capillaries also seen.

*SHAWL SIGN : Photosensitivity rash in chest and neck

*MECHANIC’S HANDS : thickened erythematous scaly rash over the palms – associated with anti-Jo-1 antibodies.

*Periungual telangiectasia.

*Cutaneous ulcers
WEAKNESS:

* insidious in onset.
* proximal muscles - esp neck flexors, shoulder girdle & hip flexors
* Symmetric weakness
* Gower sign +ve.
* Childhood Myositis Assessment Scale (CMAS) is a clinical assessment tool that provides an objective measure of muscle strength
**COMPLICATIONS**

Esophageal muscle weakness:
* dysphonia, dysphagia, GER, aspiration.

Respiratory muscle weakness:
* respiratory failure – hypercarbia.

Cardiac muscle:
* pericarditis, myocarditis & conduction defects.

Vasculitis of GIT:
* crampy abdominal pain, pancreatitis, GI bleeding, intestinal perforation or infarction
LIPODYSTROPHY

loss of s/c & visceral fat over face & upper body +/- metabolic syndrome.

CALCINOSIS – 40%

• dystrophic deposition of calcium phosphate, hydroxyapatite or fluoroapatite crystals
• Increased local production of TNFα
• delayed diagnosis and long duration of untreated disease, a chronic disease course, and inadequate corticosteroid therapy.
*Nail fold capillary microscopy - capillary dilatation and branching

*Enzymes – diagnostic and response to Rx

Changes in CK occur first

LDH and AST – best indicators for relapse

*EMG

*Muscle biopsy

to evaluate activity/ in uncertain diagnosis
MRI

- Increasingly used to avoid the morbidity of muscle biopsy & EMG
- Abnormalities - increased signal intensity (on T2) of the affected muscle, perimuscular edema, enhanced chemical shift artifact, and increased signal intensity in subcutaneous fat.
- Higher muscle signal intensity on MRI correlated with decreased muscle strength.
- After therapy, signal intensity returned to normal.

McCann LJ et al. The Juvenile Dermatomyositis National Registry and Repository (UK and Ireland)—clinical characteristics of children recruited within the first 5 yr. Rheumatology (Oxford) 2006; 45:1255.
Brown VE, Pilkington CA, Feldman BM, Davidson JE, Network for Juvenile Dermatomyositis PRES. An international consensus survey of the diagnostic criteria for juvenile dermatomyositis (JDM). Rheumatology 2006; 45: 990-93
* Lymphopenia

* CRP, ESR may be elevated

* Immunological tests:

  ANA, Anti-Mi2 antibody

  Anti-Jo antibody – more severe disease

  von Willebrand factor – not specific.

  Blood vessel injury causes release of vWF from platelets and endothelial cells – elevated plasma levels
GOAL:

* control of the underlying inflammatory myositis

* Prevention and/or treatment of complications
* Mild: Prednisolone 2mg/kg
* Severe: IV methyl prednisolone – 30mg/kg x 5 days

oral prednisolone – 2mg/kg/day x 4 to 6 months

Taper prednisolone over 6-9 months
• Reduces the duration & cumulative dose of steroids
• Dose: 15 to 20mg/m2/week
• Combination therapy preferred
• Folic acid (1 mg/day) in order to limit toxicity.
Other options:

* IVIG: Severe cases/unresponsive to first line therapy

* Cyclosporine, cyclophosphamide, azathiprine, hydroxychloroquine

* Anti-TNFα agents – infliximab, etanercept

* Calcinosis – probenecid, diltiazem, aluminum hydroxide, alendronate, sodium thiosulfate

* PHYSIOTHERAPY, Sun screens
Mortality: < 10%

POOR PROGNOSIS:

- Disease related: Rapid onset, extensive weakness, severe cutaneous vasculitis – skin ulcers, GI vasculitis, severe end arteriopathy & infarction in biopsy
- Therapy related: Delay in diagnosis, Inadequate dose/duration of Rx, Minimal response to steroids

Cassidy JT, Lindsley CB et al. Textbook of pediatric rheumatology. 5th edn.
THANK YOU

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