Chronic Inflammatory Demyelinating Polyneuropathy – The role of accurate objective measures as feedback for medical care. A case study.

Jacinta Sharp

Introduction

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a neurological disorder characterised by areflexia, progressive weakness and impaired sensory function in the arms and legs. It is considered to be an autoimmune disorder and shares initial presentation with Guillaume-Barre Syndrome (GBS). Differentially, with CIDP the disease process continues for more than 8 weeks and can continue progressively or have a relapsing-remitting pattern for months to years (Oaklander et al 2017). Physiotherapy assessment and treatment forms a major part of the overall care and management of patients with CIDP. There is an important role for physiotherapy in informing medical management decisions through accurate and timely outcome measures, which describe disease progression.

One of the primary medical therapies for CIDP is Intra-venous (or subcutaneous) Immunoglobulin (IVIG). There is still a global shortage of IVIG, resulting in the implementation of the National Demand Management Program for Immunoglobulin (NHS England 2011). The Demand Management Program identifies CIDP as a high priority for IVIG but may need to be approved for long term use. Mr Edward Guest has had a particularly good recovery from this disease, with aggressive medical treatment from the outset and specialist, goal-oriented physiotherapeutic input ongoing.

Pathophysiology

CIDP is an idiopathic autoimmune disease. Some triggers for the similar condition GBS are known, e.g. influenza type virus, campylobacter, Epstein Barr virus (Tam et al, 2007), yet not everyone with these illnesses will develop GBS/CIDP or an autoimmune response. There is potentially a familial link which gives predisposition, but not all family members, with triggering virus will go on to develop the disease. So, the development of CIDP requires a combination of factors which are not fully understood. If the right factors and conditions are present, then a complex inflammatory and auto-immune response begins. There is an increased expression of pro-inflammatory cytokines, macrophages and T-cells. Auto-antibodies are developed which can attack both the myelin cells and the axons of the nerve cells themselves, resulting in axonal damage directly, and secondarily after demyelination.

Without continuous myelin, the conduction of signals (depolarisation) along the nerve is slowed (or stopped) resulting in the typical changes in motor and sensory ability and the expected conduction velocity changes in nerve conduction studies.

The axons of nerve cells rely on axoplasmic flow, related to depolarisation at their base rate to provide nutrition from end to end (Wilfred, 2017), i.e. some cell body requirements are delivered by the action of depolarisation, rather than circulation. When this is interrupted, as in demyelination

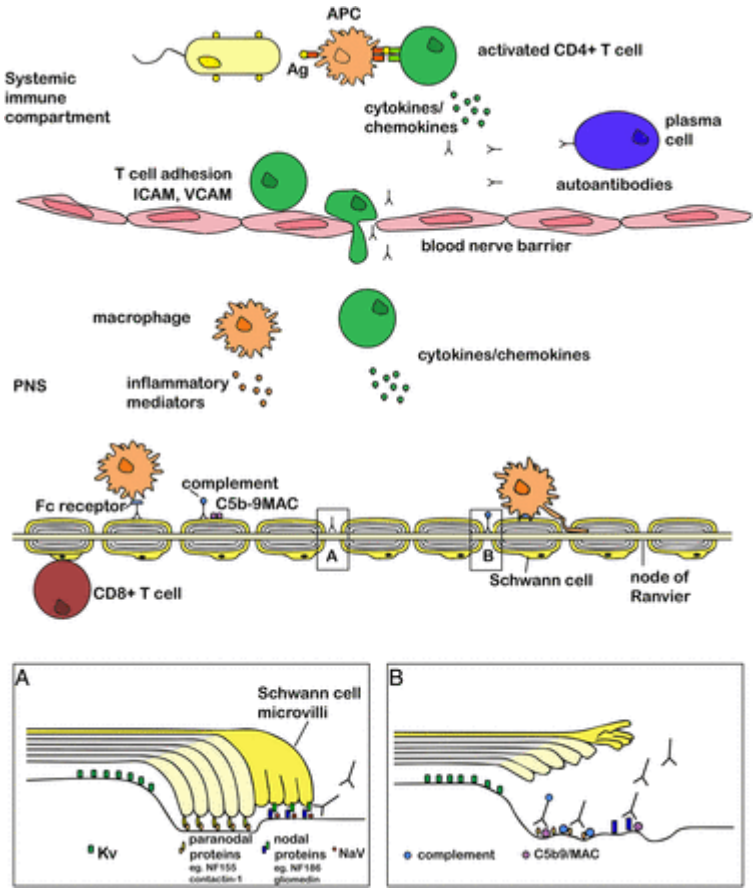

Image courtesy of Mathey et al 2015 https://jnnp.bmj.com/content/86/9/973

and inflammation, a secondary process of axon damage begins. Without the myelin sheath, it is even more likely that axon damage will occur, and this is the primary reason for close monitoring against relapse. Please copy the link above for more in-depth pathophysiology.

