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LE PATOLOGIE DELLA MIELINA: GLI STRUMENTI PER LA DIAGNOSI DIFFERENZIALE

Le patologie della Mielina: diagnosi differenziale delle malattie del SNC

ALGORITMO DIAGNOSTICO E RICADUTE TERAPEUTICHE

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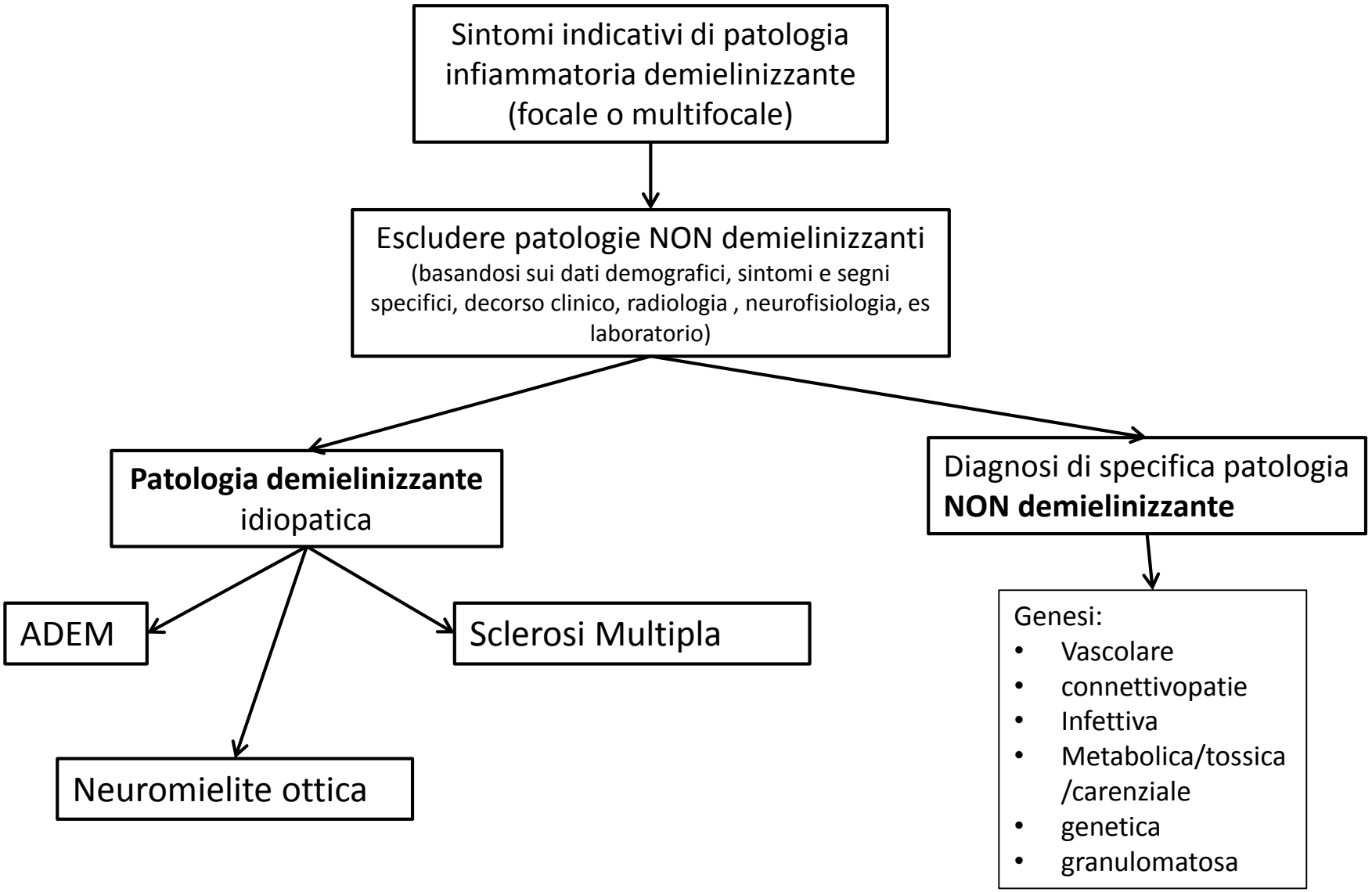
DIAGNOSI DIFFERENZIALE PATOLOGIE DEMIELINIZZANTI



Differential diagnosis of suspected multiple sclerosis: a consensus approach

Multiple Sclerosis 2008; **14**: 1157–1174 Miller et al

Table 1 Diagnoses and syndromes mistaken for multiple sclerosis

	No. (%)
Migraine alone or in combination with other diagnoses	24 (22)
Fibromyalgia	16 (15)
Nonspecific or nonlocalizing neurologic symptoms with abnormal MRI	13 (12)
Conversion or psychogenic disorder	12 (11)
Neuromyelitis optica spectrum disorder	7 (6)
Clinically isolated syndrome	3 (3)
Neurodegenerative cerebellar syndrome	2 (2)
MRI changes caused by vascular disease	2 (2)
Parkinsonism with nonspecific white matter abnormalities	2 (2)
"Radiologically isolated syndrome"	2 (2)
Cervical spondylosis with myelopathy	2 (2)
Genetic leukodystrophy	2 (2)
Idiopathic transverse myelitis	2 (2)
Noninflammatory myelopathy	2 (2)
Nonspecific symptoms with positive CSF OCBs	2 (2)
Stroke, nonembolic	2 (2)
Anti-Ma2 paraneoplastic syndrome	1 (1)
Acute disseminated encephalomyelitis	1 (1)
Astrocytoma	1 (1)
Mitochondrial disorder	1 (1)
Neurosarcoidosis	1 (1)
Moyamoya disease	1 (1)
Hypertension and alcohol abuse	1 (1)
Neuropathy	1 (1)
Unclear diagnosis; complaints of paresthesias	1 (1)
Nonspecific or nonlocalizing neurologic symptoms with normal MRI	1 (1)
Viral meningoencephalitis with subsequent abnormal MRI and acute labyrinthitis	1 (1)
White matter lesions due to TNF-α inhibitor use for psoriasis	1 (1)
Behçet syndrome	1 (1)
CADASIL	1 (1)
Degenerative joint disease of lumbar spine	1 (1)

The contemporary spectrum of multiple sclerosis misdiagnosis

A multicenter study

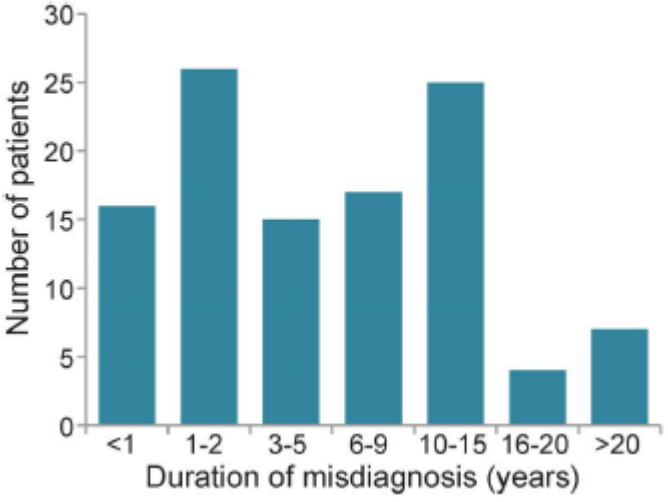
Neurology® 2016;87:1393-1399

Solomon et al.

Identificati 110 pazienti con diagnosi errata di SM, afferenti a 4 poli ospedalieri/universitari americani

non nota la percentuale di diagnosi errate- non ricavabile per il tipo di studio (affermazione esplicitata dagli autori)

Durata di diagnosi errata



The contemporary spectrum of multiple sclerosis misdiagnosis

A multicenter study

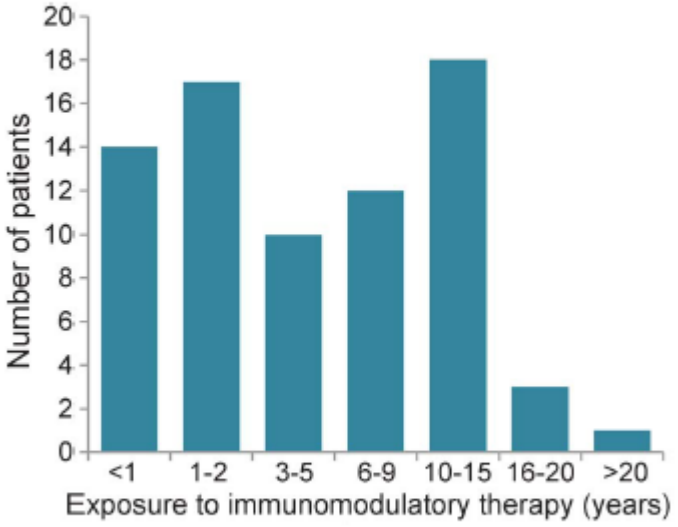
Neurology® 2016;87:1393-1399

Solomon et al.

tp immunomodulanti somministrate erroneamente

	No. (%)
Interferon beta-1a or interferon beta-1b	58 (53)
Glatiramer acetate	44 (40)
Natalizumab	14 (13)
Dimethyl fumarate	7 (6)
Fingolimod	5 (5)
Teriflunomide	3 (3)
Mitoxantrone	2 (2)
Cyclophosphamide	1 (1)
IV immunoglobulin	1 (1)
Repository corticotropin injection	1 (1)
Unknown	1 (1)

Anni di esposizione a tp immunomodulante



The cumulative number of years misdiagnosed patients had been exposed to any immunomodulatory therapy.

