Typically atypical: when optic neuritis is not

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A typical vs atypical

• Differentiating between
  – typical (demyelinating) optic neuritis
  – Atypical optic ‘neuritis’
A typical vs atypical

• Differentiating between
  – typical (demyelinating) optic neuritis
  – Non-typical optic ‘neuritis’
Typical (demyelinating) optic neuritis

- 20-50 years old
- Unilateral
- Pain comes on over few days, made worse by eye movements
- Blurring of vision 2-3 days after onset on pain, stabilising by 2 weeks
- No anterior/posterior segment inflammation
- Vision improves over several weeks, 80% back to 6/12 or better
Non-typical optic neuritis

- Under 20 or over 50 years old
- Bilateral
- Painless or painful for more than 2 weeks
- Sudden loss of vision or progressive deterioration of acuity over more than 2 weeks
- Anterior/posterior inflammatory signs
- Poor visual recovery
- Steroid dependent
Patient JR

- 75 year old male

- 1/12 hx painless loss of vision in left eye

- PMH Nil
Patient JR

• O/E

6/9       6/36
L RAPD (grade 3)
6/9

6/36

SYPHILIS ?
Diagnosis?

- Syphilis ??
  - Serology positive for a recent infection
Disbelief!!

• GU medicine initially refused to accept patient
  – ‘75 year old cannot have a recently acquired syphilis infection’
Disbelief!!

• GU medicine initially refused to accept patient
  – ‘75 year old cannot have a recently acquired syphilis infection’

• Admitted to a visit to local sauna to celebrate 75th birthday
The EPIDEMIC

**Figure 2**

Diagnoses of Infectious syphilis* made in GUM clinics, United Kingdom, 1995-2003†

* Infectious syphilis constitutes primary, secondary and early latent syphilis
† Data source: routine surveillance data, apart from Scotland for 2001, 2002 and 2003 where routine data were not available and data from the enhanced surveillance were used.
How non-typical was this?

- Age
- Bilateral
- Painless visual loss..
- ..over 1 month
- More swollen nerve had better vision
Investigations for non-typical optic neuritis

- FBC / Calcium
- LFT including GGT
- Glucose
- ESR / CRP / ?viscosity
- Cholesterol / triglycerides
- ANA / ACE / ANCA / RhF/dsDNA
- Anti-cardiolipin antibodies
- T.Pallidum / lymes / bartonella serology
- B1 B6 B12 Folate
- Immunoglobulins / Electrophoresis
- CXR / CT head / MRI head
- Leber’s mutations / OPA1
- LP
- Blood film
- T-spot
- Hu / Yo / Ri / LDH / PSA / PET scan
- Heavy metal screen
- Toxoplasma serology
- HIV / Hep A / Hep B
Investigations for non-typical optic neuritis

- **FBC / Calcium**
- LFT including GGT
- Glucose
- **ESR / CRP / ?viscosity**
- Cholesterol / triglycerides
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Patient RH

• 81 year old female ex-smoker

• 2009: Sudden painless loss of vision LE over night

• Bilateral pseudophake

• PMH  CCF / COPD
Patient RH

- O/E
  - 6/6 NPL
  - L RAPD
  - 16 T 16

- Left swollen disc
Patient RH

- O/E
  - 6/6 NPL
  - L RAPD
  - 16 T 16
  - Left swollen disc
  - ESR 83, CRP 139 (No symptoms of GCA)
Patient RH

- DD: AION ?arteritic
  - TABx negative

- Referred to myself
  - Steroids tapered
  - MRI head / carotid dopplers normal
3 months later: BAD

- Presented back with loss of vision in the other eye
- CF  NPL
- No RAPD
- Right swollen disc
3 months later

- ESR / CRP normal
- 2\textsuperscript{nd} TAB\textsubscript{x}  
  - ? Suggestive of healed GCA
- Steroids restarted
1 month further: REALLY BAD

- Urinary incontinence
- Bilateral leg weakness

- Spinal cord infarction
  - ? In context of active GCA
  - Admitted under neurology
• Bilateral sequential non-typical optic neuritis
• ‘Spinal cord process’
• A diagnostic test was performed
• Aquaporin 4 antibody POSITIVE

• Bilateral non-typical optic neuritis and transverse myelitis

= Devic’s disease
The Aquaporins

- Dr Peter Agre (Nobel laureate 2003)
  - Aquaporins – water channels
  - Allows movement of water only and blocks charged particles
Devic’s disease

- Bilateral sequential optic neuritis and transverse myelitis
- Demyelination
  - Respond to immunosuppression e.g. azathioprine
- Prognosis
Devic’s disease

• Aquaporin 4
Dovic's disease

- Anti-Aquaporin 4 antibody
- 75% sensitive
- 99% specific
Optic neuritis

• Recurrent unilateral optic neuritis
  – All other Ix normal
  – 25% Aq4 antibody positive
  – Positivity assoc with poor visual outcome

• Immunosuppression
  – Reduce risk of recurrence?
Optic neuritis

• Recurrent unilateral optic neuritis
  – All other lxa normal
  – 25% Aq4 antibody positive
  – Positivity assoc with poor visual outcome

• Immunosuppression
  – Reduce risk of recurrence?
  – Reduce risk of progressing to transverse myelitis and severe disability?
Aq4 ab – when to request

• Non-typical optic neuritis
• Recurrent optic neuritis
• Optic neuritis with poor visual outcome
Patient CM

- 45 year old male
- Oct 2009
  - 10/7 constriction of right visual field
  - 2/7 similar rapid constriction of left visual field
  - Painless / white eyes
Patient CM

