A young woman with complex regional pain syndrome

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The care of a patient with complex regional pain syndrome of several years' duration and clear dystrophic changes in one leg is discussed from the pain medicine and rehabilitation medicine perspectives.

Case scenario

Rebecca is a 23-year-old university student who studies online as she has been confined to her home for the past 18 months because of severe left leg pain. She had a netball injury to the left knee when aged 17 years and, following an arthroscopy, developed complex regional pain syndrome (CRPS) with obvious dystrophic changes of the leg.

Rebecca uses a wheelchair to get around at home. Lately she has been experiencing right shoulder pain (she is right-handed), possibly due to difficulty transferring from bed to chair. She maintains her independence in matters of personal hygiene, and enjoys cooking meals for the family. She has contemplated giving up her studies in social sciences but enjoys the online interaction. Her father works from home and her mother is a vocational education lecturer. Her older brother is studying overseas and the family plan to join him for his graduation ceremony next year.

Rebecca's current medications are the oral contraceptive pill, which she uses to delay her periods, duloxetine 30 mg twice daily, pregabalin 150 mg twice daily and oxycodone 5 to 10 mg fortnightly before the physiotherapist visits her at home. Her family doctor is considering a trial of sustained-release tapentadol. Rebecca has gained 10 kg and is lethargic and drowsy at times.

Would Rebecca benefit from a change in medications and admission to a rehabilitation unit?

Commentary from a pain medicine specialist

Dr Michael Veltman

CRPS remains a poorly understood entity that relies on clinical skill for diagnosis. It involves not only the nervous system but also the microcirculation, bone and inflammatory pathways, and there are differing degrees of central sensitisation, cortical sensorimotor changes and sympathetic autonomic changes.[1-3] Although medications remain important in the management of CRPS, these variations are the reason that there is no single medication or combination of medications that is universally effective.

Assessment

The diagnosis of CRPS seems fairly likely in this patient but it is important to identify any signs of other treatable illnesses (red flags) such as infection, oligoarthritis or saphenous infrapatellar branch neuropathy. She may have an occult knee injury or patellar–femoral pain syndrome (e.g. maltracking), which is common in younger women.

The Budapest criteria are the clinical gold standard for diagnosing CRPS and have

Key points

- **Complex regional pain syndrome (CRPS) is poorly understood and is diagnosed clinically using the Budapest criteria.**
- **It involves the nervous system, microcirculation and bone and also inflammatory pathways, and there are differing degrees of central sensitisation, cortical sensorimotor changes and sympathetic autonomic changes.**
- **Medications alone (analgesics and anti-inflammatories) are unlikely to provide effective treatment. Also required are physiotherapy, exercise programs, self-management training, psychological assessment and patient education.**
- **Multidisciplinary rehabilitation plans should be developed for patients with CPRS.**

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good sensitivity (85%) and specificity (69%); they are listed in Box 1.[4-6]

Laboratory investigations

There is no diagnostic test for CRPS. A three-phase bone scan may show increased bone metabolism, with high specificity (83 to 100%) but low sensitivity (31 to 50%) even in experienced imaging units.[7] In this patient, in whom CRPS is well established, a bone scan would be unlikely to alter management.

1. Budapest clinical diagnostic criteria for complex regional pain syndrome[4]

- Continuing pain, which is disproportionate to any inciting event
- Must report at least one symptom in three of the four following categories:
  - sensory: reports of hyperalgesia and/or allodynia
  - vasomotor: reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry
  - sudomotor/oedema: reports of oedema and/or sweating changes and/or sweating asymmetry
  - motor/trophic: reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
- Must display at least one sign* at time of evaluation in two or more of the following categories:
  - sensory: evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
  - vasomotor: evidence of temperature asymmetry and/or skin colour changes and/or asymmetry
  - sudomotor/oedema: evidence of oedema and/or sweating changes and/or sweating asymmetry
  - motor/trophic: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
- There is no other diagnosis that better explains the signs and symptoms

* A sign is only counted if it is observed at time of diagnosis.

Management

The use of medication alone is very unlikely to provide effective treatment of a patient with CRPS, particularly when the condition is longstanding with altered behaviours such as wheelchair use.

Physiotherapy to improve function is essential in patients with CRPS.[8] Progressively increasing the intensity of workload while managing the fear and avoidance of pain will significantly reduce disability.[9] Specific strategies such as graded motor imagery ('mirror box therapy') are also of benefit. Clinical psychology programs for pain management strategies (acceptance/commitment therapy) are beneficial.

The various medications used to treat CRPS need to be tailored to the individual. It is generally better to make gradual dosage changes and review after each change. Medications of possible use in patients with CRPS include over-the-counter painkillers, opioids, antidepressants and anticonvulsants effective against neuropathic pain, corticosteroids (to reduce inflammation and improve mobility), bone-loss medications, sympathetic nerve-blocking medication and intravenous ketamine.[10] Topical analgesics may also be of use.

