Complex regional pain syndrome, and related entities: Pain Amplification Syndromes

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Pain is famously defined by Margo McCaffery (1968) as "whatever the experiencing person says it is, existing whenever he says it does" (McCaffery & Pasero, 1999, p. 17).
Evaluation of musculoskeletal pain

History and physical examination
• Character of the pain
• Other symptoms
• Family history
• Family, social, emotional and educational environment

Laboratory and imaging

Pain assessment
• Physiological measures
• Behavioral measures
• Self-report measure
History of musculoskeletal pain

*What is the character of the pain?*
Is the pain sharp, aching, deep, boring, etc?
How long has the pain been present?
Which body parts are painful? Does the pain radiate, migrate, or spread?
Is the pain getting better, worse, or staying the same?
What makes the pain better? What makes the pain worse?
Is there diurnal variation in the severity of the pain?
Is the pain present at night and, if so, does it wake the child?
Does the pain interfere with function, and, if so, which one?
Is the painful area tender to touch or clothing?
Is the painful area either cold or hot to the touch?
Does the painful part look abnormal or swollen?
What is the child’s or parent’s assessment of the pain severity?
History of musculoskeletal pain

Are there other symptoms?
Fever?
Rash?
Change in gastrointestinal function?
Weight loss?
Upper or lower respiratory tract symptoms?
Muscle weakness?
Sleep disturbance?
Depression?
Anxiety?
History of musculoskeletal pain

*Family and social history*
Ankylosing spondylitis, reactive arthritis, or inflammatory bowel disease?
Back pain, heel pain, or acute iritis?
Psoriasis?
Fibromyalgia or other chronic pain condition?
Is there an identifiable stressor in the family, school, or peer group?
Are there significant or recent life changes?
Where is the child sleeping?
What activities does the child participate in?
How do the parents describe the child’s personality?
Does the child look well or ill?
Is the child’s affect commensurate with the level of reported pain?
Does the child have an air of *la belle indifférence* about him or her?
Is there any joint swelling, muscle weakness or atrophy?
Is there any tenderness to palpation and, if so, is it over joints, entheses, or muscles?
Is there any body area of allodynia, and, if so, is the area constant or does it vary over time?
Is there any color, temperature, or perspiration change?
Are there any inconsistencies in the examination?
Is there any neurological dysfunction?
Are there abnormal child-parent interactions, such as enmeshment, hostility, or berating?
Is there evidence of concurrent conversion symptoms?
In children with back pain, are signs of nonorganic back pain present?
Pain Assessment

PHYSIOLOGICAL MEASURES
Heart rate, blood pressure, palmar sweating, transcutaneous oxygen tension, and cutaneous blood flow.
Most of these tests have little or no data to support their reliability, validity, sensitivity, specificity, or practicality

BEHAVIORAL MEASURES
Physicians routinely interpret the child’s behavior as an indicator of the severity of pain.
A number of different scales of pain behavior have been developed. These include various assessments of crying or other verbal responses, facial expressions, and limb movements: CHEOPS, Pain Behavior Observation Method, FLACC scale, and others.
Pain Assessment

SELF-REPORT MEASURES

*Unidimensional Pain Measures*

The most frequently used simple unidimensional pain scale is the visual analog scale (VAS).

*Multidimensional Pain Measures*

These are questionnaires that collect information about a number of domains relevant to pain, including pain severity; psychological well-being, such as levels of anxiety and depression; coping strategies; and self-efficacy. The best known of these is the Varni/Thompson Pediatric Pain Questionnaire.
### Translations of Wong-Baker FACES™ Pain Rating Scale

