Case Number 1
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

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Case summary:

Demographic details:
Mr. AB, male, Birkirkara
Referred from: Orthopaedics

This previously healthy, right-handed, 61-year-old, gentleman presented with a history of weakness that resulted in a number of futile nerve release procedures in an attempt to alleviate symptoms that were initially thought to be due to nerve entrapment. The muscle weakness, most prominent in both upper limbs, especially his left hand was accompanied with left intrinsic hand muscle wasting and some paraesthesia in the left fingertips. Marked hyporeflexia was also present. Neurological investigations led to the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) being established

Presenting complaint:

Slowly progressive bilateral weakness in the upper limbs, particularily marked in his left hand.

History of presenting complaint:

This weakness was first noticed back in 2002 while the patient was having supper with his family and was unable to grip his fork.

Over the course of the years, his weakness progressed, gradually depriving him of significant power in his left hand. On presentation the patient had marked muscle wasting in his left (non-dominant) hand. Additionally, the patient also had muscle twitching in both upper limbs and frequent muscle cramps in his thigh and calf muscles bilaterally when lying immobile for long periods.

He had some paraesthesia in the fingertips of his left hand and numbness in both upper limbs on prolonged flexion of the elbows. Oherwise, no other sensory deficits were noted. The patient's condition never caused him any pain. His symptoms showed no fluctuation during the day and his sleep was not impaired in any way. A week ago, the patient had an isolated episode of sudden unsteadiness whilst walking.

He denies any stiffness in his wrist and finger joints. He also denies having any loss of consciousness, vertigo, diplopia, dysarthria, dysphasia or dysphagia. The patient is alert, responsive and ambulant without the need for walking aids. He has no problems with speech and eats well without choking.

Past medical and surgical history:

Past medical history:

- Mild hypercholesterolaemia which is controlled by diet and exercise.
- Hypothyroidism which is controlled with replacement therapy.

Negative for: - Diabetes Mellitus
- Hypertension

Past surgical history:

- Anal stretch for anal fissure.
- Right knee replacement.
- Left carpal tunnel and left cubital tunnel release.

Drug history:

No known drug allergies.
The patient is compliant with his medication and does not complain of any side-effects.

Drug Name (Generic)	Dosage	Frequency	Type	Reason
Levothyroxine	100 µg	Daily	Thyroid hormone replacement	For hypothyroidism

Family history:

Paternal cousin has congenital monoparesis. None of the patient's seven siblings have any neuromuscular problems. His mother died of a myocardial infarction and his father died due to colon cancer.

Social history:

A married, non-smoking, boarded out gentleman. He used to work in construction but had to change his job due to his condition and now works as a watchman. He drinks occasionally and walks on a regular basis. The patient is completely independent although his weakness does make his activities of daily living more labourious. He lives with his wife and daughter. He can drive an automatic car safely.

Systemic inquiry:

- General Health: Looks well in general; no weight loss or diminished appetite noted
- Cardiovascular System: Nil to note
- Respiratory System: Nil to note
- Gastrointestinal Tract: Nil to note
- Genitourinary System: Nil to note
- Central Nervous System: See above
- Musculoskeletal System: Nil to note
- Endocrine System: Nil to note

Discussion of results of general and specific examination:

Upper limbs:

Inspection
Fasciculations in right upper arm.
Asymmetry between right and left; complete wasting of the left intrinsic hand muscles, mild clawing in the left hand. Froment's sign in the left hand.
Scars of cubital tunnel release and carpal tunnel release.