Table 3 Contributors to MS misdiagnosis

	Yes	No	Unknown
	n (%)	n (%)	n (%)
Inappropriate application to MS diagnostic criteria of neurologic symptoms atypical for a demyelinating attack	72 (65)	24 (22)	14 (13)
Inappropriate application to diagnostic criteria of a historical episode of neurologic dysfunction without corroborating objective evidence of a lesion (on neurologic examination, evoked potentials, or imaging)	53 (48)	38 (35)	19 (17)
Overreliance on the presence of MRI abnormalities meeting DIS to confirm a diagnosis of MS in a patient with "nonspecific neurologic symptoms"	66 (60)	28 (25)	16 (15)
Erroneous determination of juxtacortical or periventricular lesion location to fulfill DIS	36 (33)	43 (39)	31 (28)
Erroneous determination of DIT because of variability of MRI slice orientation (i.e., MRIs performed on different scanners leading to the appearance of new lesions)	13 (12)	64 (58)	33 (30)

REVIEW Multiple Sclerosis 2008; 14: 1157–1174

Differential diagnosis of suspected multiple sclerosis: a consensus approach

DH Miller[1], BG Weinshenker[2], M Filippi[3], BL Banwell[4], JA Cohen[5], MS Freedman[6], SL Galetta[7], M Hutchinson[8], RT Johnson[9], L Kappos[10], J Kira[11], FD Lublin[12], HF McFarland[13], X Montalban[14], H Panitch[15], JR Richert[16], SC Reingold[16,17] and CH Polman[18]

Gruppo internazionale di esperti di Sclerosi Multipla focalizzato sulla diagnosi differenziale di SM.
Diagnosi di SM prevede l'esclusione di altre patologie che potrebbero meglio giustificare segni e sintomi

Raccomandazioni:

1. «**red flags**» cliniche e paracliniche indicative di diagnosi alternative di SM
2. Definizione più precisa di **CIS** e algoritmi diagnostici
3. Classificazione e diagnosi per altre **patologie infiammatorie demielinizzanti** del SNC

Identificati 79 CAMPANELLI D'ALLARME- RED FLAGS
Indicativi di DIAGNOSI ALTERNATIVE

Caratteristiche :

- Cliniche
- demografiche
- Laboratoristiche
- radiologiche

Ognuno di qs è stato valutato da 6 sottogruppi della Commissione con punteggi:

- 1-2: basso rischio di una diagnosi alternativa
- 3: intermedio
- 4-5: elevata probabilità di una diagnosi alternativa

Per ognuno è stato calcolato la deviazione standard

MAJOR RED FLAGS

Red flag	Type	Total score	SD	Red flag[a]	Examples of alternative diagnosis
Bone lesions	Clinical	30	0.00	Major	Histiocytosis; Erdheim Chester disease
Lung involvement	Clinical	30	0.00	Major	Sarcoidosis; Lymphomatoid granulomatosis
Multiple cranial neuropathies or polyradiculopathy	Clinical	30	0.00	Major	Chronic meningitis, including sarcoidosis and tuberculosis; Lyme disease
Peripheral neuropathy	Clinical	30	0.00	Major	B12 deficiency; adrenoleukodystrophy; metachromatic leukodystrophy, Lyme disease
Tendon xanthomas	Clinical	30	0.00	Major	Cerebrotendinous xanthomatosis
Cerebral venous sinus thrombosis	MRI	30	0.00	Major	Behçet's disease; vasculitis; chronic meningitis, antiphospholipid or anticardiolipin antibody syndromes
Cardiac disease	Clinical	29	0.41	Major	Multiple cerebral infarcts; brain abscesses with endocarditis or right to left cardiac shunting
Myopathy	Clinical	29	0.41	Major	Mitochondrial encephalomyopathy (e.g., MELAS); Sjögren's syndrome
Renal involvement	Clinical	29	0.41	Major	Vasculitis; Fabry disease, systemic lupus erythematosus
Cortical infarcts	MRI	29	0.41	Major	Embolic disease; thrombotic thrombocytopenic purpura; vasculitis
Hemorrhages/ microhemorrhages	MRI	29	0.41	Major	Amyloid angiopathy; Moya Moya disease; CADASIL; vasculitis
Meningeal enhancement	MRI	29	0.41	Major	Chronic meningitis; sarcoidosis; lymphomatosis; CNS vasculitis
Extrapyramidal features	Clinical	28	0.52	Major	Whipple's disease; multisystem atrophy; Wilson's disease
Livedo reticularis	Clinical	28	0.52	Major	Antiphospholipid antibody syndrome; systemic lupus erythematosus; Sneddon's syndrome
Retinopathy	Clinical	28	0.52	Major	Mitochondrial encephalomyopathy; Susac, and other vasculitides (retinal infarction); neuronal ceroid lipofuscinosis
Calcifications on CT scans	MRI	28	0.52	Major	Cysticercosis; toxoplasmosis, mitochondrial disorders
Diabetes insipidus	Clinical	28	0.82	Major	Sarcoidosis; histiocytosis; neuromyelitis optica
Increase serum lactate level	Clinical	27	0.55	Major	Mitochondrial disease
Selective involvement of the anterior temporal and inferior frontal lobe	MRI	27	0.55	Major	CADASIL

Red flag	Type	Total score	SD	Red flag[a]	Examples of alternative diagnosis
Hematological manifestations	Clinical	27	0.84	Major	Thrombotic thrombocytopenic purpura; vitamin B12 deficiency; Wilson's disease (hemolytic anemia); copper deficiency
Lacunar infarcts	MRI	27	0.84	Major	Hypertensive ischemic disease; CADASIL; Susac syndrome
Persistent Gd-enhancement and continued enlargement of lesions	MRI	27	0.84	Major	Lymphoma; glioma; vasculitis; sarcoidosis
Mucosal ulcers	Clinical	27	1.22	Major	Behçet's disease
Myorhythmia	Clinical	27	1.22	Major	Whipple's disease
Hypothalamic disturbance	Clinical	26	0.52	Major	Sarcoidosis; neuromyelitis optica; histiocytosis
Recurrent spontaneous abortion or thrombotic events	Clinical	26	0.52	Major	Antiphospholipid antibody syndrome; thrombotic thrombocytopenic purpura; metastatic cancer with hypercoagulable state
Simultaneous enhancement of all lesions	MRI	26	0.52	Major	Vasculitis; lymphoma; sarcoidosis
Rash	Clinical	26	0.82	Major	Systemic lupus erythematosus; T-cell lymphoma; Lyme disease, Fabry disease
T2-hyperintensity in the dentate nuclei	MRI	26	0.82	Major	Cerebrotendinous xanthomatosis
Arthritis, polyarthalgias, myalgias	Clinical	26	1.63	Major	Systemic lupus erythematosus; Lyme disease; fibromyalgia
Amyotrophy	Clinical	25	0.75	Major	Amyotrophic lateral sclerosis; syringomyelia; polyradiculpathy
Headache or meningismus	Clinical	25	0.98	Major	Venous sinus thrombosis; chronic meningitis; lymphoma or glioma, vasculitis, systemic lupus erythematosus
T1-hyperintensity of the pulvinar	MRI	25	0.98	Major	Fabry disease; hepatic encephalopathy; manganese toxicity
Persistently monofocal manifestations	Clinical	24	0.63	Major	Structural lesion (e.g., Chiari malformation); cerebal neoplasm
Large and infiltrating brainstem lesions	MRI	24	1.10	Major	Behçet's disease; pontine glioma
Predominance of lesions at the cortical/subcortical	MRI	23	0.41	Major	Embolic infarction; vasculitis; progressive multifocal leukoencephalopathy

