The Neurology of General Medicine

Dr Tim Lavin
Consultant Neurologist
Honorary Clinical Lecturer
Manchester Centre for Clinical Neuroscience
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North of England Acute Neurology Update

@timlavin4
Tim.lavin@srft.nhs.uk

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Content

- 3 case vignettes
- Opposite end of the Nervous System

Case 1

- 26yr old, R handed
- Psychology Graduate
- Working as a teacher in 4 yr in Asia, 1 yr in Vietnam
- Vegan
- Reports no illicit drug or risky sexual behaviour
- No preceding infection

- Presents with 8 weeks of
  - Fatigue
  - Mouth Ulcers
  - Ache across abdomen – appendix removed
  - Loss of sensation in feet

Acute worsening over 1 week

Poor balance
Difficulty mobilising
Ascending paraesthesia to knees and hands
Bilateral leg weakness
Normal sphincter

Further Hx

- ½ stone of weight loss
- No fever
- No rash/arthralgia
- Mouth ulcer but not genital ulcers
- No CVS/Renal/Resp/GU
- No insect bites

Investigated by Neurologist in Vietnam

“French Name”

Normal EMG and MR Spine

Clinical Examination

Higher Mental Function N
CN included VA, fields and fundi N
Gait Ataxic

		R	L
Insp	UL	Pseudoathetosis	
	LL		
Tone	UL	N	N
	LL	N	N
Power	UL	5	5
	LL	5	5
Coord	UL	Ataxic	Ataxic
	LL	Ataxic	Ataxic
Reflexes	UL	+	+
	LL	-	-
Plantar		UP	UP
Clonus		6 beats	6 beats

		R	L
PP	UL	Wrist	Wrist
	LL	Thigh	Thigh
Vib	UL	Wrist	Wrist
	LL	ASIS	ASIS
JPS	UL	PIP	PIP
	LL	Knee	Knee

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Where is the Lesion

A. Central
B. Peripheral
C. Both
D. Neither she is functional

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B. Peripheral
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Where is the lesion- Single best Answer

A. Cortex and peripheral nerve
B. Subcortical White Matter and Peripheral Nerve
C. Brainstem and Peripheral Nerve
D. Cord and Peripheral Nerve
E. Cord and Sensory Neuron

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- Myeloneuropathy

- Hb 130
- WCC 7, normal diff
- Plt 240
- U+E and LFT N
- HIV N
- Hep N
- Syphilis N
- Folate 15
- CRP and ESR N

- Normal CXR
- Normal 12 lead ECG
- Normal Spirometry

Vit B12 213 (211-911ng/L)

CSF Analysis
No cells
Normal Protein and Glucose Ratio
Negative Virology

NCS
Abnormal study.
There is a sensory neuropathy. There is a suspicion of a non-length dependent pattern with, at least, an equal
degree of attenuation of upper limb digital sensory responses and lower limb sensory responses.

- Any other tests?

- Methylmalonic Acid 0.48 (<0.42)
- Homocysteine 42.8 ng/L (0–12)

B12 Deficiency

- Vitamin B_{12} deficiency is relatively common, affecting up to 6% of those aged under 60 years and around 20% of those over 60 years in the UK and USA

- Megaloblastic Anaemia , Glossitis, Depression/Mania , Infertility , Thrombosis (high homocysteine)

- Anaemia appears inversely correlates to neurological dysfunction

- pernicious anaemia, gastric and intestinal malabsorption, pancreatic insufficiency, malnutrition and various drugs including alcohol and proton pump inhibitors

Dobson R, Alvares D. The difficulties with vitamin B_{12}. *Practical Neurology* 2016;16:308-311

Neurological Manifestations of B12 deficiency

- Essential for
  - Development and Maintenance of Myelin
- Affects
  - Optic Nerves
  - Dorsal Column of Cord (and lateral to lesser degree)
  - Peripheral Nerve (demyelination and axonal loss)
- Optic Neuropathy, Myelopathy (dorsal column) or Peripheral Neuropathy or combination

