Classification of Juvenile Myositis

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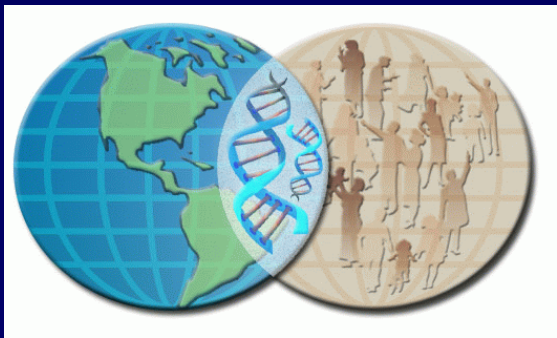

IIM - Adult and Juvenile - Classifications

- *Clinical groups*
  - Dermatomyositis
  - Polymyositis
  - Myositis with other CTD
  - Inclusion body
  - Cancer-associated
  - Focal / Nodular
  - Ocular / Orbital
  - Eosinophilic
  - Granulomatous

Rider and Miller, Rheum Dis Clin N Amer, 1997: 23: 619-655

- *Serologic groups*
  - Myositis-specific (MSA)
    - Anti-synthetases
    - Anti-SRP
    - Anti-Mi-2
  - Myositis-associated (MAA)
    - Anti-U-RNP (U1, U2, U5)
    - Anti-Ro52
    - Anti-PM/Scl
    - Anti-Ku
    - Anti-155kD
    - Anti-MJ
    - Anti-PMS-1, PMS-2
  - MSA and MAA negative

Bohan and Peter are Primary Criteria Used in JDM Research Studies

Study Type	***Definite B&P***	***Probable B&P***	***Possible B&P***	***Not defined***
Clinical/ natural history/ epidemiol	3*	31	12**	5***
Pathology/ pathogenesis	4*	4	1	4
Immunogenetics	2	9		3
Therapeutic	6	7		6

Bohan and Peter are Primary Criteria for Including JPM, JCTM in Research Studies

Study Type	***Definite B&P***	***Probable B&P***	***Possible B&P***	***Not defined***
Clinical / natural history/epidemiol	1	11	3*	3
Pathology/ pathogenesis		2		
Immunogenetics		3		
Therapeutic		1		2

Bohan and Peter Criteria are Often Present at Time of Diagnosis of JIIM

Criteria	***Positive % (n) Pachman, JDM***	***Positive % (n) Feldman, JIIM***
Rash	100% (79)	94% (120)
Proximal weakness	100% (79)	92% (120)
Any 1 enzyme ↑	90% (79)	80% (120)
•CK ↑	64% (76)	
•LDH ↑	80% (56)	
EMG	81% (43)	83% (104)
Muscle biopsy	80% (51)	92% (80)

Frequency of Cutaneous Manifestations in JDM vs. JPM, JCTM (Feldman, 2002)

Cutaneous Sign	***JDM (n=79- 105)***	***JPM (n = 5)***	***JCTM (n = 5)***
Gottron's papules	91%	0%	80%
Heliotrope rash	83%	0%	40%
Malar/facial rash	42%	0%	20%
Nailfold capillary change	80%	60%	80%
Mouth ulcers	15%	20%	60%
Skin ulcers	6%	0%	20%
Gingivitis	6%	0%	0%
Calcinosis	3%	20%	20%

Frequency of Systemic Features in JDM vs. JPM, JCTM (Feldman, 2002)

Sign or Symptom	***JDM (n=79-105)***	***JDM Pachman (n = 79)***	***JPM (n = 5)***	***JCTM (n = 5)***
Myalgia/arthralgia	25%	73%	0%	0%
Dysphonia/dysphagia	24%	44%	0%	40%
Fever	16%	65%	40%	0%
Pulmonary	11%	43%	40%	40%
Lethargy	9%	100%	40%	20%
Contractures	9%	20%	20%	60%
Adenopathy	8%	NA	0%	20%
Arthritis	6%	35%	20%	80%
Abdominal pain, GI	5%	37%	0%	40%