- Tour guide at castle
- Homosexual monogamous relationship
- Resident in France 2004-2005
  - Endocarditis ?bug
  - Aortic valve replacement – warfarinised

- FH / POH / FOH
Patient CM

- 6/6 6/6
- Isihara 17/17 BE
- L RAPD
- Optic discs…
GFOV
Ix normals

- Syphilis IgM, IgG, VDRL (performed twice) - negative
- Serology for cryptococcus negative
- HIV test negative
- Toxoplasma and toxoxcara Ig negative
- Blood cultures negative
- CMV PCR negative
- Bartonella, Borrelia, Brucella negative
- EBV IgM negative
- HepB (active infection) negative, HepC negative

- U+E, ESR, LFT, Amylase, Calcium and albumin, phosphate normal
- B12 / Folate normal, Plasma Glucose 5
- Coag screen affected by warfarin
- Anticardiolipin negative, ANTI Hu,Yo and Ri negative, ANA / ENA neg, ANCA neg
- Serum ACE normal
- Protein electrophoresis normal

- LHON negative (for 4 point mutations)
- Throat swabs for beta-haem strep negative
- Throat swabs for influenza, parainfluenza, RSV and H1N1 negative
Ix normals CSF

- 2 L.Ps both with:
  - Normal CSF cytology, microscopy, culture, cell count
  - CSF T pallidum IgM and IgG negative
  - No OCB
  - Glucose 3.5 (both times)
  - Protein 0.44
  - PCR for enterovirus, HSV1, HSV2, Mumps and VZV negative
  - Mycobacterial culture negative
  - Microscopy for fungi - negative
  - Cryptococcal antigen test negative
Ix normals radiology

- MRI
- Normal CXR
- Normal echo of valves
Ix abnormals

- Hb 10, microcytic with low ferritin and low transferrin saturation
  - (starts Fe supplements)

- Investigated for RBC destruction in heart valve - reticulocyte count raised at 214 (25-85) but urinary haemosiderin negative

- Minimally low serum IgG 5.6 (6-11) - no OCB

- LDH 526 (208-460)

- CRP 27 at presentation

- Complement screen - mildly raised C3 1.76 (0.73 to 1.4)
Jan 2010

• 6/6 6/6
• 17/17 isihara 17/17
• No RAPD
• Pale, no longer swollen optic discs
October 2010

- Tried tapering steroids x2
- L RAPD recurs
- Fields deteriorate
- Steroid dependent
- Azathioprine
December 2010

• Stable
  – RV March 2011
Patient FC

• 64 year old male
• 2 years in France with his second wife
• Dec 2010
  – C/O peripheral constriction of visual field
O/E

- 6/6 6/5
- 13/13 Ishihara 13/13
- Pale swollen optic discs
- Mildly constricted fields
• All normal

• PO pred
March 2011

• Right hemicolecctomy
  – Occult Ca colon

• Brother died Ca colon 43 years old
Ix

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  (starts Fe supplements)

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- **LDH 526 (208-460)**

- CRP 27 at presentation

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March 2011

- Hereditary non-polyposis colorectal cancer syndrome
- Paraneoplastic optic neuropathy
Patient FC

- PET scan
Patient FC

- PET scan
- Metastatic prostate Ca
Paraneoplastic optic neuropathy

- Subacute painless bilateral – over days to months
- 50% patients present with known malignancy, 50% tumour is undiagnosed at presentation
Non-typical optic ‘neuritis’

- May be a form of optic neuritis
  - Only known in retrospect

- May not be optic neuritis at all
Patient HS

• Sept 07: from Eye casualty notes
  – Left side headaches and left blurred vision
  – GP Rx as sinusitis 1/52
  – FH glaucoma
  – PMH
    • IBS
Patient HS

- **O/E**
  - 6/6  6/9
  - 17/17 isihara  8/17
  - Left RAPD
  - Normal fundoscopy

- Typical optic neuritis - discharged
Patient HS
Patient HS

• October 2007
  – 3/12 hx headaches and deteriorating vision left eye
    • ‘headaches’ = left sided facial pain
Patient HS

- October 2007
  - VA 6/6  6/12
  - Isihara  17/17  0/17
  - Left RAPD
  - Fundus: mild temp pallor left

- Getting progressively worse over months
  - ?compression
Compressive optic neuropathy

• Anterior vs posterior compression

• Both cause
  – Mild reduction in acuity
  – Loss of colour vision
  – Proptosis
  – RAPD
Compressive optic neuropathy

• Anterior compression eg optic nerve sheath meningiomas
  – Disc swelling

• Posterior compression
  – No swelling
  – ‘Foggy’ ‘Dim’ vision
  – Slowly progressive
  – Can cause cupping
• Non-typical optic neuritis – appropriate treatment can be sight saving
  – Give steroids – also be sight saving
• Treatment may be life saving: Aq4 ab
• Fading vision over months ?compression
• Don’t forget syphilis
Typical optic neuritis…Do you scan?

• Optic neuritis ≠ MS

• No treatment – no scan

• MacDonald criteria
  – Plaques on scan of different ages in different places = other subclinical attacks
  – USA: Treat
Typical optic neuritis…Do you scan?

- Not in UK
  - Treat cumulative disability
- BENEFIT study
- IFN ‘snake oil’ backlash
Typical optic neuritis…Do you scan?

• Disease modifying treatments
  – Dimethyl fumarate (*Tecfidera*)
    • Fungicide in shoes
  – Fingolimod

• More confused…..