Problem with B12 testing

- False negative and false positive results at a rate of up to 50%
- Elevated Methylmalonic acid (MMA) and plasma homocysteine levels can be used as surrogate measures for vitamin B_{12} deficiency
- MMA is more specific
- Homocysteine can be increased in renal failure, folate deficiency

Stabler SP Vitamin B12 deficiency. N Engl J Med 2013;368:149–60

Key Points

- NO use is common in young people, rarely volunteered
- Ask about diet
- Functional B12 deficiency requires additional tests (MMA and Homocysteine)
- serum B12 is not perfect- suspect if low normal or risk factor
- Presentations can be dramatic and severe, mimicking inflammatory demyelination
- Remember COPPER in older people

- 62 yr old men
- Referred to MAU
- 6/52 of
  - Diffuse heaviness of the limbs
  - Unbalanced
  - Paresthesia affecting feet and hand
  - Left hand worse then R.
  - Gradually worsening, but ambulant
- Over past 2/7
  - Bedbound with diffuse limb weakness
  - No sensory loss
  - No sphincter/ No autonomic/ No bulbar/No ocular
  - Systemically no change
  - Severe Neuropathic pain in feet

Exam

- Higher cortical function normal
- Mild bilateral facial weakness
- Bulbar/tongue/palate/uvula normal
- EOM full

- Areflexic
- Wasted interossei

- Vibration to knee
- JPS lost at hallux
- PP lost to thigh
- Lost to Wrist on R and elbow on L

	R	L
SA	3	3
EF	3	2
EE	4	4
WF	3	1
FDIO	3	1
ADM	3	1
FDP	4	2
HF	2	2
KF	3	3
KE	2	2
ADF	0	0

Where is the Lesion

A. Hemispheric Lesion

B. Cervical Cord

C. Polyradiculopathy

D. Polyneuropathy

E. Neuromuscular Junction

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- Next test?

Investigations

- CSF Protein 2.05g No cells, Normal cytology. CSF viral PCR inc CMV
- HIV/Hep Neg
- CRP 20
- NCS: Severe bilateral, asymmetrical sensorimotor neuropathy. Mixed axonal demyelinating features

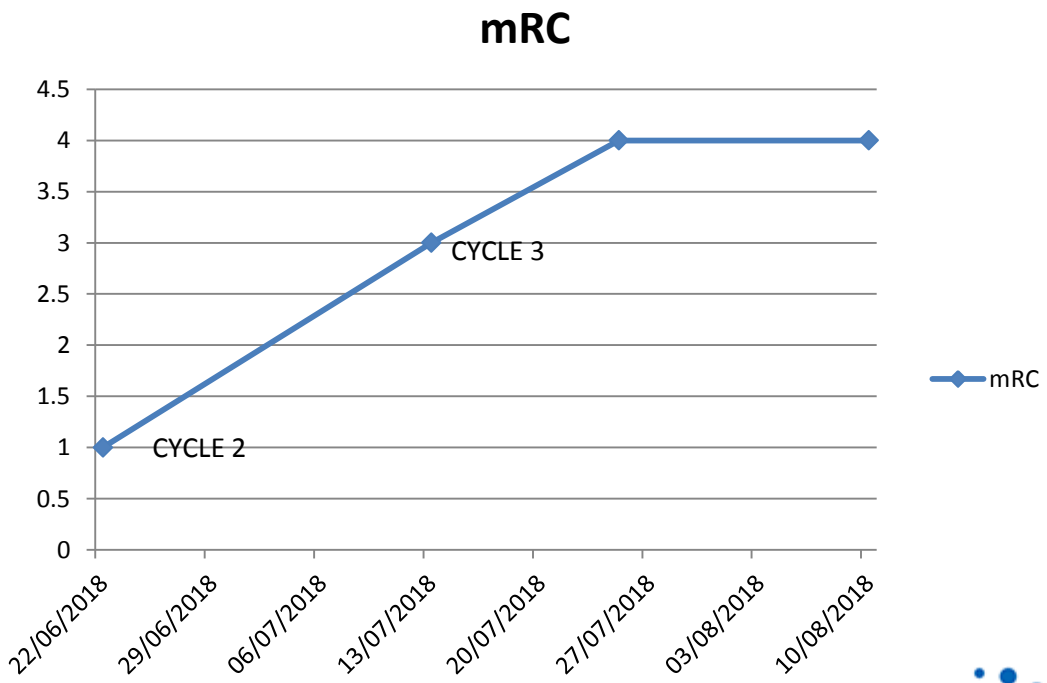
More History

- Known Kappa light chain myeloma
- Elevated free kappa light chains
- What additional history would we like?