Tone
Normal bilaterally

Power (MRC grading)

	Right	Left
Deltoid	5/5	5/5
Biceps brachii	5/5	5/5
Triceps brachii	5/5	5/5
Wrist extension	5/5	4/5
Wrist flexion	5/5	4/5
Finger extension	5/5	2/5
Abductor pollicis brevis	4/5	0/5
Abductor digiti minimi	4/5	0/5
Finger adduction	4/5	2/5

Sensation
Normal throughout

Reflexes (tested with Jendrassik maneouvre):
Biceps brachii, triceps brachii and brachioradialis were all hyporeflexic (bilaterally)

Lower limbs:

Inspection
No wasting
No fasciculations
Knee arthroplasty scar on right knee
Can stand on toes and heels

Tone
Normal bilaterally

Power (MRC grading)

	Right	Left
Hip flexion	5/5	5/5
Hip extension	5/5	5/5
Knee extension	5/5	5/5
Knee flexion	5/5	5/5
Ankle dorsiflexion	5/5	5/5
Big toe dorsiflexion	5/5	5/5
Ankle plantar flexion	5/5	5/5

Sensation
Normal throughout

Reflexes
Knee and ankle jerk were both hyporeflexic
Gait
Normal

Differential diagnosis

- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Amyotrophic Lateral Sclerosis (ALS) / Motor Neurone Disease (MND)
- Multifocal motor neuropathy with conduction block
- Paraneoplastic syndrome
- Polyneuropathy secondary to a paraproteinaemia
- Vasculitic polyneuropathy
- Radiculopathy (but usually not bilateral)
- Motor neuropathy secondary to lead (Pb) poisoning
- Diabetic peripheral neuropathy
- Hereditary peripheral neuropathy
- Old polio

Diagnostic procedures:

Laboratory exams:

Test: Thyroid function tests, Liver function tests and Blood Glucose level
Justification for test: Looking for metabolic/biochemical causes.
Result: Normal.
Conclusion: Metabolic/biochemical causes not implicated.

Test: Erythrocyte Sedimentation Rate
Justification for test: Looking for evidence of extensive inflammation.
Result: 11mm; not elevated.
Conclusion: No evidence of systemic inflammation.

Test: B12 and folate levels
Justification for test: Looking for deficiency.
Result: Within range.
Conclusion: Not deficient.

Test: Serum Immunoglobulin analysis
Justification for test: Looking for evidence of a polyneuropathy due to a paraproteinaemia.
Result: No monoclonal band present.
Conclusion: The neuropathy is probably not due to a paraproteinaemia.

Test: Vasculitic screen
Justification for test: Looking for evidence of a vasculitic polyneuropathy.
Result: Negative.
Conclusion: The cause is probably not a vasculitic polyneuropathy.

Test: Tumour markers
Justification for test: Looking for evidence of a neoplasm.
Result: Negative.
Conclusion: The cause is most likely not a paraneoplastic syndrome.

Test: Antiganglioside antibodies (anti-GM1)
Justification for test: May indicate evidence of a multifocal motor neuropathy with conduction block.[1]

Result: Mildly elevated.
Conclusion: Multifocal motor neuropathy may be present.

Test: Lumbar Puncture
Justification for test: Looking for abnormal CSF analysis.
Result: Normal, however, the protein level was on the high side of the normal range (borderline).
Conclusion: The fact that the protein level was borderline high might indicate an inflammatory polyneuropathy.

Instrumental exams:

Test: Electromyography (EMG)
Justification for test: Looking for abnormalities in neuronal conduction.
Result: Consistent with generalised demyelinating sensory motor polyneuropathy with secondary axonal change and denervation in the muscles tested.
Conclusion: Polyneuropathy confirmed.

Therapy:

Drugs:

Drug Name (Generic)	Dosage	Frequency	Type	Reason
Intracet® (IVIG)	0.4mg/kg	For five days	IV	CIDP responds to IVIG

Diagnosis:

The slowly progressive course of the symptoms and signs indicate that the problem at hand is a chronic one. Symptoms were generalised in affecting various parts of the body, namely the upper and lower limbs with motor weakness being the main feature, together with a slight sensory impairment (paraesthesia noted in the history, however normal sensation on examination) and markedly diminished tendon reflexes. This points towards a generalised problem of lower motor neuron pathology. Thus a polyneuropathy should be considered. Furthermore, the patient suffered from a fall recently which might reflect impaired coordination or possible autonomic nervous system involvement resulting in dizziness (since lower limb power is normal).