INTERMEDIATE RED FLAGS

Red flag	Type	Total score	SD	Red flag[a]	Examples of alternative diagnosis
Hydrocephalus	MRI	23	0.98	Intermediate	Sarcoidosis or other chronic meningitis; lymphoma or other CNS neoplasm
Punctiform parenchymal enhancement	MRI	23	0.98	Intermediate	Sarcoidosis; vasculitis
Sicca syndrome	Clinical	23	1.33	Intermediate	Sjögren's syndrome
T2-hyperintensities of U-fibers at the vertex, external capsule and insular regions	MRI	22	1.37	Intermediate	CADASIL
Gastrointestinal symptoms	Clinical	22	1.51	Intermediate	Whipple's disease; celiac disease and other malabsorptive states that lead to B12 or copper deficiency
Regional atrophy of the brainstem	MRI	21	0.55	Intermediate	Behçet's disease; adult onset Alexander's disease
Diffuse lactate increase on brain MRS	MRI	21	0.84	Intermediate	Mitochondrial disease
Marked hippocampal and amygdala atrophy	MRI	21	0.84	Intermediate	Hyperhomocystinemia
Loss of hearing	Clinical	21	1.38	Intermediate	Susac's syndrome; glioma; vertebrobasilar infarction
Fulminant course	Clinical	20	0.82	Intermediate	Thrombotic thrombocytopenic purpura; intravascular lymphoma; acute disseminated encephalomyelitis
Symmetrically distributed lesions	MRI	20	0.82	Intermediate	Leukodystrophy
T2-hyperintensities of the basal ganglia, thalamus and hypothalamus	MRI	20	1.03	Intermediate	Behçet's disease; mitochondrial encephalomyopathies; Susac's syndrome; acute disseminated encephalomyelitis
Diffuse abnormalities in the posterior columns of the cord	MRI	20	1.37	Intermediate	B12 deficiency; copper deficiency; paraneoplastic disorder
Increase serum ACE level	Clinical	20	1.86	Intermediate	Sarcoidosis; histiocytosis
Prominent family history	Clinical	19	0.41	Intermediate	Depending on pattern of inheritance suggested by family history: hereditary spastic paraparesis; leukodystrophy; Wilson's disease; mitochondrial disorder; CADASIL

Red flag	Type	Total score	SD	Red flag[a]	Examples of alternative diagnosis
Constitutional symptoms	Clinical	19	1.17	Intermediate	Sarcoidosis; Whipple's disease, vasculitis
Lesions across GM/WM boundaries	MRI	19	1.17	Intermediate	Hypoxic-ischemic conditions; vasculitis; systemic lupus erythematosus
T2-hyperintensities of the temporal pole	MRI	19	1.17	Intermediate	CADASIL
Complete ring enhancement	MRI	18	0.63	Intermediate	Brain abscess; glioblastoma; metastatic cancer
Progressive ataxia alone	Clinical	18	1.10	Intermediate	Multisystem atrophy; hereditary spinocerebellar ataxia; paraneoplastic cerebellar syndrome
Central brainstem lesions	MRI	17	0.75	Intermediate	Central pontine myelinolysis; hypoxic-ischemic conditions; infarct
Predominant brainstem and cerebellar lesions	MRI	17	0.75	Intermediate	Behçet's disease; pontine glioma
Neuropsychiatric syndrome	Clinical	17	1.33	Intermediate	Susac's syndrome; systemic lupus erythematosus; Wilson's disease, GM2 gangliosidosis
Lesions in the center of CC, sparing the periphery	MRI	17	1.33	Intermediate	Susac's syndrome
Seizure	Clinical	16	1.63	Intermediate	Whipple's disease; vasculitis; metastases
Dilation of the Virchow-Robin spaces	MRI	15	0.55	Intermediate	Hyperhomocystinemia ; primary CNS angiitis
Uveitis	Clinical	15	0.84	Intermediate	Sarcoidosis; lymphoma; Behcet's disease
Cortical/subcortical lesions crossing vascular territories	MRI	14	1.21	Intermediate	Ischemic leukoencephalopathy; CADASIL; vasculitis
Pyramidal motor involvement alone	Clinical	13	0.75	Intermediate	Primary lateral sclerosis variant of ALS; hereditary spastic paraparesis
Large lesions with absent or rare mass effect and enhancement	MRI	13	0.98	Intermediate	Progressive multifocal leukoencephalopathy
Gradually progressive course from onset	Clinical	13	1.17	Intermediate	HTLV-1 associated myelopathy; adrenomyeloneuropathy; adrenoleukodystrophy; metachromatic leukodystrophty, B12 deficiency
No "occult" changes in the NAWM	MRI	13	1.33	Intermediate	Lyme disease, isolated myelitis, CADASIL

MINOR RED FLAGS

Red flag	Type	Total score	SD	Red flag[a]	Examples of alternative diagnosis
No spinal cord lesions	MRI	10	0.52	Minor	Multiple infarcts; vasculitis; progressive multifocal leukoencephalopathy
Abrupt onset	Clinical	11	1.17	Minor	Cerebral infarction; cerebral hemorrhage; cerebral venous sinus thrombosis
Large lesions	MRI	11	0.75	Minor	Glioblastoma; lymphoma; progressive multifocal leukoencephalopathy
No T1 hypointense lesions (black holes)	MRI	11	0.75	Minor	Ischemic degenerative leukoencephalopathy; progressive multifocal leukoencephalopathy
Onset after age 50	Clinical	12	0.89	Minor	Cerebral infarction; amyloid angiopathy; lymphoma
Marked asymmetry of WM lesions	MRI	12	0.89	Minor	Glioblastoma; lymphoma; cerebral infarction
Brainstem syndrome	Clinical	7	0.41	Minor	Pontine glioma; cavernous angioma; vertebrobasilar ischemia
No enhancement	MRI	8	0.52	Minor	Progressive multifocal leukoencephalopathy; ischemic lesions; metachromatic leukodystrophy
Myelopathy alone	Clinical	9	0.55	Minor	Chiari type 1 malformation; cord compression including cervical spondylosis; B12 or copper deficiency; HTLV1
No optic nerve lesions	MRI	9	0.55	Minor	Metastatic carcinoma; gliomatosis cerebri; toxoplasmosis
Onset before age 20	Clinical	10	0.52	Minor	Mitochondrial encephalomyopathy; leukodystrophy; Friedrich's ataxia

Criteri diagnostici SCLEROSI MULTIPLA Mc Donald 2010

At least two attacks with objective clinical evidence of at least two lesions
None

At least two attacks with objective clinical evidence of one lesion
Dissemination in space shown by:
- At least one T2 lesion in at least two of four areas of the CNS typically affected in demyelination: periventricular, juxtacortical, infratentorial, and spinal cord
- Further clinical attack at a different site

One attack with objective clinical evidence of at least two lesions
Dissemination in time shown by:
- Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions on a single scan or a new T2 and/or gadolinium-enhancing lesion on follow-up MRI
- Second clinical attack

One attack with objective clinical evidence of one lesion
Dissemination in space shown by:
- At least one T2 lesion in at least two of four areas of the CNS typically affected in demyelination: periventricular, juxtacortical, infratentorial, and spinal cord
- Second clinical attack at a different site

Dissemination in time shown by:
- Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions on a single scan or a new T2 and/or gadolinium-enhancing lesion on follow-up MRI
- Second clinical attack

1 year of disease progression (retrospectively or prospectively determined)
Presence of two of:
- At least one T2 brain lesion in at least one multiple sclerosis-characteristic region: periventricular, juxtacortical, or infratentorial
- At least two T2 spinal cord lesions
- Positive CSF (at least two oligoclonal bands not present in serum, elevated IgG index, or both)

Modified from Polman and colleagues.[1]

The contemporary spectrum of multiple sclerosis misdiagnosis

A multicenter study *Neurology®* 2016;87:1393-1399 Solomon et al.

Diagnosi di sclerosi multipla:
Sintomi e segni neurologici che dimostrano la disseminazione nello spazio e nel tempo delle lesioni

- in caso di lesioni tipiche con sindrome tipica **RMN** è sufficiente per confermare la diagnosi
- alcuni pazienti necessitano di **esame LCR e test neurofisiologici**

- **Ma.. No better explanation**

Criteri di DISSEMINAZIONE NELLO SPAZIO (DIS) proposti da MAGNIMS

DIS può essere dimostrata dal coinvolgimento* almeno di 2 di 5 aree del SNC
> o = 3 lesioni periventricolari
> o = 1 lesione sottotentoriale
> o = 1 lesione midollo spinale
> o = 1 lesione **nervo ottico**
> o = 1 lesione **corticale**/iuxtacorticale §

* Se un paziente presenta una sindrome midollare o del tronco encefalo, o la neurite ottica, le **lesioni sintomatiche non** vengono escluse dai criteri e contribuiscono al conto delle lesioni

§ nuove sequenze di RMN sono state proposte per meglio evidenziare le lesioni corticali Double Inversion recovery DIR e phase sensitive inversion recovery PSIR

Tali criteri devono essere utilizzati sia per la forma recidivante/remittente (RR) che primariamente progressiva (PP)

MRI CRITERIA FOR THE DIAGNOSIS OF MULTIPLE SCLEROSIS: MAGNIMS CONSENSUS GUIDELINES

Lancet Neurol. 2016 March ; 15(3): 292–303.