Investigations

- MRI with contrast of spine: no change
- Free kappa light chains fallen from 3000 to 400

- Velcade/Cyclophosphamide/Dex/Thalidomide- 2 cycles



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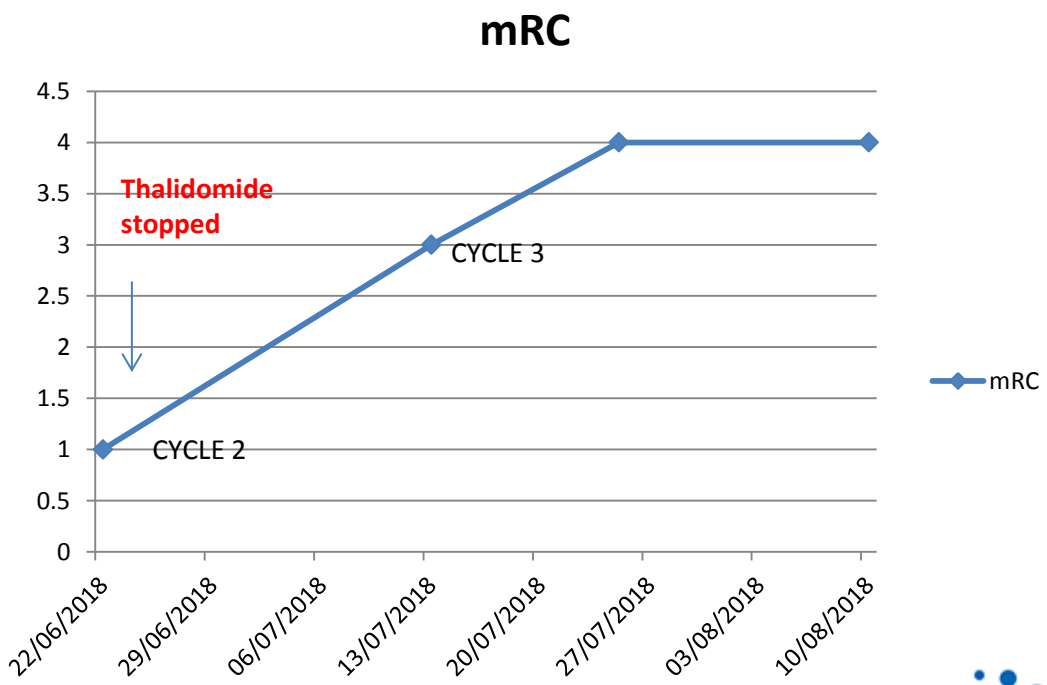
- Velcade/Cyclophosphamide/Dex- cycle 3



