Azienda Ospedaliera Nazionale
SS. Antonio e Biagio e Cesare Arrigo
Alessandria

A case of chronic relapsing inflammatory optic neuropathy in a young girl: which diagnosis?

D. Ferrandi, G. Ursino*, R. Bottaro*, M. Melato*, M. Mascolo*, E. Fiorina*, M. Palermo*, C. Prevost*, F. Passantino*, R. Schizzi^, L. Ruiz**
*Department of Neurology, ^ Department of Neuroradiology. SS Antonio and Biagio Hospital, ASO Alessandria

BACKGROUND

Chronic relapsing inflammatory optic neuropathy (CRION) is an entity described in 2003. The question has arisen over the last ten years, if CRION was part of NMO spectrum disease. A recent review demonstrated that CRION is a nosological distinct entity. The proposed diagnostic criteria are: ON and at least one relapse; objective evidence for loss of visual function; NMO-IgG seronegative; contrast enhancement of the acutely inflamed optic nerves; response to immunosuppressive treatment and relapse on withdrawal or dose reduction of immunosuppressive treatment

DIAGNOSTIC CRITERIA - CRION vs NMO

CRION

1) **History: ON and at least one relapse**
2) **Clinical: Objective evidence for loss of visual function**
3) **Labor: NMO-IgG seronegative**
4) **Imaging: Contrast enhancement of the acutely inflamed optic nerves**
5) **Treatment: Response to immunosppressive treatment and relapse on withdrawal or dose reduction of immunosppressive treatment**

Table 1 NMOSD diagnostic criteria for adult patients

Diagnostic criteria for NMOSD with AQP4-IgG
1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses[a]

Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status
1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
   b. Dissemination in space (2 or more different core clinical characteristics)
   c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses[a]

Core clinical characteristics
1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions (figure 3)
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions (figure 3)

Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status
1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm (figure 1)
2. Acute myelitis: requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM) OR ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis (figure 1)
3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions (figure 2)
4. Acute brainstem syndrome: requires associated periependymal brainstem lesions (figure 2)

Abbreviations: AQP4 = aquaporin-4; IgG = immunoglobulin G; LETM = longitudinally extensive transverse myelitis lesions; NMOSD = neuromyelitis optica spectrum disorders.
[a] See table 2 and text discussion on serologic considerations for recommendations regarding interpretation of clinical and serologic testing.

CASE REPORT

A 30 year's old girl presented a loss of vision in left eye and pain **not responsive to i.v. steroids** in 2009, hesitated with a deficit of the lower altitude visual field. Several years later she presented to our attention again **with acute onset loss of vision in the right eye associated with pain during ocular movement**. No other neurological deficits on examination. Several investigations were performed: haematological screening for immuno-mediated diseases, Aquaporin-4 autoantibodies (AQP4) and NMO, Myelin oligodendrocyte glycoprotein antibodies (MOG) were all negative. Visual Evoked potential: P100 with increased latency and irregular morphology in the right eye (Fig 1). Fluoroangiography: normal pattern in the right eye, in the left eye marked hypo-fluorescence of the optical papilla in atrophic issue. Brain, cervical and dorsal MRI: normal (Fig 2). Visual Field: lower altitude defect in the right eye. Fundus Oculi: bilateral diffuse slight pallor, oedema RNFL 1+. Optical disc: small bilateral excavation in optic disk. OCT: Increased thickness in right eye, reduced in left eye. CSF examination (normal), genetic test for Leber disease in progress. The patient was first treated with high doses of methilprednisolone i.v. for 5 days without response, then with 5 days of i.v. Ig (0,4g/Kg/die) with no response.