Diagnosis

Diagnosis is primarily clinical, based on the presentation with areflexia, progressive weakness and impaired sensation. Tests are performed to exclude other conditions, usually MRI of the spine and CSF tap. Nerve conduction studies are then performed to confirm a demyelinating process, as demonstrated by patterns of reduced conduction velocity and sometimes conduction loss.

Medical management

The mainstay of treatment for CIDP is similar to that for other autoimmune diseases, with the aim to repress the damaging inflammatory process and to support healthy immune response. Therefore, a common treatment regime will include initial high dose IV steroids, Intravenous Immunoglobulin g (IVIG) and sometimes Plasmapheresis. As CIDP is a chronic condition, the timeframes, frequency and dose can change over the course of the disease. It is usual to reach a point of disease stability/remission where the decision to reduce treatment is made. At that point, dosage and intensity are titrated down slowly. In the case of steroid treatment, this helps manage withdrawal and dependency. With IVIG, an abrupt stop to treatment is not dangerous or damaging, but treatment is still reduced slowly to monitor for regression/reliance on the treatment. The use of sensitive and valid objective outcome measures can help guide this dose reduction.

Epidemiology

CIDP is a relatively rare condition with a prevalence of 2-3 cases per 100 000 people (Oaklander et al 2017). It typically affects people aged between 40 and 60 years old but can occur in children and the elderly. Within this set, there are several phenotypes of CIDP, suggesting that it may be a spectrum

of related conditions rather than a single disease (Mathey et al 2015). This makes diagnosis and management difficult for both the medical team and allied health professionals. In CIDP where the prognosis is uncertain, it becomes more difficult to make appropriate predictions of recovery/progression and therefore harder to set realistic goals or select appropriate treatment. The tools which improve this problem are objective measures. Measures which are more specific, sensitive and individually tailored, combined with appropriate frequency of reassessment, will start to give an accurate picture of disease progression. It is not usual care to have repeat nerve conduction studies which would give similar information about disease progression/regression, so relying on objective measures helps address the problems of prognosis and goal setting.

Because the choice of IVIG, steroid treatment or Plasmapheresis is also individually determined, accurate feedback about recovery or progression can help improve drug choice. This has become even more relevant recently with the international shortage of human plasma products. This shortage has caused a review of IVIG provision which is now decided upon through the Demand Management Programme.

The patient

Mr Guest (or Ed), a 65yo gentleman was previously fit and well, recently retired and had worked as an Engineering Consultant. His only medical concerns were ocular hypertension and mild OA knee, he is a non-smoker and moderate drinker. Medications of note: Lisinopril, Latanoprost. In 2017 at the onset of symptoms, he developed gradually worsening gait and an inability to manage the stairs, with gradual deterioration of sensation. This led to a hospital admission during which his condition continued to deteriorate with resulting global areflexia, altered sensation, muscle weakness and wasting, to the point of becoming bed-bound.

Investigations (as per medical report): Normal PET scan. Normal CT scan abdomen and pelvis. Retroviral screen negative. Normal immunoglobulins and electrophoresis. Normal antiganglioside antibody analysis. Raised CSF protein. MRI showed smooth enhancement of all the lumbar intradural nerve roots, likely to indicate an inflammatory process. Nerve conduction studies showed reduced conduction velocity and conduction block. He was diagnosed with classic CIDP.

Medical care: Mr Guest's CIDP was treated with initial 5-day course of IVIG with oral Gabapentin for pain of neural origin. This was followed by a second course of IVIG one month later and Pregabalin replaced Gabapentin.

At this point, Mr Guest was transferred to a University Hospital with a specialist neurological unit. The next dose of IVIG was given with the addition of IV methylprednisolone.

At first, Mr Guest was an inpatient and was followed up by neurological specialist consultant after discharge. At 4 months after discharge, he was seen by a CIDP specialist consultant to manage his ongoing care.