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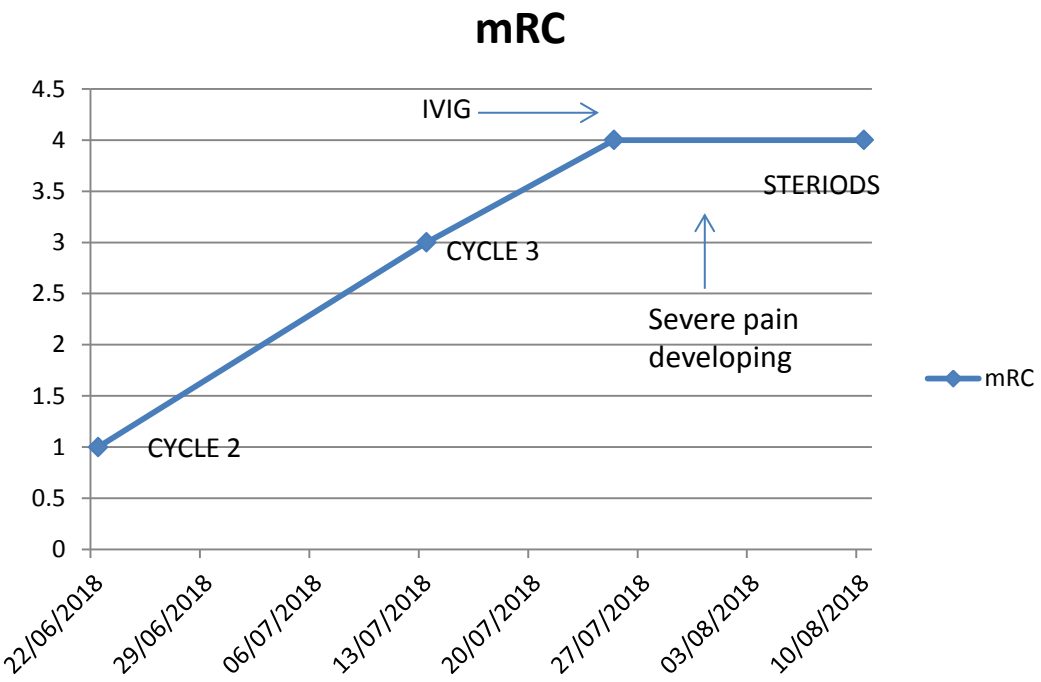
Primary Demyelinating Neuropathy
with secondary axonal injury

Treatment and Progress



Treated as GBS like syndrome- poor response.

Latterly developed severe neuropathic pain

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Summary

- Subacute demyelinating neuropathy due to Velcade

Toxic Neuropathy

- In General
  - Length Dependent
  - Axonal
  - Painful
  - Dose dependent (cumulative)
- Common Culprits
  - Chemotheurapeutics
  - Amiodarone
  - Allopurinol
  - Phenytoin
  - Alcohol

ACUTE NUTRITIONAL AXONAL NEUROPATHY

JOHANNA HAMEL, MD and ERIC L. LOGIGIAN, MD

University of Rochester Medical Center, 601 Elmwood Avenue, Rochester, New York, 14642, USA

Accepted 23 May 2017

- Mimic GBS
- Post Bariatric Surgery
- Alcoholics
- Anorexia
- Multiple defiencies

Case 1

67yr old- previously well

Initially presented in 2014 with a

- 4 month history of ascending sensory disturbance (numbness, paraesthesia and neuropathic pain)
- sensory ataxia
- mild LL proximal and distal weakness, but mobile with frame.
- No sphincter disturbance,

- Examination demonstrated – symmetrical findings
  - Normal UL
  - LL areflexia
  - Vib to iliac crest
  - JPS lost at toes
  - PP lost to mid thigh

Results

- NCS suggests demyelinating neuropathy
- CSF protein 2.7g
- IgG Lambda band small, unquantifiable
  - normal bone marrow
  - Normal skeletal survey
- CT TAP small mesenteric nodes and root oedema

Progress

- Treated as CIDP
- Independently mobile
- Mesenteric nodes and oedema resolved on repeat CT

- This deteriorated clinically and electrophysiologically after 3-4 months
- Started on Mycophenolate 1500 bd and steroids - again appears to be clinical improvement
- No reported change over following year

What is the relevance of the IgG lambda

MGUS vs Myeloma (or Waldentroms)