Fig 1: Visual evoked potential

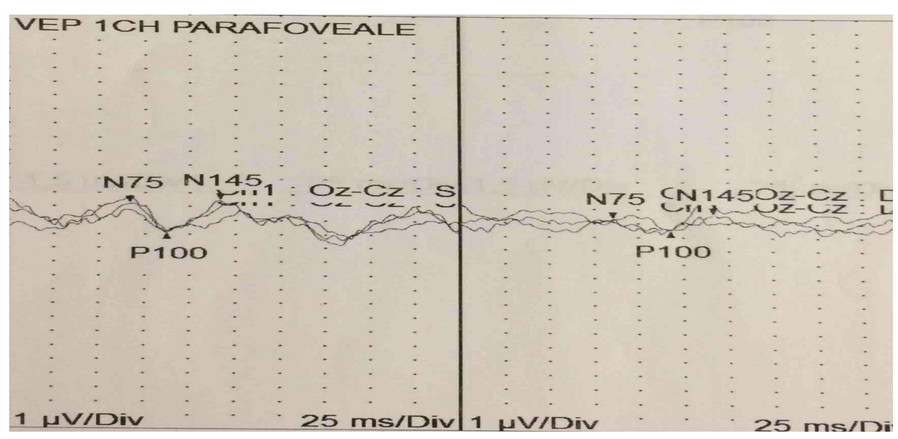
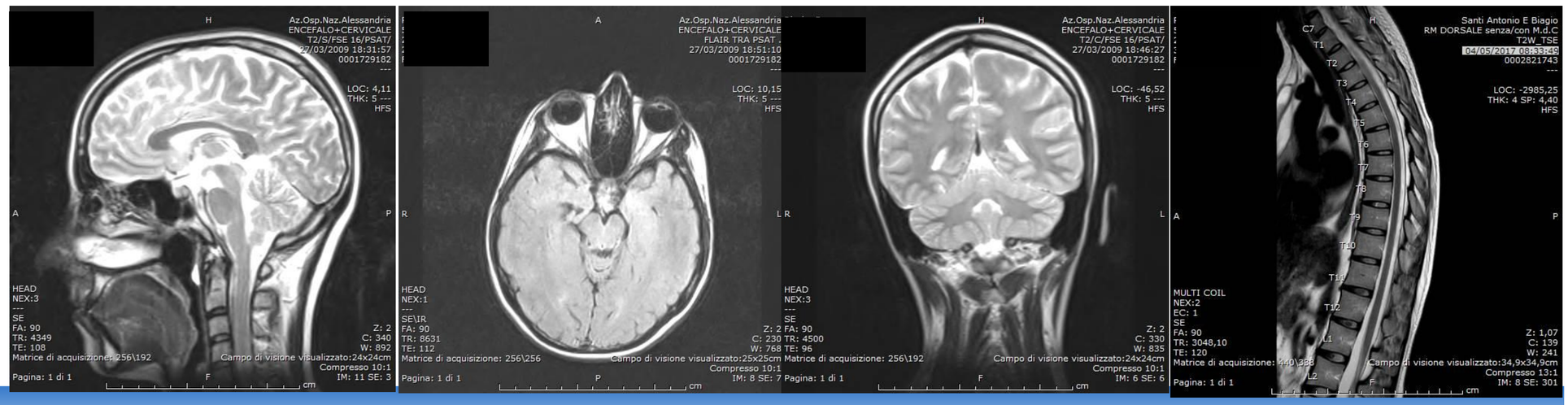


Fig 2 Normal brain, cervical and dorsal MRI



DISCUSSION

In this case the clinical and instrumental picture are unclear. Clinically the most likely hypothesis is that it can be a CRION, even if there was a poor response to steroid therapy. What casts doubt on the diagnosis of NMO is the negativity of AQP4 and the absence of spinal cord injuries after a long time from the first ON. The others hypothesis we have taken into consideration were a genetic entity (Leber optic neuropathy, however unlikely because usually not painful and more frequent in male) and ischemic optic neuropathy due to anatomical features of the optical disk (very rare in young people and not painful). **Recurrent consecutive optic neuropathy is a diagnostic challenge for clinicians**. An extensive clinical and instrumental evaluation is necessary to achieve a correct diagnosis excluding the more frequent and known pathologies. Often diagnosis remain uncertain.