Survey of Pediatric Rheumatologists Suggests Biopsy, EMG Often Not Used in JDM Diagnosis

Finding	***Extremely or Very Important***	***Not important***
Skin rash	90%	
Proximal weakness	87%	
Muscle enzyme elevation	69%	
EMG	(used 26%)	54%
Muscle Biopsy	(used 25%)	41%
MRI	43% (used 39%)	

Moenkemoeller, A&R, 2001, S293

Survey of Pediatric Rheumatologists Suggests Biopsy Not Important in JDM Diagnosis

- Classic rash, weakness, abnormal enzymes: 61% expect abnormal biopsy
- 58% say normal biopsy would not change their therapy

Moenkemoeller, A&R, 2001, S293

Revision of the Diagnostic Criteria for JDM

Virginia Brown, Liz Halkon, Joyce Davidson and Clarissa Pilkington, on behalf of the Network for Juvenile Dermatomyositis

Background

- Bohan and Peter,1975

– don't necessarily fit in with modern day clinical practice

-individual diagnostic criteria in JDM patients can be normal

- International collaboration agreed at PReS 2002:

"to derive a core set of criteria through a consensus process, leading to the development of a revised set of criteria that would be recognised and applied internationally"

Part 1: Methodology

- Statistician and clinician designed survey:

-Listed those criteria felt to be helpful in diagnosis of JDM (excluding overlap patients)

- Individuals also asked to list all criteria felt to be useful, even if they did not use themselves

- Question of accessibility

- Survey circulated to all members of the Network for JDM and to members of PRINTO network

- 237 individuals in >100 centres in 35 countries across Europe, Asia, North and South America

NETWORK FOR JUVENILE DERMATOMYOSITIS
A Working Group of PRES
REVISION OF DIAGNOSTIC CRITERIA FOR JUVENILE DERMATOMYOSITIS

- Please look at the list of diagnostic criteria listed below, tell us whether you use this variable in your regular clinical practice.
- Please tell us whether you have easily available access to use each variable.
- Then, in the blank spaces list any further variables you feel may be used in the diagnosis of juvenile dermatomyositis. Please continue on further page(s) if necessary.

CRITERIA	USED BY YOU ROUTINELY?	DO YOU HAVE EASY ACCESS TO THIS?
Proximal Muscle Weakness		
Changes on muscle biopsy typical of myositis		
Elevated Muscle Enzymes/Other Laboratory Markers:		
Creatine Kinase		
Aldolase		
Transaminases		
Lactate dehydrogenase		
Myopathic Changes on Electromyogram		
Characteristic Skin Rash		
Abnormalities on magnetic resonance imaging suggestive of inflammatory myositis		

Please answer the following questions:

1. Do you have any patients with classical juvenile dermatomyositis under your care currently?
2. On average, how many new patients with classical juvenile dermatomyositis do you see per year?

Part 1: Response

- Response from *~90 centres*
- *in **32 (91.4%)** countries*
- *Response rate 50.2% (119)*

- 113 responders had at least 1 DM patient under care

Part 1: Results

Proposed Diagnostic Criteria	Use (%)	Access (%)
Proximal Muscle Weakness	100	100
Characteristic Skin Rash	100	100
Elevated Muscle Enzymes (Aldolase; Creatine Kinase; Transaminases; Lactic Dehydrogenase)	86.8	87.2
Myopathic Changes on Electromyogram	55.5	89.1
Changes on Muscle Biopsy Typical of Myositis	61.3	87.4
Abnormalities on MRI Suggestive of Inflammatory Myositis	58	70.6
Other (Nailfold Capillaroscopy; Factor VIII; Muscle Ultrasound; Calcinosis; Neopterin; Dysphagia; Dysphonia; Myalgia; Myositis specific/related antibodies; Skin Biopsy; Skin Ulcerations)	35.3	-