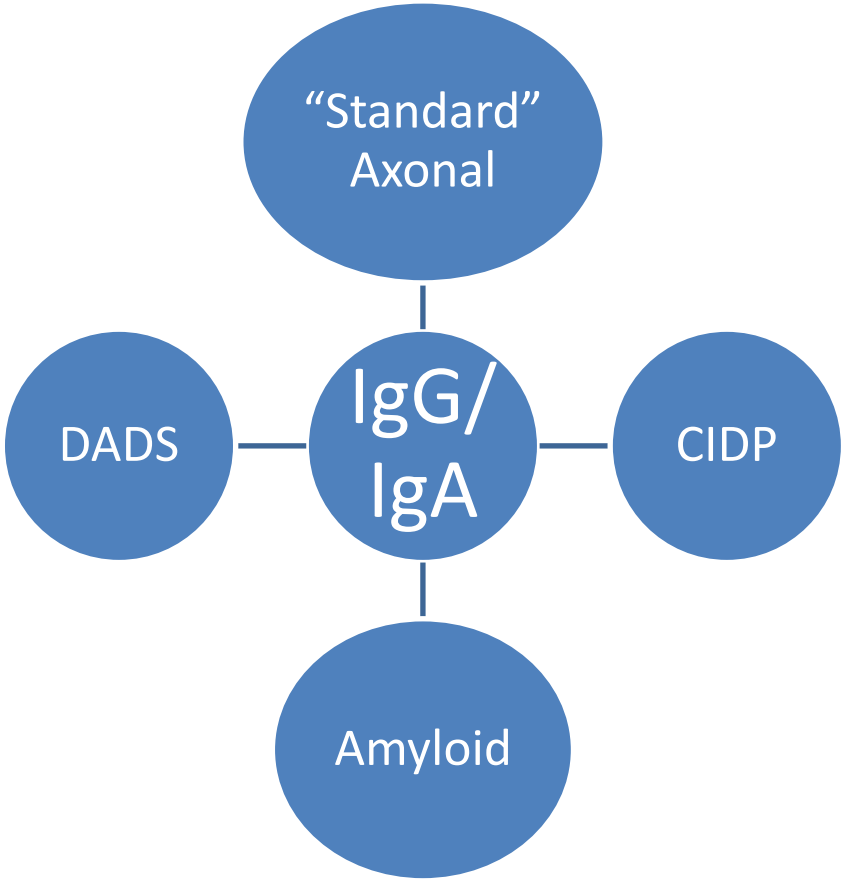
- IgG/IgA MGUS defined by
  - <30g/l
  - BJP <1g/24hr
  - No lytic/sclerotic lesions
  - No anaemia, renal disease, hypercalcaemia
  - Plasma cell infiltration <10%