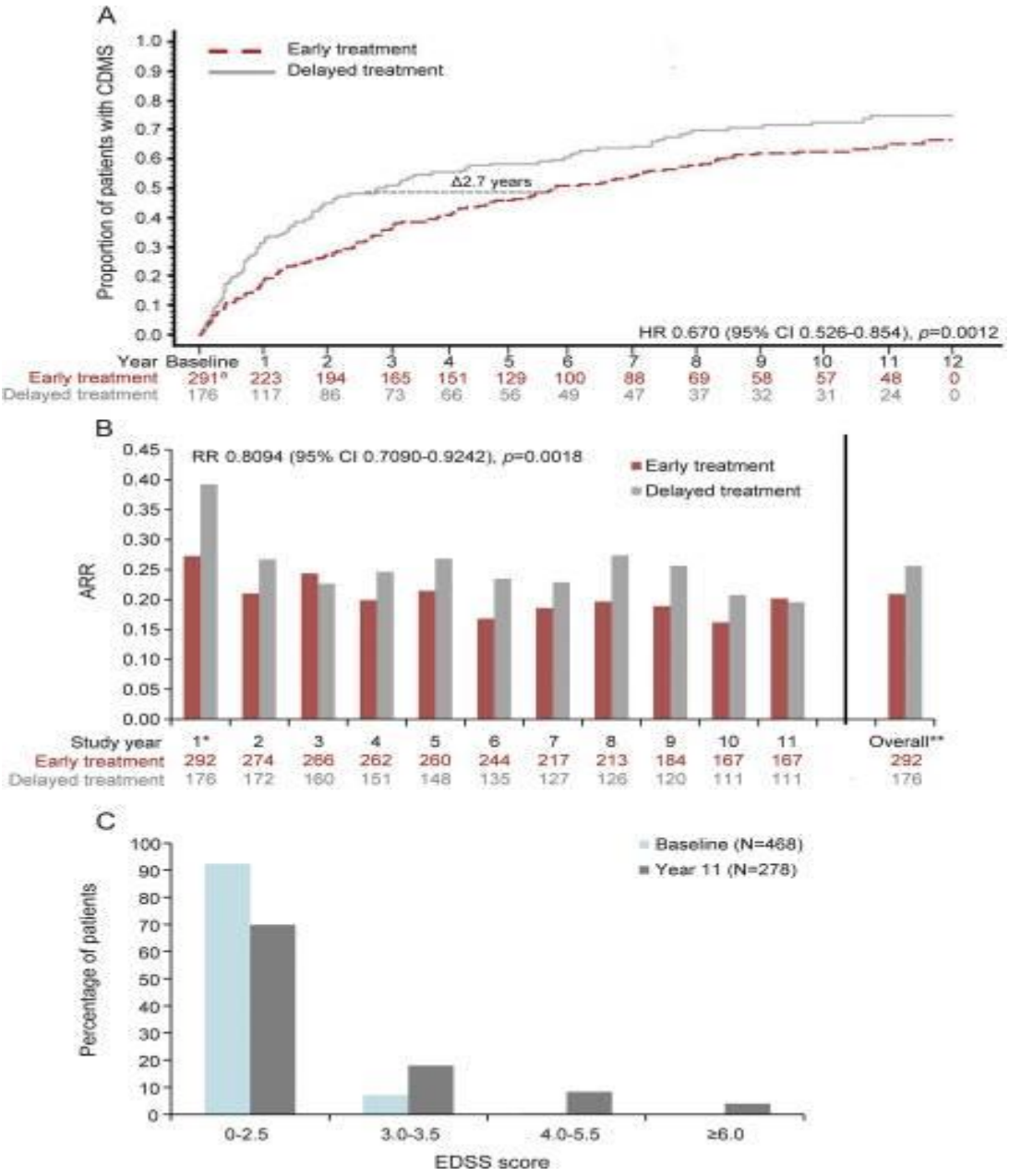
Studi placebo-controllo in pazienti con primo episodio clinico suggestivo di SM

	CHAMPS[5]	ETOMS[2]	BENEFIT[6]	PreCISe[3]	REFLEX[4]	ORACLE
Study design						
Treatment groups	Intramuscular interferon beta-1a 30 µg once a week (n=193); placebo (n=190)	Subcutaneous interferon beta-1a 22 µg once a week (n=154); placebo (n=155)	Subcutaneous interferon beta-1b 250 µg every other day (n=292); placebo (n=176)	Subcutaneous glatiramer acetate 20 µg once a day (n=243); placebo (n=238)	Subcutaneous interferon beta-1a 44 µg three times a week (n=175); subcutaneous interferon beta-1a 22 µg three times a week (n=171); placebo (n=171)	Oral cladribine 5·25 mg/kg cumulative dose (n=204); oral cladribine 3·5 mg/kg cumulative dose (n=206); placebo (n=206)
Switch to active treatment in patients who converted to multiple sclerosis in the placebo group	No: patients who converted were withdrawn	Optional: open-label subcutaneous interferon beta-1a 22 µg once a week	Yes: subcutaneous interferon beta-1b 250 µg every other day	Yes: subcutaneous glatiramer acetate 20 µg once a day	Yes: subcutaneous interferon beta-1a 44 µg three times a week	Yes: subcutaneous interferon beta-1a 44 µg three times a week (included patients from all treatment groups who converted)
Duration of double-blind period	Stopped after 18 month interim analysis	2 years	2 years	3 years	2 years	2 years; early termination
Primary endpoint	CDMS	CDMS	CDMS and McDonald MS (2001)	CDMS	McDonald MS (2005)	CDMS
Maximum time from FCDE to screening	27 days	3 months	60 days	90 days	60 days	75 days
Age range, years	18–50	18–40	18–45	18–45	18–50	18–55
Baseline characteristics						
Age, years	33 (7)	NR	NR	31 (7)	31 (8)	32 (9)
Time from FCDE to randomisation, days	19 (16–23)	NR	NR	74 (14)	58 (4)	79 (17)
Number of T1 gadolinium-enhancing lesions	NR	1 (0–3)	0·0 (0–1)	0 (0–20)*	0 (0–1)	0 (0–1)
Number of T2 lesions	NR	1 (0–3)	NR	22 (2–265)*	NR	18 (9–37)

Data are range, mean (SD), or median (IQR) unless otherwise stated. CDMS=clinically definite multiple sclerosis. FCDE=first clinical demyelinating event. NR=not reported. *Median (range).

***Table 5:* Overview of placebo-controlled trials in patients with a first clinical event suggestive of multiple sclerosis**

Effect of oral cladribine on time to conversion to clinically definite multiple sclerosis in patients with a first demyelinating event (ORACLE MS): a phase 3 randomised trial. Thomas P Leist et al. Lancet Neurol 2014; 13: 257–67



Studio Benefit a 11 anni Neurology 2016 sept 978-987

Cochrane Database Syst Rev. 2017 Apr

Treatment with disease-modifying drugs for people with a first clinical attack suggestive of multiple sclerosis.

Filippini G[1], Del Giovane C[2], Clerico M[3], Beiki O[4,5], Mattoscio M[6], Piazza F[3], Fredrikson S[4], Tramacere I[1], Scalfari A[6], Salanti G[7]

SELECTION CRITERIA:

We included randomised and observational studies that evaluated one or more drugs as monotherapy in adult participants with a first clinical attack suggestive of MS. We considered evidence on alemtuzumab, azathioprine, cladribine, daclizumab, dimethyl fumarate, fingolimod, glatiramer acetate, immunoglobulins, interferon beta-1b, interferon beta-1a (Rebif®, Avonex®), laquinimod, mitoxantrone, natalizumab, ocrelizumab, pegylated interferon beta-1a, rituximab and teriflunomide.

Studi dal 2010 al 2016

AUTHORS' CONCLUSIONS:

Very low-quality evidence suggests a small and uncertain benefit with early treatment compared with placebo in reducing disability-worsening and relapses. The advantage of early treatment compared with delayed on disability-worsening was heterogeneous depending on the actual drug used and based on very low-quality evidence. Low-quality evidence suggests that the chances of relapse are less with early treatment compared with delayed.

