Optic Neuritis
The Lancet Neurology
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Disclosures

Stichting MS Research NL
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Novartis, Roche, Heidelberg Academy
The ICON 2022 story

Imaging of the optic nerve: technological advances and future prospects
The Lancet Neurology
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Optic neuropathies and autoimmune optic neuropathies: advances in diagnosis and treatment
Jeffrey L Bennett, Fiona Costello, John J Chen, Axel Petzold, Valérie Brousse, Nancy J Newman, Steven L Galetta
The Lancet Neurology
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Understanding the molecular basis and pathogenesis of hereditary optic neuropathies: towards improved diagnosis and management
Nancy J Newman, Patrick-Yu Wai-Man, Valérie Brousse, Valerio Carelli
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Position Paper
Diagnosis and classification of optic neuritis
Axel Petzold, Clare L Fraser, Mathias Albig, Raed Alroushani, Daniela Alischowo, Regina Alviaronga, and others
The Lancet Neurology
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PERSONAL VIEW
Myelin-oligodendrocyte glycoprotein antibody-associated disease
Romain Marignier, Yael Hacohen, Alvaro Cobo-Cobo, Anne-Katrin Pröbstel, Orhan Aktaş, Harry Alpers.., and others
The Lancet Neurology, Vol. 20, No. 9
Published: September 2021
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REVIEW
Mitochondrial disease in adults: recent advances and future promise
Vi Shiao Ng, Laurence A Blindoff, Gavraine S Gorman, Thomas Klöpstock, Cornelia Kombium, Michelangelo Mancuso, and others
The Lancet Neurology, Vol. 20, No. 7
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A Diagnosis of optic neuritis

- Diagnosis based on clinical assessment and paraclinical tests (panel 1)

(a) Subacute monocular loss of vision, dyschromatopsia, pain worsening on eye movements, RAPD + 1 paraclinical test
(b) Like (a) without pain + 2 paraclinical tests
(c) Like (a) or (b) but binocular (RAPD unreliable) + MRI and another paraclinical test

(d) Clinically seen in acute phase, with features of (a), (b), or (c), with fundus examination consistent with optic neuritis classical disease course and no available paraclinical tests
(e) Retrospective typical history + paraclinical test(s)

(f) Loss of vision with features from panel 3 being present that suggest alternative pathology and paraclinical tests showing alternative pathology

Definite optic neuritis
Possible optic neuritis
Not optic neuritis
ICON 2022 Classification

B Classification of optic neuritis

Level 1 dichotomisation to guide general management

- Optic neuritis
  - Autoimmune (usually relapsing)
  - Infectious or systemic (usually monophasic)

Level 2 consensus opinion

- AQP4-ON
- CRMP5-ON
- MOG-ON
- MS-ON
- SION
- RION
- CRION
- Infectious optic neuritis
  - Post-infectious optic neuritis
  - Post-vaccination optic neuritis (panel 4)
- Systemic disorders (panel 4)

Level 3 expert opinion

List of disorders that might in a future revision of the classification be considered to reach level 2 (appendix pp 23–25)
1st Case

- 34y old Caucasian female patient
- 7d RE pain, worsening on eye movements
- Dyschromatopsia & VA RE 6/9, LE 6/5
- Right RAPD
- Reports: fatigue, cognitive problems, urinary incontinence, depression
- PmHx: right sided numbness lasting 1m, 3y ago
- MRI: DIS & DIT & 3 Gd+ non-symptomatic lesions
2nd Case

- 28y old, Afrocaribbean male
- Painless loss of vision LE (6/38)
- Dyschromatopsia
- L RAPD
- Several steroid responsive episodes over ~20y fup
- OCT: pRNFL atrophy LE (IEPD >5%)
- MRI a swollen, Gd+, left optic nerve. Brain & spinal cord normal
- AQP4 seropositive
3rd Case

- 72 year old male develops febrile illness in Vietnam
- 2-3 weeks later bilateral, sequential, painless loss of vision (PL)
- no RAPD (but both pupils constrict with accommodation)
- Fundus:
  - Bilateral disc edema
  - RE hemorrhages
  - LE macular scar, CMO
- No recovery @ 6m fup (IVMP given ~6w after onset)
3 Scenarios