At this point, the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) should come to mind. Many consider a duration of symptoms for more than 8 weeks to be adequate for diagnosing the condition[2]. Investigations ruled out important differentials, and the fact that the patient was found positive for anti-GM1 antibodies increases the likelihood of a multifocal motor neuropathy being present. EMG changes were typical of what one would expect in CIDP, thus confirming the diagnosis.

Final treatment and follow ups:

The immunoglobulin course was five days long and during the first few days of treatment the patient was already experiencing some improvements in motor function of his upper limbs. Subsequently the patient was to have a number of outpatient sessions for IVIG pulses and follow-up at MOP where the improvement was to be confirmed clinically.

Fact Box 1

Title: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

CIDP is the most common treatable chronic neuropathy in the western world. This autoimmune polyradiculoneuropathy is acquired over a period of 2 or more months and typically targets the peripheral nervous system (PNS) proximally, with involvement of nerve roots and major plexuses.

Clinicl Features: The natural course of CIDP is that of a progressive or relapsing condition, with predominant symmetrical motor deficits occuring in a proximal to distal pattern. Other presentations of CIDP include evolution from a subacute monophasic path or, rarely, as the acute Guillain-Barre' syndrome (GBS), only to be followed by progression of the disease or relapse. Hypo- or arfelexia is a feature since this is a lower motor neuron disorder[3,4].

Risk factors: Family history

Diagnosis:

- Appropriate clinical features
- Demyelinating picture on electrophysiological studies, as specified by the EFNS and PNS Task Force (2010) criteria, which request proof of any of the features listed below in at least 2 nerves:
- Prolongation of distal latency
    - Reduction in motor conduction velocity
    - Prolongation of F wave latency
    - Absence of F waves
    - Partial conduction block
    - Abnormal temporal dispersion
    - CMAP reduction in amplitude

- Additional features to back the diagnosis

Raised CSF protein and normal leucocytes

- Nerve root or plexus hypertrophy as evidenced by gadolinium enhancement on MRI
- Primary demyelination on nerve biopsy
- Amelioration with immunotherapy

Pathogenesis:

The endoneurium and perivascular regions are invaded by T (CD4 & CD8) and B lymphocytes as well as macrophages, which together orchestrate phagocytic demyelination. Of note is the high expression of MHC on Schwann cells and the increasingly leaky blood nerve barrier (BNB) [5, 6,7] . The inadequately high permeability of the BNB to autoantibodies derives from T-cell transmigration occurring through interaction of T-cell adhesion molecules VLA-4 and LFA-1 with their counterparts VCAM-1 and ICAM-1 on endothelial cells, in association with chemokines, cytokines and matrix metalloproteinases. As a result, nodal and paranodal sites lose their structural integrity with concomitant early conduction block[8,9].