Possible medication changes

This patient is currently taking the oral contraceptive pill, duloxetine, pregabalin and oxycodone, and her family doctor is considering a trial of sustained-release tapentadol. Considering these medications:

- pregabalin is known to cause both early and late weight gain in 18% of patients;[11] switching to gabapentin (off-label use) may prove worthwhile for this patient to see if it is better tolerated
- the serotonin and noradrenaline reuptake inhibitor duloxetine can produce somnolence (or insomnia) and could also be causing the sedation; it usually does not require twice-daily dosing, and changing to once-daily dosing would usually be helpful
- the evidence for benefit from opioids in chronic pain is limited; if they are used then there needs to be functional benefit, no escalation of dose and no aberrant behaviour, and patients thought to be at high risk of abuse should avoid opiates for chronic pain management.[12] If opioids are used then it makes sense to prescribe buprenorphine or tapentadol rather than oxycodone because of their lower rates of abuse.[13,14] Tapentadol has 5:1 equivalence with oral oxycodone.

Other medications to consider

Medications with specific benefit in CRPS that could be considered in this patient's case include the following:

- high-dose vitamin C – has been shown to be beneficial in preventing CRPS in the early post-injury phase but is untested in patients with longstanding CRPS[15]
- bisphosphonates – have been shown to be effective in reducing or preventing bone loss in both early and long-standing CRPS;[16,17] calcitonin injections have also been used (off-label use) and may be of benefit[10]
- prednisolone – may have benefit in reducing inflammation during the first weeks of an acute CRPS presentation, with typical dosage ranges of 20 to 60 mg for two to three weeks in most studies[18]
- intravenous ketamine – short courses of this anaesthetic (off label-use) have been shown to improve pain in patients with CRPS[19]
- intravenous lidocaine plus clonidine (off-label uses) – is occasionally of use
- topical analgesic creams, including the free radical scavengers dimethyl-sulfoxide and N-acetyl cysteine, and also lignocaine and capsaicin and various combination therapies (off-label uses) – may improve pain[20,21]
- low-dose naltrexone – there are case reports of low dose naltrexone (off-label use) improving CRPS;[22] this correlates with the increasing understanding of neuroinflammation and opioid use as a significant factor in chronic pain.

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Commentary from a rehabilitation specialist

Dr Michael Vagg

This case concerns a young woman with established CRPS of several years' standing and clear dystrophic changes in the left leg. She has become a wheelchair user as her main form of indoor mobility, and it is a critical part of her rehabilitation goal setting to determine the plan by which she can return to weight bearing and ultimately walk.

Rebecca's current analgesia regimen seems to be contributing little to improving her level of function. Weight gain and daytime somnolence are identified as particular issues and may be due to a lack of physical activity and deconditioning, medication side effects and/or a mood disorder. Use of pregabalin may be associated with weight gain and fluid retention and may, in rare cases, worsen depression in young patients. Duloxetine is relatively 'neutral' in term of weight gain.

The patient's right shoulder pain is concerning as she is right-handed and uses a self-propelled wheelchair. It is unclear how she is transferring into and out of her wheelchair but it could be expected that she is using a pivot transfer by pushing up on the arms of the wheelchair and pivoting on her right leg. This type of transfer places significant stress on the shoulders, and her technique may need to be assessed and modified if the pain is to be allowed to settle.

Investigations such as an ultrasound examination to exclude rotator cuff disorders, subacromial bursitis, adhesive capsulitis or occult fractures should be requested. Treatments may include analgesia (such as short courses of NSAIDs), shoulder-strengthening exercises targeting the scapular stabilising muscles and shoulder depressors and retraining in wheelchair transfer. Periarticular corticosteroid injections should be given if indicated by clinical or imaging findings.

Rebecca should be strongly encouraged to continue her online tertiary studies, which could lead to vocational development or employment. It would be helpful for her to attend the university to facilitate social interaction. Discussions regarding vocational options must form part of any rehabilitation planning.

Rehabilitation plan

A rehabilitation plan should be developed for Rebecca, taking into account the significant milestones identified so far. An example plan, showing interdisciplinary goals, is shown in Box 2.

What could be done with rehabilitation physician consultation alone?