Early treatment reduced the hazard of conversion to CDMS compared either with placebo, no treatment or delayed treatment, both in short- and long-term follow-up. Low-quality evidence suggests that early treatment is associated with fewer participants with at least one serious AE compared with placebo.

Diagnosis of multiple sclerosis: progress and challenges

Wallace J Brownlee, Todd A Hardy, Franz Fazekas, David H Miller

Lancet 2017; 389: 1336–46

PRESENTAZIONI TIPICHE della forma recidivante remittente di SM

Panel 1: Typical presentations of relapsing-remitting multiple sclerosis and selected atypical or red flag presentations that are more suggestive of an alternative diagnosis

Typical presentations

- Acute unilateral optic neuritis
- Double vision due to an internuclear ophthalmoplegia or sixth nerve palsy*
- Facial sensory loss or trigeminal neuralgia*
- Cerebellar ataxia and nystagmus
- Partial myelopathy
- Sensory symptoms in a CNS pattern
- Lhermitte's symptom
- Asymmetric limb weakness
- Urge incontinence or erectile dysfunction

PRESENTAZIONI ATIPICHE
RED FLAGS

Atypical or red flag presentations

- Bilateral optic neuritis or unilateral optic neuritis with a poor visual recovery
- Complete gaze palsy or fluctuating ophthalmoparesis
- Intractable nausea, vomiting, or hiccups
- Complete transverse myelopathy with bilateral motor and sensory involvement
- Encephalopathy
- Subacute cognitive decline
- Headache or meningism
- Isolated fatigue or asthenia
- Constitutional symptoms

Diagnosi differenziale SM: patologie con decorso RECIDIVANTE REMITTENTE

	Clinical features	MRI findings	CSF findings	Other investigations
Neuromyelitis optica spectrum disorder	Optic neuritis, especially bilateral or with poor visual recovery; transverse myelitis; intractable nausea and vomiting; paroxysmal tonic spasms	Longitudinally extensive optic nerve lesions (involving >50% of the optic nerve) with or without extension into the optic chiasm; brain lesions in diencephalon, dorsal midbrain, or periependymal regions; cloud-like enhancement; longitudinally extensive spinal cord lesions extending over three or more vertebral segments	Mild CSF pleocytosis sometimes with neutrophils or eosinophils; OCBs present in 20% of patients	AQP4-IgG; MOG-IgG; sometimes OCT
Neurosarcoidosis	Optic neuropathy and myelopathy; facial palsy; early relapse after stopping steroids; with or without systemic involvement	Meningeal enhancement; enhancement of the optic nerve sheath; persistent, nodular enhancement within lesions; enlarged lacrimal glands	OCBs sometimes present; raised CSF ACE (not sensitive or specific for neurosarcoidosis)	Serum ACE concentration; chest radiograph, HRCT, lung function tests; CT/PET scan; slit-lamp examination; tissue biopsy
CNS vasculitis (primary or secondary)	Headache; acute CNS syndromes including hemiparesis and ataxia; early cognitive impairment; with or without systemic involvement	Punctate or larger lesions in the grey and white matter, often enhancing, sometimes with restricted diffusion and evidence of microhaemorrhages	OCBs sometimes present	Serum ANCA (systemic vasculitis); tissue biopsy at systemic site or brain biopsy (if possible)
Susac's syndrome	Encephalopathy, visual loss, deafness	"Snow-ball" lesions in the corpus callosum associated with restricted diffusion in the acute phase and then T1-hypointensity; also icicle and spoke lesions	OCBs usually absent	Fluorescein angiogram looking for branch retinal artery occlusions; OCT; audiometry
CADASIL	Migraine, especially with complex or prolonged aura; recurrent acute hemiparesis and other vascular syndromes; neuropsychiatric disturbance; dementia	Extensive white matter abnormalities; prominent involvement of the temporal poles and external capsule	OCBs absent	Testing for *NOTCH3* gene mutation; skin biopsy
Connective tissue disorders (systemic lupus erythematosus, Sjögren's syndrome, antiphospholipid syndrome)	Optic neuritis; longitudinally extensive transverse myelitis; systemic involvement; recurrent miscarriage, thrombosis (antiphospholipid syndrome)	Variable	OCBs usually absent	Serological testing: ANA, ENA, antiphospholipid antibodies; AQP4-IgG
Behçet's disease	Brainstem syndrome; myelopathy (rare); oral and genital ulceration; intraocular inflammation	Mass-like enhancing lesions, predilection for the midbrain, thalami, and internal capsules	Significant pleocytosis (white count >50 cells per cm^3), might be neutrophil predominant; OCBs usually absent	Pathergy testing; HLA typing
CLIPPERS	Subacute ataxia, double vision, and slurred speech; early relapse after stopping steroids	Punctate gadolinium-enhancing lesions within the brainstem and cerebellum; with or without lesions in the basal ganglia, supratentorial white matter, and spinal cord	OCBs sometimes present	Brain biopsy
Leber's hereditary optic neuropathy	Bilateral sequential optic neuropathies with poor visual recovery; more common in men than in women	Normal or might show white matter lesions (Harding's disease)	OCBs absent	Genetic testing

CSF=cerebrospinal fluid. OCBs=oligoclonal bands. AQP4=aquaporin 4. MOG=myelin oligodendrocyte glycoprotein. OCT=optical coherence tomography. ACE=angiotensin-converting enzyme. HRCT=high resolution CT. ANCA=antineutrophil cytoplasmic antibodies. CADASIL=cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy. ANA=antinuclear antibodies. ENA=extractable nuclear antigen. CLIPPERS=chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids.

Algoritmi diagnostici per le più comuni

CIS (Clinically Isolated Syndrome)

suggestive di SM

CIS in diagnosi differenziale con SM

Tipo 1 CIS: clinicamente monofocale, almeno 1 lesione asintomatica in RMN
Tipo 2 CIS: clinicamente multifocale, almeno 1 lesione asintomatica in RMN
Tipo 3 CIS: clinicamente monofocale, RMN potrebbe essere normale, nessuna lesione asintomatica in RMN
Tipo 4 CIS: clinicamente multifocale, RMN potrebbe essere normale, nessuna lesione asintomatica in RMN
Tipo 5 CIS: nessuna presentazione clinica di patologia demielinizzante, ma RMN suggestiva

Le lesioni presentano caratteristiche tipiche per demielinizzazione; localizzate a livello cerebrale o del midollo spinale

Differential diagnosis of suspected multiple sclerosis: a consensus approach
Multiple Sclerosis 2008; **14**: 1157–1174 Miller et al

NEURITE OTTICA

Tipico per SM

- Perdita di visione unilaterale
- Instaurarsi del disturbo < 2 settimane
- Edema lieve della papilla ottca o retrobulbare
- Difetto pupillare afferente

RMN encefalo

Normale

Rischio SM < 20%

Alterazioni compatibili con lesioni demielinizzanti

Elevato rischio SM 60-90%
→ Criteri di Mc Donald

Atipico per SM:

- Assenza di dolore
- Essudati retinici
- Emorragie retiniche
- Edema severo della papilla ottica
- Disturbo visivo bilaterale
- Assenza di recupero dopo 1 mese