Most Useful/Important/Clinically Relevant Diagnostic Criteria

- Proximal Muscle Weakness
- Characteristic Skin Rash
- Elevated Muscle Enzymes
- **These criteria will automatically be included in the revised diagnostic criteria for JDM**

Part 2: Methodology

- Purpose to rank ***other*** proposed diagnostic criteria from 1-6 in order of most useful/important/clinically relevant in diagnosis

- 1 = most useful, 6 = least useful

- Participants asked to leave blank those criteria that were not felt to be useful or relevant in clinical practice

- Survey sent to all responders of first survey

- 131 individuals in >100 centres in 35 countries across Europe, Asia, North and South America

NETWORK FOR JUVENILE DERMATOMYOSITIS
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All respondents to the initial survey used proximal muscle weakness, elevated muscle enzymes and characteristic skin rash as diagnostic criteria for classical JDM. They will therefore be included in the revised diagnostic criteria

Please look at the list below: these are **other** diagnostic criteria proposed in the initial survey.

We would like you to rank these in order of usefulness from numbers 1 to 6; 1 being the most useful in the diagnosis of JDM, 6 the least useful.

Please leave blank those criteria that you feel to be less useful than 6.

CRITERIA	USEFULNESS RANKING (1-6)
Abnormalities on magnetic resonance imaging suggestive of inflammatory myositis	
Calcinosis	
Changes on muscle biopsy typical of myositis	
Dysphagia	
Dysphonia	
Factor VIII (von Willebrand antigen)	
Myalgia	
Myopathic changes on electromyogram	
Myositis specific/related antibodies	
Muscle Ultrasound	
Nailfold Cappillaroscopy/Capillaroscopy/Periungal erythema	
Neopterin	
Skin Biopsy	
Skin Ulcerations	

Part 2: Results

- 90 (68.7%) responders from ~70 centres in 31 countries

Median Values of Other Proposed Diagnostic Criteria for JDM

MRI	2
Muscle Biopsy	2
Electromyogram	2.5
Nailfold Capillaroscopy	3
Calcinosis	3
Dysphonia	3.5
Dysphagia	4
Factor VIII	4
Myalgia	4
Myositis Specific/ Myositis Related Antibodies	4
Muscle Ultrasound	4
Skin Biopsy	4
Skin Ulcerations	4
Neopterin	5

Conclusions

- First survey confirmed that in diagnosis of JDM all clinicians use:
  - Proximal Muscle Weakness
  - Characteristic Skin Rash
  - Elevated Muscle Enzymes
- Good accessibility
- Second ranking survey outlines several other clinically important and/or useful diagnostic criteria:
  - Abnormalities detected on MRI
  - Changes on Muscle Biopsy typical of myositis
  - Myopathic changes on electromyogram
  - Calcinosis
  - Nailfold Capillaroscopy

Discussion

From first survey 3 clear criteria:

Skin rash, proximal muscle weakness and raised muscle enzymes

From second survey we have top 5 rankings of other criteria

Questions

1. Do we need any more than the top 3 criteria?
   Should these be classed as major criteria?
2. Is it worth sorting out the ranking of the other 5?
   Should these be classed as minor criteria?
3. How would we sort out the JDM overlaps?
   Would the last 5 be any better than the top 3?

Diagnostic Criteria – Proposed Study

- Retrospective
- Each site to enroll 2 patients with…
  - JDM (diagnosis certain)
  - Myositis NOT JDM
  - Other muscle disease
- Chart review for all diagnostic items
- Sensitivity, specificity, likelihood ratios, AUC of the ROC
- Define the BEST diagnostic algorithm
- Prospective validation

Conclusions

- No uniform classification criteria used in research studies of juvenile myositis
- Bohan and Peter criteria most often used, but applied variably (and mis-applied)
- Clinical features of juvenile myositis and initiative for new diagnostic criteria for JDM suggest additional features and tests to include in classification criteria