Physiotherapy: After a hospital stay of 22 weeks, he was discharged home with a stair lift and a package of care. He lives at home with his wife who has health concerns as well. At this point, he was referred to community NHS physiotherapy but also self-referred to private specialist neuro-physiotherapy to ensure specialist assessment and treatment with a view to maximise recovery. He later also accessed NHS neuro-physiotherapy and the treating therapists were able to work collaboratively for best patient care.

At Initial physiotherapy assessment - shortly after discharge home. Mr Guest presented with wasting of all muscle groups in all four limbs with "flat" appearance to hands. He had low tone throughout with some development of stiffness and contracture (calves). He had mild weakness proximally in all four limbs, mildly reduced core stability and marked weakness of all four limbs

distally. He was able to transfer with a frame (despite poor grip) and close supervision. He used a wheelchair for all mobility around the house, self-propelling with legs and hands, or assisted.

Goals discussed initially were: walking, access to the shower and improved use of his hands. As therapy and recovery continued, goals and treatment plans were adjusted incrementally. Ed's overarching goal was to return to independent living, including driving. To establish if progress was being made towards these goals, and to best reflect any neurological changes, outcome measures were taken at initial presentation and repeated at relevant intervals. Outcome measures were selected to demonstrate changes in **power, function and sensation**.

The table shows changes in key observations over time.

	Measure	Initial PT Assessment	2 months	4 months	6 months	8 months
POWER	Left ankle DF	0/5 oxford scale	1+/5	3/5	4/5	4/5
	Left toe extension	1/5	1/5	2/5	3/5	4/5
	Left and right wrist extension	2/5	4/5	-	-	4/5
	Left and right thumb abduction	0/5	3/5	-	-	3/5
	Grip Strength	-	-	L - 17kg R - 17kg	-	L - 31kg R - 29kg
FUNCTION	Opposition	To middle finger	To ring finger	-	-	To little finger
	Independent static standing	0 seconds	5 seconds	1 minute+ no AFO Single leg – 1 and 3 seconds.	Single leg 6 and 9 seconds	Single leg now: 8 and 12 seconds
	RODS *	14	17	38	44	44
	Gait speed -from video analysis	0.25m/s (with WZF, AFO)	0.35m/s (with WZF, AFO)	0.58m/s (no walking aids, AFO on)	0.9m/s No aids, no AFO	-
	Functional goals **achieved**.		Access to shower with assistance of carer	Independent gait with a frame.	Shaving. Walk with crutches.	Return to Gym and swimming
SENSATION	Nottingham sensory assessment	Intact at tested points.	Intact pressure and light touch, no extinction.	-	-	Intact pressure and light touch, no extinction
	Sharp/Blunt		50%	Intact (>90%)	80%	-
	2-point discrimination		Across 2-3 joints (distal)	60% accurate within segment	Over 2 joints	
MEDICATION CHANGES	IV 150mg Octogam IV methylpred	IV 150mg Octogam IV methylpred	IV methylpred Ceased IVIG	Ceased IV methylpred IV 150g Octogam (restarted)	110g Octogam	90g Octogam

*RODS is a GBS-CIDP validated measure of ADLs (Vanhoutte et al 2015)

Intervention

To guide and achieve these improvements, physiotherapy input varied in frequency and content over the period. It was always goal oriented, patient focussed and adaptable.

For initial goals:

Access to shower with assistance of carer and appropriate equipment
Independent gait with frame
Initial therapy intervention included:
1: Develop and progress to a daily maintenance program which included joint passive range of movement exercises, long finger flexor stretches, hamstrings and calf stretches, massage or passive movements for circulation.
2: AFO for left ankle and taping to hands as splint.
3: Sensory stimulation program for the hands and feet to be repeated during therapy sessions.
4: Strengthening home program for knee extensors, dorsiflexors, calf muscles, core stability, intrinsic hand muscles and finger flexors/extensors.
5: Gait practice with frame and crutches.
6: Fatigue management advice.

As function, power and sensation improved, the goals were reviewed, and therapy was progressed:

Next set goals:

Improved use of mobile phone, cutlery and shaving.
Improved balance with a view to walking with crutches.
Intervention:
1: Progressed home exercise program for strengthening knee extensors, ankle dorsiflexors, plantar flexors, inverters and everters, hip extensors, core stability.
2: Hand focussed program of active and assisted movements, putty and other strengthening tools.
2: Patients own exercise bike with simultaneous UL elastic band exercises for core.
3: Continued sensory stimulation for the hands and feet.
4: Gait practice with single crutch and walking stick.
5: Stepping up a step.