<table>
<thead>
<tr>
<th>English</th>
<th>0 Hurt</th>
<th>2 Hurts Little Bit</th>
<th>4 Hurts Little More</th>
<th>6 Hurts Even More</th>
<th>8 Hurts Whole Lot</th>
<th>10 Hurts Worst</th>
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</thead>
<tbody>
<tr>
<td>Spanish</td>
<td>No Duole</td>
<td>Duele Un Poco</td>
<td>Duele Mucho Más</td>
<td>Duole Mucho Más</td>
<td>Duele El Máximo</td>
<td>Très Très Mal</td>
</tr>
<tr>
<td>Italian</td>
<td>Nessun Dolore</td>
<td>Dolore Lieve</td>
<td>Dolore Moderato</td>
<td>Dolore Forte</td>
<td>Dolore Molto Forte</td>
<td>II Più Forte Dolore Immaginabile</td>
</tr>
<tr>
<td>Portuguese</td>
<td>Não Doi</td>
<td>Doi Um Pouco</td>
<td>Doi Um Pouco Mais</td>
<td>Doi Muito</td>
<td>Doi O Máximo</td>
<td>Boli Najviše</td>
</tr>
<tr>
<td>Bosnian</td>
<td>Ne Boli</td>
<td>Boli Same Malo</td>
<td>Boli Malo Više</td>
<td>Boli Puno</td>
<td>Boli Puno</td>
<td>Boli Najviše</td>
</tr>
<tr>
<td>Vietnamese</td>
<td>Kình Dau</td>
<td>Dau Hồn Chút</td>
<td>Dau Nhiều Hồn</td>
<td>Dau Thật Nhiều</td>
<td>Dau Gáa Dô</td>
<td>Boli Najviše</td>
</tr>
<tr>
<td>Chinese</td>
<td>無痛</td>
<td>微痛</td>
<td>疼痛</td>
<td>更痛</td>
<td>難痛</td>
<td>劇痛</td>
</tr>
<tr>
<td>Greek</td>
<td>Δέν Πονάη</td>
<td>Πονάη Λιγό</td>
<td>Πονάη Πολύ</td>
<td>Πονάη Πολύ</td>
<td>Πονάη Πολύ</td>
<td>Πονάη Πολυ</td>
</tr>
<tr>
<td>Romanian</td>
<td>No Doare</td>
<td>Doare Pujin</td>
<td>Doare Un Pic Mai Mult</td>
<td>Doare Şi Mai Mult</td>
<td>Doare Foarte Tare</td>
<td>Doare Cel Mai Mult</td>
</tr>
<tr>
<td>Mongolian</td>
<td>Зовнуруүгий байна</td>
<td>Бага зарзг овдож байна</td>
<td>Энэгийн омдогдож байна</td>
<td>Их овдож байна</td>
<td>Маш их овдож байна</td>
<td>Тэнзэхий эргэгий овдож байна</td>
</tr>
<tr>
<td>Japanese</td>
<td>痛みはない</td>
<td>わずかに痛い</td>
<td>もう少し痛い</td>
<td>かなり痛い</td>
<td>ひどく痛い</td>
<td>耐えられないほど痛い</td>
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<tr>
<td>Bahasa Malaysia</td>
<td>Tidak Sakit</td>
<td>Sangat Sedikit Sakit</td>
<td>Sedikit Sakit</td>
<td>Sakit</td>
<td>Sangat Sakit</td>
<td>Teramat Sakit</td>
</tr>
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</table>
Definition of these conditions

I use *pain amplification syndromes or amplified musculoskeletal pain* in these talks because:

- it is descriptive
- does not presume an etiology
- differentiates these children from adults with chronic pain
- does not “label” the child with a disease

When reading a particular study, it is important to know what criteria were used to classify children with various forms of amplified musculoskeletal pain.
Complex Regional Pain Syndrome, Type I (reflex sympathetic dystrophy [RSD], Sudeck's atrophy, reflex neurovascular dystrophy [RND], or algoneurodystrophy)

Criteria 2-4 must be satisfied.

1. The presence of an initiating noxious event, or a cause of immobilization
2. Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event
3. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain
4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degrees of pain and dysfunction
Classification

**Complex Regional Pain Syndrome, Type II (Causalgia)**

*All three criteria must be satisfied.*

1. The presence of continuing pain, allodynia, or hyperalgesia after a nerve injury, not necessarily limited to the distribution of the injured nerve
2. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain
3. This diagnosis is excluded by the existence of conditions that would otherwise account for the degrees of pain and dysfunction
Classification

Fibromyalgia (ACR, 1990)
Both criteria must be satisfied.
1. Widespread pain (bilateral, and above and below the waist and axial pain) present for at least 3 months
2. Pain (not tenderness) on digital palpation with 4 kg of pressure on 11 of the following 18 sites:
   a. Occiput: at insertion of suboccipital muscle. b. Low cervical: at anterior aspect of the intertransverse spaces of C5-C7. c. Trapezius: at the midpoint of the upper border. d. Second rib: just lateral to the second costochondral junction at the upper rib border. e. Scapula: the medial border just above the spine of the scapula. f. Lateral epicondyle: 2 cm distal to the epicondyle. g. Gluteal: in the upper outer quadrant of the buttocks. h. Greater trochanter: 1 cm posterior to the trochanteric prominence. i. Knees: at the medial fat pad 1 cm proximal to the joint mortise
Fibromyalgia trigger points
Classification

Yunus and Masi Criteria for Childhood Fibromyalgia
All 4 major and 3 minor, OR the first 3 major, 4 painful sites, and 5 minor need to be satisfied.

Major:
1. Generalized musculoskeletal aching at 3 or more sites for 3 or more months
2. Absence of underlying condition or cause
3. Normal laboratory tests
4. Five or more typical tender points (1990 ACR criteria)

Minor:
1. Chronic anxiety or tension. 2. Fatigue. 3. Poor sleep. 4. Chronic headaches.
   5. Irritable bowel syndrome. 6. Subjective soft tissue swelling.
10. Pain modulation by anxiety or stress
Classification

**Diffuse Idiopathic Pain**
Both criteria must be satisfied.
1. Generalized musculoskeletal aching at 3 or more sites for 3 or more months
2. Exclusion of disease that could reasonably explain the symptoms.