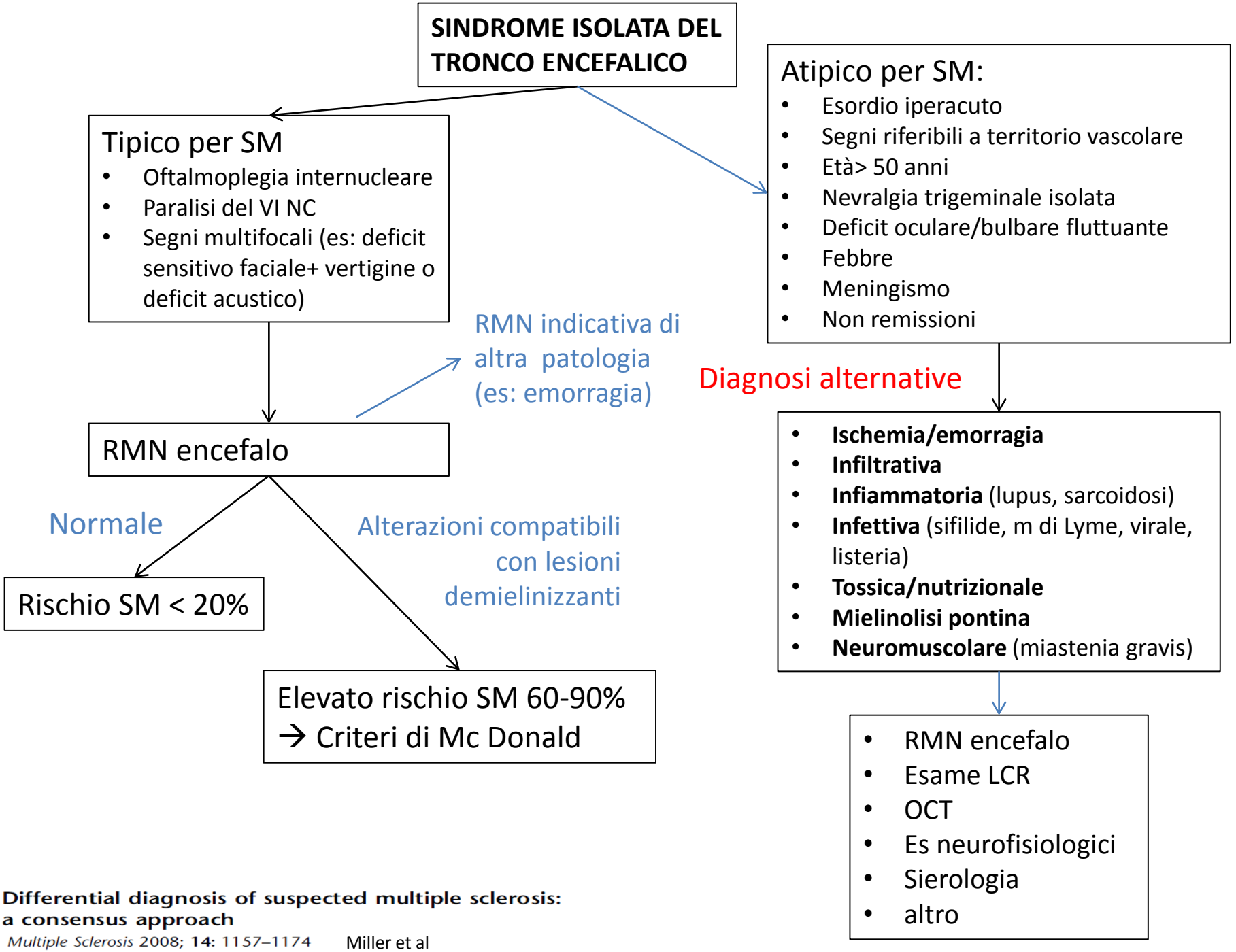
Diagnosi alternative

- **NO ischemica**
- **NO Ereditaria**
- **NO Infiltrativa**
- **Infiammatoria** (lupus, sarcoidosi)
- **Infettiva** (sifilide, m di Lymne, virale, neuroretinite)
- **Tossica/nutrizionale**
- **Disturbo retinico**

- RMN encefalo
- Esame LCR
- OCT
- Es neurofisiologici
- Sierologia
- altro

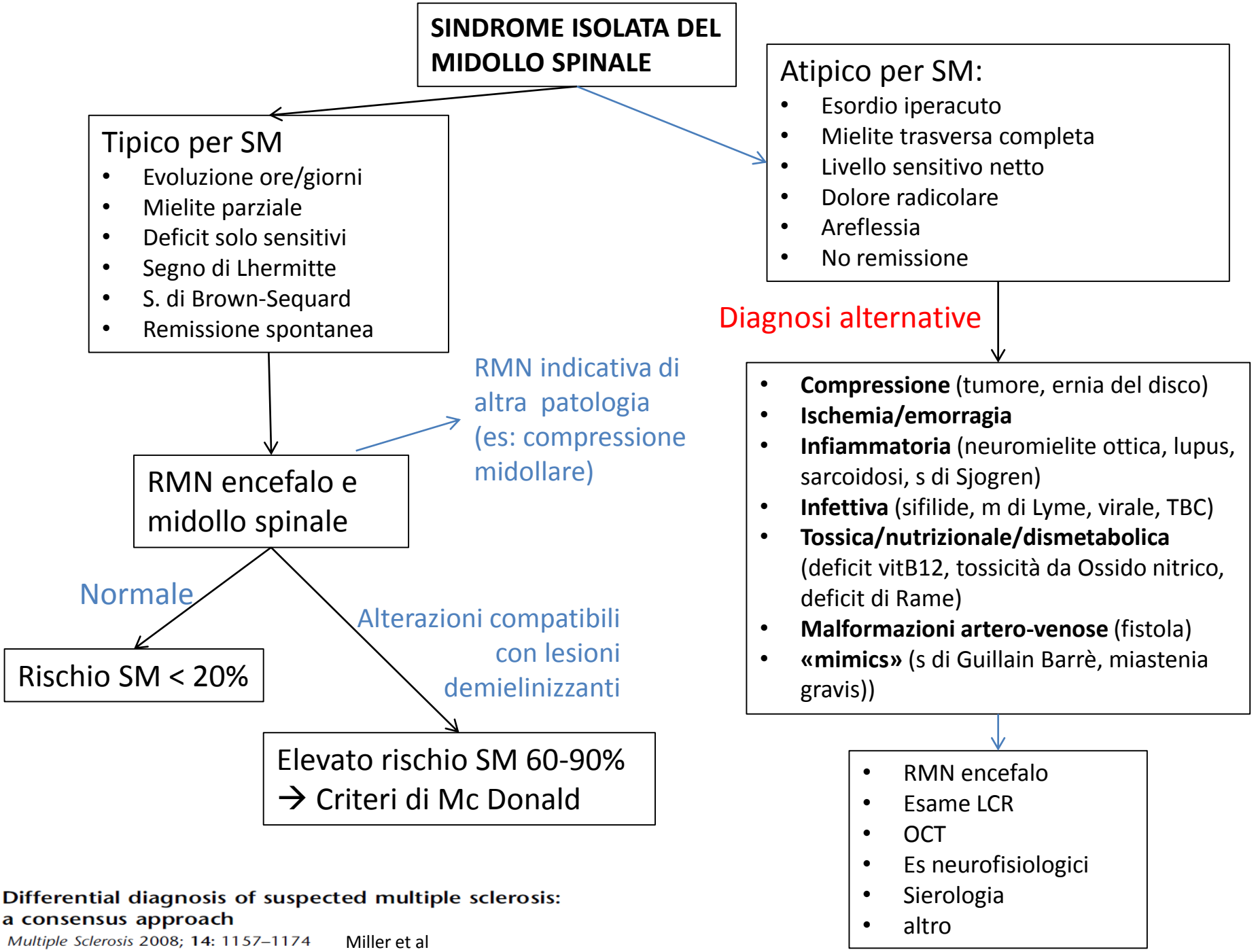
Differential diagnosis of suspected multiple sclerosis: a consensus approach

Multiple Sclerosis 2008; **14**: 1157–1174 Miller et al



Differential diagnosis of suspected multiple sclerosis: a consensus approach

Multiple Sclerosis 2008; **14**: 1157–1174 Miller et al



Differential diagnosis of suspected multiple sclerosis: a consensus approach

Multiple Sclerosis 2008; **14**: 1157–1174 Miller et al

Algoritmo diagnostico per le più comuni patologie con decorso progressivo

Criteri Mc Donald 2010 - SM

PROGRESSIONE DI PATOLOGIA DI ALMENO 1 ANNO (determinato retrospettivamente o prospettivamente):
Almeno 2 tra

- Almeno 1 lesione cerebrale in T2 in una regione tipica per SM: periventricolare, iuxtacorticale o sottotentoriale
- Almeno 2 lesioni midollari in T2
- LCR positivo (almeno 2 bande oligoclonali assenti nel siero, incremento indice IgG o entrambi)