● **Case 1: is this MS?**
  
  **Scenario A**: painful, monocular, subacute LOV, dyschromatopsia, RAPD

● **Case 2: is this NMO?**
  
  **Scenario B**: no pain, monocular, subacute LOV, dyschromatopsia, RAPD

● **Case 3: what is this?**
  
  **Scenario C**: binocular, subacute LOV, dyschromatopsia, no pain, RAPD unreliable
Panel 1: Diagnostic criteria for optic neuritis

Clinical criteria
- A: Monocular, subacute loss of vision associated with orbital pain worsening on eye movements, reduced contrast and colour vision, and relative afferent pupillary deficit
- B: Painless with all other features of (A).
- C: Binocular loss of vision with all features of (A) or (B).

Paraclinical criteria
- OCT: Corresponding optic disc swelling acutely or an inter-eye difference in the mGCIPL of >4% or >4 μm or in the pRNFL of >5% or >5 μm within 3 months after onset.
- MRI: Contrast enhancement of the symptomatic optic nerve and sheaths acutely or an intrinsic signal (looking brighter) increase within 3 months.
- Biomarker: AQP4, MOG, or CRMP5 antibody seropositive, or intrathecal CSF IgG (oligoclonal bands).

Application of the clinical and paraclinical criteria

Definite optic neuritis
- (A) and one paraclinical test
- (B) and two paraclinical tests of different modality
- (C) and two different paraclinical tests of which one is MRI

Possible optic neuritis
- (A), (B), or (C) if seen acutely but in absence of paraclinical tests, with fundus examination typical for optic neuritis and consistent with the natural history during follow-up
- Positive paraclinical test or tests, with a medical history suggestive of optic neuritis
OCT in MS-ON

pRNFL atrophy

TLN 2010

20.10 (17.44-22.76) µm

TLN 2017

20.38 (17.91-22.86) µm
4th Case

- 37 y old woman 18 month ago
  - expanding central scotoma
  - Periocular pain, score 9/10
  - Photo phobia
- Headaches improved with topiramate
- Visual function with 3 more attacks:
  - BCVA RE 6/9.5, LE 6/24
  - Normal colour vision
  - Left RAPD
4th Case

PmHx:
● Recurrent oral ulcers for 9 years
● Erythematous digital nodules & facial rash
● Musculoskeletal pain & fatigue
● GI problems (bloating, diarrhoea, steatorrhoea)

Management in referring hospital:
● High dose IV corticosteroids repeatedly for suspected relapsing optic neuritis & repeat MRI
MRI

1st attack L ON

2nd attack L ON

3rd attack L ON

4th attack L ON
OCT

IEPD macular = 2.5% (less than the 4% required)
IEPD disc = 3% (less than the 5% required)
4th Case

- ICON 2022: not optic neuritis
  - Not clinically
  - Not with para-clinical tests
- Dx: acute L superior BRVO pattern recognition on OCT
- DD: Behçet’s disease
- National Behçet’s Centre @Birmingham
Outlook

REVIEW

Artificial intelligence extension of the OSCAR-IB criteria

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5th case

- 32 year old woman with RRMS
- Natalizumab for > 10 years
- Develops progressive cloudy vision in right eye
- Started on corticosteroids for suspected MS-ON
- MRI: no enhancement of right optic nerve, no new lesions
- Vision continues to worsen (HM)
- 22 days after onset seen @MEH
- OCT: ...
- 5th case: VZV vitritis
- Observation: 1.71%
- Routine: 24.09%
- Semi-Urgent: 46.39%
- Urgent: 27.80%
Summary

- Clinical approach to ON differential diagnosis
- ICON 2022 Diagnostic Criteria
- ICON 2022 Classification
- 5 Cases: 4 not MS-ON
  - 3 clinical scenarios
- Outlook: AI, pattern recognition, non-supervised learning, EUNOS 2024
Wielkie dzięki