**Localized Idiopathic Pain**
All 3 criteria must be satisfied.
1. Pain localized to one limb persisting
   a. 1 week with medically directed treatment OR
   b. 1 month without medically directed treatment
2. Absence of prior trauma that could reasonably explain the symptoms
3. Exclusion of diseases that could reasonably explain the symptoms
Epidemiology

Incidence and prevalence
Musculoskeletal pain is common: back pain 20%, limb pain 16%
Fibromyalgia 2 to 6%
About 10% of new patients in PR clinics have some sort of amplified musculoskeletal pain

Age of onset
Mean age is generally at 12 or 13 years old

Gender
Ratio is about 4:1 (F:M)

Geographical and Racial distribution
All reports are from developed countries
Etiology and Pathogenesis

Causes are unknown

In adults, several hypothesis: abnormal muscle anatomy and physiology, altered sleep pattern, abnormal serotonin metabolism, hypothalamic-pituitary-adrenal axis hypofunction, decreased cerebral blood flow, trauma, and psychological distress, but there is no convincing evidence that any of these factors is of primary importance.

Different findings in bone scan of children and adults with CRPSI
Causally related to injury, illness, or psychological distress, either singly or in combination
Interdependency or enmeshment is common
Etiology and Pathogenesis

NERVE PLASTICITY (describing the ability of the brain to change easily) or CENTRAL SENSITIZATION

Changes that occur in the brain in response to repeated nerve stimulation or after repeated experiences with pain.

Following repeated stimulation, levels of neurotransmitters and brain electrical signals change as neurons develop a "memory" for responding to those signals. Frequent stimulation results in a stronger brain memory, so that the brain will respond more rapidly and effectively when experiencing the same stimulation in the future.

Thus, the brain is activated or sensitized by previous or repeated stimuli to become more excitable.
Etiology and Pathogenesis

**CLINICAL EFFECTS OF CENTRAL SENSITIZATION**

- Hyperalgesia
- Allodynia
- Pain summation
- Radiation of pain beyond the dermatomal distribution
Clinical Manifestations

Amplified Musculoskeletal Pain

Conversion symptoms are common. Numbness is frequently reported, but they also can manifest paralysis, nonepileptic episodes (pseudoseizures), muscle shaking or rigidity, blindness, or a bizarre (histrionic) gait. Eating disorders can be present, and a high index of suspicion for these need to be maintained.

*La belle indifference* can be present, even when reporting severe pain and dysfunction. A few children will demonstrate marked pain behaviors such as crying or screaming. These children seem to be mature for their age, are accomplished in school and extracurricular activities, and are described by their parents as perfectionistic, empathetic, and pleasers.
Localized Amplified Musculoskeletal Pain

Minor trauma that might not be clearly recalled is common
The pain and consequent disability increase over time
Autonomic signs (edema, cyanosis, coolness, increased perspiration) may be persistent or transient or may not occur
Allodynia can be marked (“the breeze of someone walking by hurts”) and can lead to significant impairment.
Any body part can be involved, and the child may have several areas of pain, but the lower extremity is more commonly involved than the upper, and peripheral body parts are more commonly involved than central areas. Occasionally, only one small area is involved, such as a finger, the nose, or a tooth.
Clinical Manifestations

Diffuse Amplified Musculoskeletal Pain

Onset is usually more gradual and can be vague in location and character.

Absence of autonomic signs, but affected children complain of poor sleep and depression more often than do those with localized pain.

Report a multiplicity of symptoms is common.

The pain is often centrally located, involving the back, chest, abdomen, head, and extremities.

A significant number of children with diffuse amplified musculoskeletal pain who start out with very localized pain or even clear cut complex regional pain syndrome that then spreads and may involve the entire body.
Clinical Manifestations

Physical Exam
There is no findings suggesting an underlying disease, neurological examination is normal, and allodynia is present. Careful sensory testing is required. Allodynia is present if pain is reported when lightly touching the skin, the border of the allodynia can vary dramatically. Signs of autonomic dysfunction, especially coolness and cyanosis, may only be present after exercising the limb or may become apparent if the limb is held in a dependent position for a few minutes. The distribution of painful points is outlined in the previous slide. Control points, such as the forehead, shin, and thumbnail, will define how widespread the pain is.
Differential Diagnosis

Diagnosis of exclusion

No laboratory or radiographical examination is diagnostic

A number of other painful conditions need to be excluded (Fabry disease, Neoplasia, erythromelalgia, pernio, spinal cord tumors, Raynaud, hypermobility, restless legs syndrome, CRMO, progressive diaphyseal dysplasia, peripheral neuropathy, transient migratory osteoporosis, vitamin D deficiency, thyroid disease)

Keep an eye for seronegative enthesopathy arthropathy syndrome, in children with back pain

The most common misdiagnoses for children who actually have an amplified pain syndrome are trauma, mechanical pain, or arthritis.
General Assessment

There are two major independent variables to consider when assessing pain:

1. The quality and quantity of the pain complaint itself, and
2. The amount of dysfunction as a consequence of the pain.

The report of pain is always valid because, by definition, pain is subjective. Therefore, the most useful measurement of pain is the self-report on a verbal or visual analog scale.