Diagnosi differenziale SM: patologie con DECORSO PROGRESSIVO

	Clinical features	MRI findings	CSF findings	Other investigations
HTLV1-associated myelopathy	Progressive myelopathy; residence or travel to an endemic area (especially West Indies or Japan)	Spinal cord atrophy (thoracic more than cervical); T2-hyperintense brain lesions in some patients	OCBs sometimes present	CSF HTLV1 antibody testing
Dural arteriovenous fistula	Subacute, progressive myelopathy	Extensive spinal cord T2-hyperintensity often extending to the conus, with or without gadolinium enhancement; dilated veins over the dorsal surface of the cord (often subtle); brain MRI normal	OCBs absent	Spinal angiography
Nutritional myelopathy (vitamin B12 or copper deficiency)	Subacute progressive myelopathy or myeloneuropathy; optic atrophy (severe B12 deficiency); anaemia or pancytopenia	T2-hyperintensity upper cervical cord classically affecting the posterior columns; brain MRI normal	OCBs absent	Serum B12, methylmalonic acid; serum copper levels, caeruloplasmin
Primary lateral sclerosis (or upper motor neuron predominant ALS)	Spastic quadriparesis or hemiparesis; with or without bulbar involvement; with or without development of lower motor neuron signs	MRI normal or showing T2-hyperintensity in the corticospinal tracts	OCBs absent	Electromyography looking for lower motor neuron involvement
Leukodystrophies: adrenomyeloneuropathy; Krabbe's disease; Alexander's disease; hereditary diffuse leukoencephalopathy with axonal spheroids	Progressive myelopathy (adrenomyeloneuropathy, Krabbe's); bulbar symptoms, ataxia (Alexander's disease); early cognitive impairment (hereditary diffuse leukoencephalopathy with axonal spheroids)	Highly variable; diffuse, symmetrical T2-hyperintensity sparing subcortical U fibres; with posterior hemispheric predominance (adrenomyeloneuropathy); spinal cord MRI normal or showing atrophy	OCBs absent	Very-long-chain fatty acids (adrenomyeloneuropathy); genetic testing available for some leukodystrophies
Hereditary spastic paraplegia (especially *SPG5*)	Slowly progressive myelopathy (spasticity greater than weakness) with or without other neurological symptoms and family history	Spinal cord atrophy; supratentorial and infratentorial white matter lesions (*SPG5*); atrophy of the corpus callosum	OCBs absent	Genetic testing
Spinocerebellar ataxias	Progressive cerebellar ataxia, with or without other neurological symptoms and family history	Early, prominent cerebellar, with or without spinal cord, atrophy	OCBs absent	Genetic testing

CSF=cerebrospinal fluid. HTLV1=human T-lymphotropic virus type 1. OCB=oligoclonal band. ALS=amyotrophic lateral sclerosis.

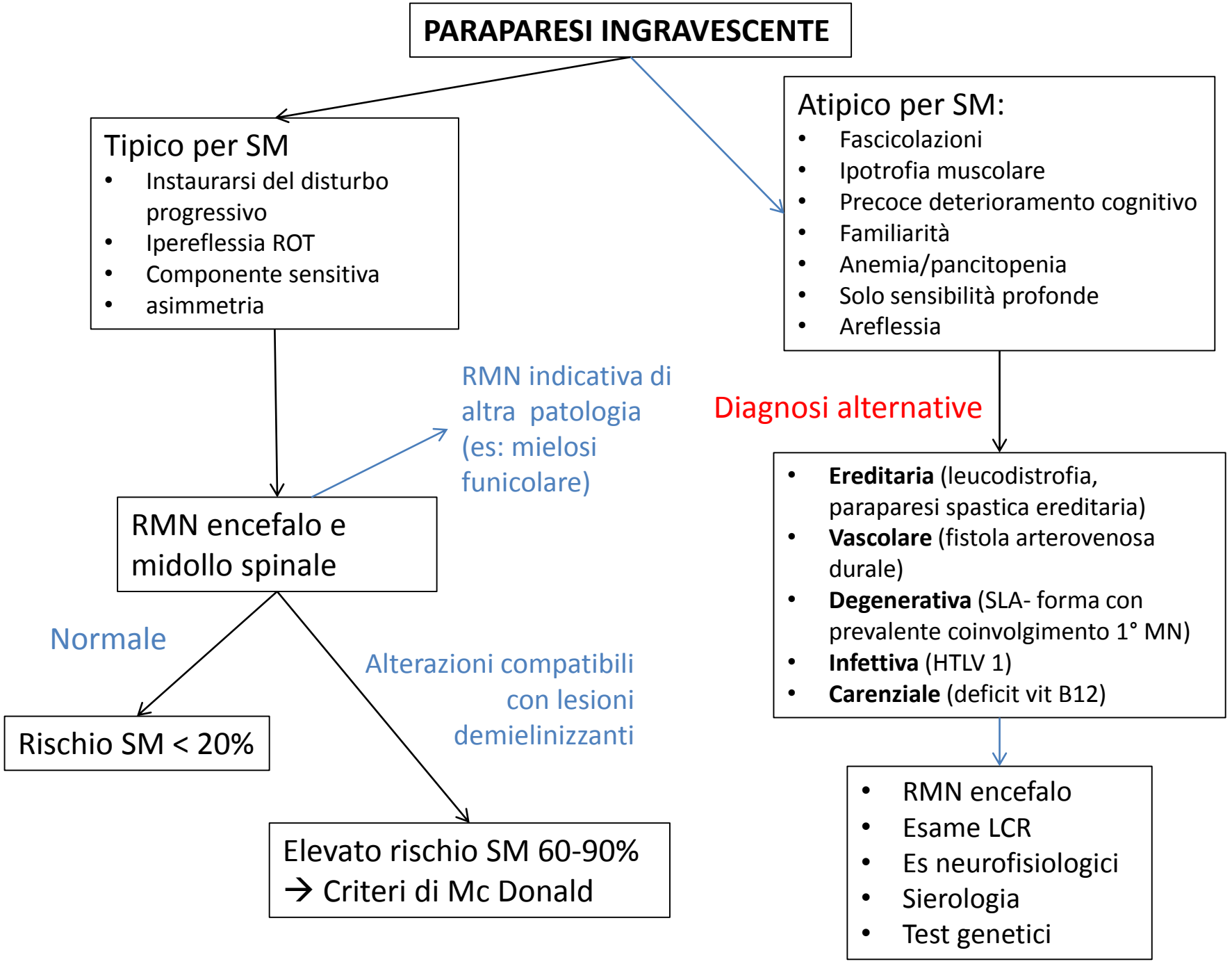
PROGRESSIONE DI PATOLOGIA DI ALMENO 1 ANNO (determinato retrospettivamente o prospettivamente):
Almeno 2 tra

- Almeno 1 lesione cerebrale in T2 in una regione tipica per SM: periventricolare, iuxtacorticale o sottotentoriale
- Almeno 2 lesioni midollari in T2
- LCR positivo (almeno 2 bande oligoclonali assenti nel siero, incremento indice IgG o entrambi)

Diagnosis of multiple sclerosis: progress and challenges

Wallace J Brownlee, Todd A Hardy, Franz Fazekas, David H Miller

Lancet 2017; 389: 1336–46


PARAPARESI INGRAVESCENTE
Tipico per SM
• Instaurarsi del disturbo progressivo
• Ipereflessia ROT
• Componente sensitiva
• asimmetria
Atipico per SM:
• Fascicolazioni
• Ipotrofia muscolare
• Precoce deterioramento cognitivo
• Familiarità
• Anemia/pancitopenia
• Solo sensibilità profonde
• Areflessia
RMN indicativa di altra patologia (es: mielosi funicolare)
Diagnosi alternative
RMN encefalo e midollo spinale
• Ereditaria (leucodistrofia, paraparesi spastica ereditaria)
• Vascolare (fistola arterovenosa durale)
• Degenerativa (SLA- forma con prevalente coinvolgimento 1° MN)
• Infettiva (HTLV 1)
• Carenziale (deficit vit B12)
Normale
Alterazioni compatibili con lesioni demielinizzanti
Rischio SM < 20%
Elevato rischio SM 60-90%
→ Criteri di Mc Donald
• RMN encefalo
• Esame LCR
• Es neurofisiologici
• Sierologia
• Test genetici

Algoritmo diagnostico per le **malattie demielinizzanti idiopatiche** suggestive di SM

	ADEM	NMOSD	MS
Età di esordio	Principalmente soggetti giovani < 10 anni	30-40 anni	Adolescenti e giovani adulti
genere	Prelante in M	Prevalenza in F (F:M= 4-9:1)	Prevalente in F
MRI	Lesioni large (>1-2 cm), confluenti, cotonose, captanti mdc; scompaione nel tempo; coinvolgimento della sostanza bianca (< sost grigia profonda)	Lesioni midollari > 3 segmenti, centrali area postrema, periventricolari/ tronco (periependimali), talamiche Nervo ottico	Periventricolari, iuxtacorticali, sottotentoriali, perpendicolari ai ventricoli (Dawson fingers), ovoidali, ben definite; lesioni corticali, coinvolgimento fibre a U; nuove lesioni al F.U.
LIQUOR	pleiocitosi (neutrofili e linfociti) BOC talora presenti (ma incostanti)	Pleiocitosi solitamente lieve (>25 GB/mcL), BOC < 20%	Bande oligoclonali > 80 % dei pazienti
Test visivo	NO bilaterale	NO bilaterale/unilaterale	NO unilaterale
Esami ematici	Leucocitosi IgG anti MOG	Ab anti AQP4 (70 -80%) IgG anti MOG (pz più giovani, donne, decorso favorevole)	Non significativi
Presentazione	Encefalopatia (alterazioni coscienza, comportanmento, cognitive) polisintomatici, acuta, grave all'esordio, Febbre, cefalea, segni meningei, crisi comiziali, segni neurologici focali associata a recenti infezioni/vaccinazioni	Sindromi tipiche: NO Mielite acuta S. area postrema (singhiozzo, nausea, vomito) S. del tronco encefalo Narcolessia sintomatica o s diencefalica acuta	Monosintomatica, esordio acuto o subacuto
decorso	Prevalentemente monofasico	ricadute	Ricadute o progressiva