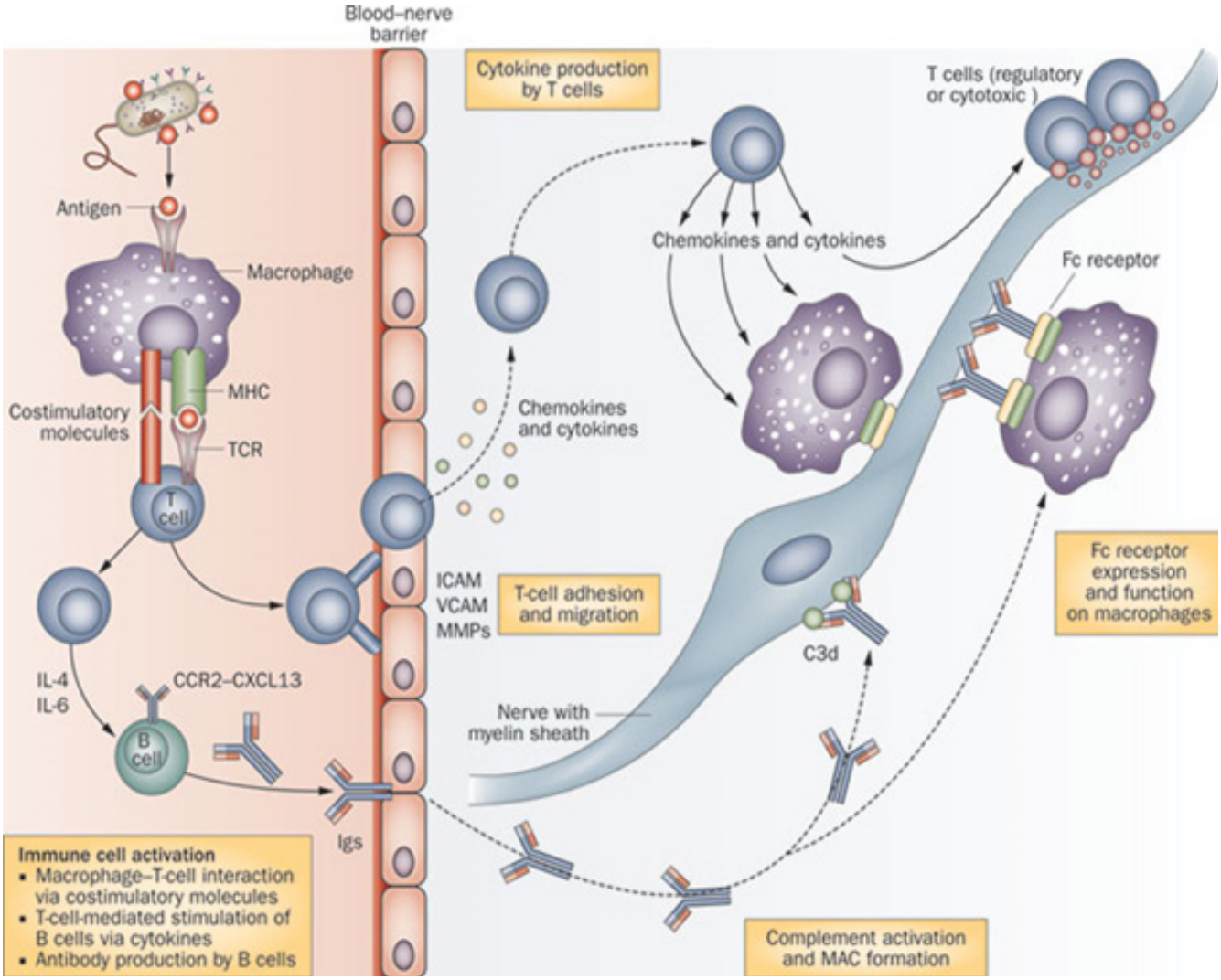

Figure 1: Immunopathology of CIDP

Treatment: A variety of treatment options exist, the best of which is chosen on the grounds of efficacy, cost, availability and safety[3].

One suggested approach to treatment involves administering IVIg as first line, particularly in patients with pure motor CIDP (in whom corticosteroids can aggravate the condition) [10]. In case of resistance, plasmapheresis would be the next option. If the patient still does not respond, a combination of a corticosteroid and immunosuppressives is tried. The mentioned treatment options provide short-term resolution, hence they must be supplemented by a maintenance course of IVIg.

Whichever treatment is opted for, patients on the road to remission should be put on lower doses or have their treatment withdrawn completely since it is known that a substantial number of patients need no long-term maintenance therapy [11, 12, 13] .

Early recognition of the disease and adequate treatment can help prevent debilitating and disabling outcomes.

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