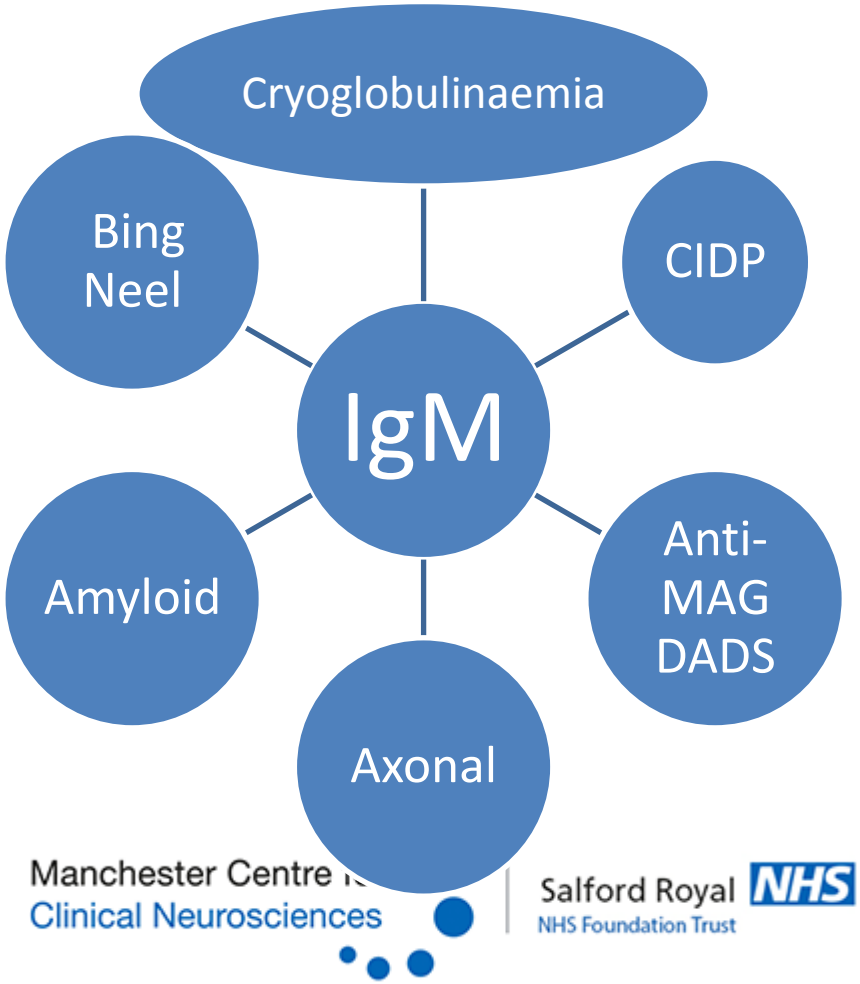
- Therefore MGUS

- What is the relevance of MGUS to Neuropathy?

Paraproteinaemic Neuropathies

- 10% of patients with sensorimotor neuropathy have MGUS
- **30-70% of patients** with MGUS will have neuropathy
- 3.5% myeloma patients pre Rx


"Standard"
Axonal
DADS
IgG/
IgA
CIDP
Amyloid


Cryoglobulinaemia
Bing
Neel
CIDP
IgM
Amyloid
Anti-
MAG
DADS
Axonal

General Deterioration

- Develops swallow ulcers of the lower leg secondary to PVD
- Pedal Oedema
- General Malaise
- Skin changes
- More falls- advanced CVD

Haematology

- Low B12- 110
- Low Plts around 120
- Low level lambda band- but no concerns raised

Endocrine

- Hypothyroid
- Adrenal insufficiency (steroids)
- Hirsute

Repeat Bone Marrow

- Normocellular for age. Megakaryocytes increased, left shifted. Conclusion: **No evidence of myeloma or lymphoproliferative disorder** F

- Trephine:

- There is active haempoiesis with megakaryocyte expansion. **The latter show some morphological changes and occasional small cluster**

- **VEGF: 1658 (N <700)**

In Summary

- Polyneuropathy
- Lymphadenopathy
- Endocrinopathy
- M protein
- Skin changes

- Unexplained low B12, fracture, oedema and previous mesenteric nodes

- Polyneuropathy
- Lymphadenopathy (Organomegaly)
- Endocrinopathy
- M protein
- Skin changes

- Unexplained low B12, fracture, oedema and previous mesenteric nodes

Diagnosis:

POEMS syndrome secondary to plasmacytoma/osteosclerotic myeloma

POEMS syndrome diagnostic criteria

Polyneuropathy and monoclonal plasma cell disorder present in all patients; to make diagnosis at least one other major criterion and 1 minor criterion is required.

- Major Criteria
  - Polyneuropathy
  - Monoclonal plasma cell disorder (almost always λ – 95%)
  - Sclerotic bone lesions
  - Castleman disease
  - VEGF elevation
- Minor Criteria
  - Organomegaly (spleno-, hepato- or lymphadenopathy)
  - Oedema, pleural effusion or ascites
  - Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic*
  - Skin changes (pigmentation, nails, hair, plethora, cyanosis)
  - Papilloedema
  - Thrombocytosis or polycythaemia**
- Other symptoms or signs
  - Clubbing
  - Weight loss
  - Diarrhoea
  - Low vitamin B12
  - Pulmonary hypertension or restrictive lung disease
  - Thrombotic episodes
  - Hyperhydrosis
- Possible associations
  - Arthralgia
  - Cardiomyopathy
  - Fever

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Dispenzieri 2007

Lessons from Case

- For the Neurologist: Early testing VEGF, look for systemic clues

- For the Physician:
  - Be wary of blind obedience!
  - we get it wrong, we miss the systemic clues!
  - investigate the medical clues if we don't.

What we have learnt

- B12 deficiency- its neurological presentation and investigation
- The spectrum of chemotherapy induced neuropathy
- MGUS and how it affects the peripheral nerves
- How in rare syndromes- systemic clues such as haematological, dermatological, endocrine are vital