- Discuss priorities and goal setting.
- Suggest Rebecca's pregabalin dose is reduced to see if 150 mg twice daily is still effective, and whether dose reduction improves her sedation. Gabapentin could be trialled if pain increased with weaning of pregabalin.
- Consolidation of her duloxetine doses to a single 60 mg dose at night may improve her daytime sedation.
- Examine Rebecca's left knee to exclude saphenous infrapatellar branch neuralgia, which is common after knee injury and arthroscopy and may be a driver for CRPS.
- The GP could trial tapentadol (has mu-opioid receptor agonist and

noradrenaline reuptake inhibitor actions), which may be a better choice than a pure mu-opioid receptor agonist strong opioid such as oxycodone due to its efficacy in neuropathic pain and lower potential for sedation and abuse. The risk of interactions between tapentadol and duloxetine (such as serotonin syndrome) is negligible. The goal of low-dose tapentadol is to enable Rebecca to participate fully in a new exercise program, with a view to weaning in three to six months.

- A topical or systemic NSAID may be appropriate to help manage Rebecca's shoulder pain, depending on the diagnosis. Subacromial corticosteroid injections may be performed with ultrasound guidance. Consideration of neuromodulation could be appropriate.

2. A rehabilitation plan for complex regional pain syndrome

Long-term goals (two to five years)

- Achieve social independence (move out of home)
- Have a manageable level of pain
- Sustainably self-manage mobility and domestic and community activities of daily living (ADLs)
- Develop and execute a long-term career plan (get a long-term job)

Medium-term goals (six to 24 months)

- Complete current studies or begin vocational training as decided
- Trial medical treatments appropriate to rehabilitation goals
- Reduce weight and increase aerobic capacity
- Rehabilitate right shoulder and prevent left shoulder problems
- Undertake training in pursuit of optimal skill set for self-management (pacing skills, mindfulness, acceptance and cognitive reframing, healthy food preparation)
- Travel overseas to attend brother's graduation

Short-term goals (up to six months)

- Complete trials of medications appropriate to goals
- Decide how much lower limb weight bearing is achievable or necessary
- Plan overseas travel if wheelchair will be required for all transfers
- Diagnose and treat cause of right shoulder pain
- Undertake basic pain education
- Develop an exercise routine that is effective and sustainable

Immediate goals (less than one month)

- Organise right shoulder ultrasound and detailed examination
- Review medication
- Refer to a community rehabilitation centre

What could be done in a community rehabilitation setting?

- Physiotherapy to assess transfers, wheelchair and seating prescription, review current activity patterns and prescribe a reconditioning program. If increased lower limb weight bearing is decided upon, a graded desensitisation program, potentially in combination with clinical psychology, can be commenced. Hydrotherapy can be a successful means to improve conditioning long-term without excessive lower limb weight bearing, and this can be trialled at low intensity as an outpatient.
- An exercise physiologist can supervise progression of a prescribed exercise program at home or in a community gym/pool setting.
- An occupational therapist can review pressure care and seating system if predominant wheelchair use is decided upon. Vocational advice and assessment, advice on suitable accommodation modifications to improve independence and training in energy conservation and pacing strategies are also within the occupational therapist's field. The occupational therapist may also need to liaise with airlines and travel agents to ensure Rebecca's planned overseas trip is feasible.
- A clinical psychologist can screen for mood disorder as a cause of fatigue and weight gain due to low motivation, and also assess Rebecca's current level of knowledge about CRPS and her use of effective self-management strategies.
- A dietitian can provide information about effective dietary interventions to promote healthy eating choices and prevent excessive weight gain. This maximises the long-term ability of wheelchair users to avoid shoulder injuries as well as preventing them becoming completely sedentary, with the cardiovascular risk this carries.
- If local expertise (physiotherapist or occupational therapist) is available, cortical retraining, mirror therapy or virtual reality techniques for CRPS could be performed as an outpatient.

What could be done in an inpatient rehabilitation setting?

- Ketamine or lignocaine infusion, calcitonin injection or a tunnelled lumbar epidural catheter for infusion of local anaesthetic and adjunctive clonidine (all off-label uses) could provide effective short-term analgesia (up to a week) and facilitate rapid establishment of new routines if increased lower limb weight bearing is decided upon as a medium-term goal.
- Intensive reconditioning, with daily hydrotherapy and twice-daily gym sessions, would be possible as an inpatient.
- Gait retraining on a treadmill with body weight support may be available in some centres and would enable high-volume walking with partial weight bearing.
- Intensive education and skills training is possible as an inpatient if a suitably experienced team is available.
- Inpatient rehabilitation after implantation of a neuromodulation device may be appropriate.

Conclusion

This young woman with CRPS would likely benefit both in the short- and long-term from the involvement of an interdisciplinary rehabilitation team, especially one with expertise in persistent pain management. An ideal plan for her would certainly involve a community rehabilitation centre; inpatient rehabilitation is probably not relevant in this case. Co-ordination of efforts and monitoring of the goals over time requires a well-organised approach from an appropriately skilled and resourced team. **PMT**

COMPETING INTERESTS: None.