The quality of pain can be assessed using various instruments such as the McGill Pain Questionnaire or Pediatric Pain Questionnaire.
General Assessment

The amount of reported pain does not directly correlate with the degree of incapacity, which vary from almost none to being bedridden. With treatment, function usually returns before the pain diminishes. Functional measurements vary depending on the location of the pain and the presence of coexisting conditions.

Children with amplified musculoskeletal pain suffer more than children with other musculoskeletal conditions do, which may indicate the degree to which the disorder is a manifestation of psychological distress. Psychological dysfunction is almost universally present by the time these children are identified. Even though these syndromes are not psychological in cause, the psychological toll on the child and family is often severe.
PReS Latin America Basic Rheumatology Course

Social Life
“I don’t see friends anymore. I can’t keep up”

Education
“I used to love school but have missed 80% in the last year”

Sleep
“I go to bed at 11 but don’t fall asleep until 3. I keep waking up”

Family
“Mum worries about me. She’s had to give up work”

Fitness
“I used to run for the school. Now I can’t even walk without pain and tiredness”

Appetite/eating
“I feel too sick for breakfast. I just eat junk in the day”

Moods
“I get angry and frustrated. I just go to my room, I don’t want to talk to anyone”

Independence
“I even need my mum to help me go to the toilet. It’s not fair – I’m 16”

Pain and fatigue

Jacqui Clinch, and Christopher Eccleston Rheumatology 2009;48:466-474
Treatment Goals

1. Restoration of function

2. Relief of pain

- Physical and occupational therapy with desensitization maneuvers
- Psychological evaluation and cognitive behavioral evaluation
- Cheerleading
- Adjuvant therapy
Treatment

PHYSICAL AND OCCUPATIONAL THERAPY

Aggressive physical and occupational therapy aimed at reversing immobility and increasing function.

One-on-one therapist, encouraging both speed and quality of movement.

Exercises are focused on normal function and aerobic training, such as walking times, rope jumping, climbing stairs, dressing, and other activities of daily living.

Allodynia is treated with desensitization maneuvers, deep muscle massage using towel and lotion rubs, vibration, and wearing normal clothing and footwear.
COUNSELING

Psychological evaluation to determine co-morbid situations (i.e. mood, anxiety and sleep disorders) and formal psychotherapy to treat these conditions.

Cognitive Behavioral Therapy (CBT): relaxation training, setting and working toward behavioral goals (typically including systematic increases in exercise and other activities), behavioral activation, guidance in activity pacing, problem-solving training, and cognitive restructuring (Thorn, 2004; Turner & Romano, 2001).

CBT typically includes between-session activities to practice and apply new skills (e.g., completion of thought records, relaxation practice, work toward behavioral goals).
Treatment

COUNSELING

Goals of Cognitive Behavioral Therapy (CBT):

- Reduce pain and psychological distress
- Improve physical and role function (by helping individuals decrease maladaptive behaviors, increase adaptive behaviors, identify and correct maladaptive thoughts and beliefs)
- Increase self-efficacy for pain management
Treatment

**CHEERLEADING**

It is the role of the PR to monitor, set realistic goals and reassure these children and their families that they will get through this

**ADJUVANT THERAPY**

Low-dose tricyclic antidepressants
NSAIDs
Tramadol
Muscle relaxants (cyclobenzaprine)
Pregabalin
Treatment

WHAT DOES NOT SEEMS TO WORK

- Glucocorticoids
- Anticonvulsants
- Opioids
- Epidural infusions
- Lidocaine infusions
- Nerve and ganglion blocks
- Spinal cord stimulators
- Pain pumps
- Ketamine coma
Some children have amplified pain that persists for years, and yet there are children with self-limited involvement who are never evaluated in a tertiary center.

Many children have spontaneous remission of illness.

Around 90% of children diagnosed with fibromyalgia in a pediatric rheumatology center still had significant pain 15 to 60 months (mean, 33 months) later.

The frequency of relapses is rarely reported but occurs in all forms of amplified musculoskeletal pain.

The clinical manifestation of the second episode may be different from the first, even changing between localized and diffuse disease.
Thank you!

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