Then goals to:

Walking indoors and outdoors without walking aids (achieved – now walking1.5miles+)
Return to gym, swimming, cycling and driving (achieved)
Improve cardiovascular fitness and balance (ongoing)

Intervention:
1: Progressed intensity of exercise bike.
2: Outdoor cycling session.
3: High level balance home exercise program e.g. single leg standing, heel raises, plank.
4: Mr Guest accessed a high intensity exercise class.

Intervention was progressed accordingly, to finally include: a calf and foot muscle focus, exercises to improve reaction times and responses to available sensation in feet through: jumping, skipping, running and exercises with compensatory sensations removed e.g. eyes closed.

Ed Guest has had an impressive recovery through hard work, self-motivation and the combined efforts of specialist therapeutic and medical care. He is now independent in all ADLs, has returned to driving, attends the gym and has returned to outdoor cycling.

Discussion of Implications for Practice

Irregular and rare neurological conditions present to physiotherapists in such a varying way, that only shared previous experiences can give any way of predicting outcomes. Recording precise

objective measures that have an appropriate range (i.e. less floor and ceiling effect) can help inform patients whether their recovery is fitting within that prediction or if they are moving towards their goals. Or perhaps more sensitive measures can be used, changed and returned to if required.

In reviewing this case, the problem which emerged after some physical recovery was Mr Guest's ongoing sensory deficit. It was clear at the outset there was a sensory problem, but partly because of the lack of hand function and standing, the extent of the sensory deficit and the level of functional disability caused by the sensory problem was not immediately obvious. Because of this, it was not a priority to evaluate the sensory deficit in depth and so the earlier measures used (Nottingham Sensory Assessment) were quite blunt and did not help to identify changes later. The assessment of sharp/blunt and two-point discrimination was more useful in an individual case but was not taken in a way which would have good inter-rater reliability and did not use a set of tested locations, so the comparison is not as definitive as, in retrospect, would have been more useful. The last measures show a suggestion of mild regression, but not definitively enough to act on, hence more functional measures of proprioception and texture identification have been taken to give a more precise comparison at the next assessment. This indicates the need for a clinically user friendly, but more sensitive and reliable sensory assessment tool.

Quick referral to specialist care with accurate supporting information was another key point in this case. Mr Guest's neurologist referred on to a specialist centre and that is where his ongoing management including reduction of IV methylprednisolone and IVIG began. It is always beneficial to reduce unnecessary medications, but even more so in the context of global shortage. Having that reduction managed by a specialist centre helped ensure the best outcomes for this patient. It may be that specialist care is not always available locally but being aware of specialist centres and online advice could help guide the therapy and medical teams involved, particularly when it comes to the longer-term management of medication.

Summary

Appropriate medication is the key to minimising nerve damage in CIDP. Minimising axonal nerve damage and minimising the demyelination process is the key to good long-term recovery. There is no universal approach to medication or dose, which are individualised treatment decisions. Therefore, an important role of the treating therapist is to provide accurate and timely feedback to the patient and to the medical team involved to help make appropriate dosage and therapy choices. There is a selection of scales which have been reviewed for CIDP, including RODS, the Overall Neuropathy Limitation Scale or the Inflammatory Neuropathy Cause and Treatment Group, all of which offer different insights into neurological changes as the disease progresses as discussed in clinical papers (Yusuf, 2018). These scales are available to the clinician and selecting an appropriate measure from the outset, or at the time of treatment change is the challenge.

In this case, I discovered that some of the measures I had relied on had a ceiling effect and did not report sensitively enough Ed's specific problems. An easier and more sensitive sensory assessment would have been extremely useful.

Mr Guest is a single case within a large spectrum of presentations and recovery patterns. This variability limits the direct application of the same exact treatment choices. However, in a good working relationship between the therapist, patient and medical team, the goal-oriented approach described here, supported by effective review of objective measures could be applied to any CIDP case and many other heterogenous neurological conditions.

For more information: expert opinion and updates about CIDP and related conditions can be accessed through the Polyneuro Exchange website. https://www.polyneuroexchange.com/cidp

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Appendix

At 6 months post discharge:

Functional measure of lower limb proprioception.	Can detect 5-degree angle change at ankle
Functional measure of texture identification	Can detect texture changes on fine tooth combs

For information regarding Nottingham Sensory Assessment please see:

Lincoln NB, Jackson JM, Adams SA (1998) *Reliability and Revision of the Nottingham Sensory Assessment for Stroke Patients* Physiotherapy 84(8):358-365