- L’identificazione di **Anticorpi IgG anti Acquaporina4 (AQP4-IgG**) ha permesso la definizione di NMOSD (neuromyelitis optica spectrum disorder) come entità patologica specifica, che deve essere differenziata dalla SM per le importanti differenze nella *prognosi e nel trattamento*
- Necessità di *trattamento tempestivo per l’attacco acuto*
  Terapia immunosoppressiva a lungo termine
  Evitare terapia SM (può peggiorare il decorso)

- Sottogruppo di paziente AQP4-IgG sieronegativi sono risultati opositivi per Anticorpi **IgG anti Myelin Oligodendrocyte Glycoprotein (MOG-IgG)** → decorso più favorevole

International consensus diagnostic criteria for neuromyelitis optica spectrum disorders

Neurology® 2015;85:177-189

Wingercuk et al

NEUROMYELITIS OPTICA SPECTRUM DISORDER

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.

Corretta diagnosi → corretta terapia

RICADUTE TERAPEUTICHE

ORIGINAL CONTRIBUTION

Failure of Natalizumab to Prevent Relapses in Neuromyelitis Optica

Ingo Kleiter, MD; Kerstin Hellwig, MD; Achim Berthele, MD; Tania Kümpfel, MD; Ralf A. Linker, MD; Hans-Peter Hartung, MD; Friedemann Paul, MD; Orhan Aktas, MD; for the Neuromyelitis Optica Study Group

ELSEVIER

Multiple Sclerosis and Related Disorders

Volume 7, May 2016, Pages 53–57

Case report

Fingolimod-induced leukoencephalopathy in a patient with neuromyelitis optica spectrum disorder

Fumihito Yoshii, Yusuke Moriya, Tomohide Ohnuki, Masafuchi Ryo, Wakoh Takahashi

SHORT REPORT *Multiple Sclerosis* 2007; 13: 256–259

Immunosuppressive therapy is more effective than interferon in neuromyelitis optica

C Papeix[1], J-S Vidal[2], J de Seze[3], C Pierrot-Deseilligny[1], A Tourbah[1,4], B Stankoff[1,5], C Lebrun[6], T Moreau[7], P Vermersch[3], B Fontaine[1], O Lyon-Caen[1] and O Gout[8]

Neuromyelitis optica spectrum disorders in children and adolescents

Neurology® 2016;87 (Suppl 2):S59-S66

Tenembaum et al

Treatments not recommended for patients with NMOSD. Interferon-β, natalizumab, and fingolimod can precipitate dramatic flare-up of NMOSD.[23,33] Alemtuzumab has been reported as ineffective in adult patients with NMOSD. The use of mitoxantrone and cyclophosphamide also should be avoided in children considering their potential severe side effects.

ATTACCO ACUTO

IV methylprednisolone (MP). The recommended daily dose of IV MP is 30 mg/kg/d to a maximum of 1,000 mg daily, for 5 consecutive days.

Plasma exchange (PE). Retrospective studies and case series including children with NMOSD have reported marked improvement in visual and motor function following PE (5–7 cycles).[23,33]

IV immunoglobulin (IVIg) therapy. A small study has reported successful relapse improvement in half of patients with NMOSD using IVIg after lack of response to steroids.[33] Interestingly, the effect of human IgG in reducing lesion severity in a rat model has been reported recently, providing mechanistic data to encourage further clinical assessment.[35]

Neuromyelitis optica spectrum disorders in children and adolescents

Neurology® 2016;87 (Suppl 2):S59-S66

Tenembaum et al

PROFILASSI

Preventive therapy. ***Azathioprine (AZA).*** Two retrospective studies including children with NMOSD[36,37] reported marked reductions in relapse rates (89%), with 60% of patients remaining relapse-free at 18 months, using 2–3 mg/kg/d of AZA. Nevertheless, high rates of discontinuation (46%) over time were also reported.[37]

Rituximab (RTX). The recommended dose in children is 375 mg/m² weekly for 4 weeks, with additional IV infusions depending on the CD19+ B-cell count to maintain immunosuppression.[23,34] Efficacy in reducing relapse frequency has been reported in children and adults with NMOSD treated with RTX, with stabilization or improvement of disability.[23,38]

Mycophenolate mofetil (MMF). The use of MMF was well-tolerated and induced reduction of relapse frequency with improvement of disability in 2 retrospective studies including children (median dose 2,000 mg/d).[39]

Methotrexate. A sustained remission (36 months) was reported in a single child treated with methotrexate.[4]

Cyclophosphamide. Most of the few children treated with monthly IV cyclophosphamide pulse (1,000 mg/m²) for 6 months needed to be switched to other therapies due to lack of efficacy.[4,16,18]

Mitoxantrone hydrochloride. The use of mitoxantrone in pediatric NMOSD is limited to a single patient[18]

ACUTE DISSEMINATED ENCEPHALOMYELITIS

Acute disseminated encephalomyelitis

Updates on an inflammatory CNS syndrome

Neurology® 2016;87 (Suppl 2):S38-S45 Pohl et al

Table 1 ADEM and its convergence with relapsing demyelinating disorders

Diagnosis	Clinical criteria
ADEM, monophasic[7]	Single polyfocal CNS event with encephalopathy and presumed inflammatory demyelination and no new disease activity (clinical or MRI) >3 months after onset
ADEM, multiphasic[7]	ADEM followed at >3 months by second ADEM episode, but no further ADEM or non-ADEM demyelinating events
ADEM-MS[7]	ADEM followed at >3 months by non-ADEM demyelinating relapse and new MRI lesions meeting criteria for dissemination in space[8]
ADEM-NMOSD[9]	ADEM followed at >3 months by events including optic neuritis, longitudinally extensive transverse myelitis, or area postrema syndrome, meeting MRI requirements according to revised NMOSD criteria[9]
ADEM-ON	ADEM, MDEM, or multiple ADEM attacks followed by optic neuritis

Abbreviations: ADEM = acute disseminated encephalomyelitis; MDEM = multiphasic disseminated encephalomyelitis; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder; ON = optic neuritis.

Table 2 MRI characteristics in ADEM vs MS

MRI characteristics	ADEM: Typical	MS: Typical
Deep gray matter and cortical involvement	Yes	No
Bilateral diffuse lesions	Yes	No
Poorly marginated lesions	Yes	No
Large globular lesions	Yes	No
Periventricular pattern of lesions	No	Yes
Lesions perpendicular to long axis of corpus callosum	No	Yes
Ovoid lesions	No	Yes
Lesions confined to corpus callosum	No	Yes
Sole presence of well-defined lesions	No	Yes
Black holes (on T1 sequence)	No	Yes

Abbreviations: ADEM = acute disseminated encephalomyelitis; MS = multiple sclerosis.

Acute disseminated encephalomyelitis

Updates on an inflammatory CNS syndrome

Neurology® 2016;87 (Suppl 2):S38–S45 Pohl et al

TREATMENT There are no randomized studies for the treatment of ADEM. Thus, management of ADEM is based on expert opinions and observational studies.[20,26,47] Despite the lack of conclusive evidence, high-dose corticosteroids are currently widely accepted as first-line therapy.[48] A typical treatment regimen consists of IV methylprednisolone at a dose of 30 mg/kg/d (maximally 1,000 mg/d) for 5 days, followed by an oral taper over 4–6 weeks with a starting dose of prednisone of 1–2 mg/kg/d. An increased risk of relapse was observed with steroid taper of ≤3 weeks.[49] IV immunoglobulin treatment has been described in case reports and small case series, mostly in combination with corticosteroids or as a second-line treatment in steroid-unresponsive ADEM.[50,51] The usual total dose is 2 g/kg, administered over 2–5 days.[47] Plasma exchange is recommended for therapy-refractory patients with fulminant disease, e.g., using 7 exchanges every other day.[47] In single case reports, patients with fulminant ADEM and cerebral edema have been treated with hypothermia or decompressive craniotomy.[52,53]

RICADUTE TERAPEUTICHE

Acute disseminated encephalomyelitis

Updates on an inflammatory CNS syndrome

Neurology® 2016;87 (Suppl 2):S38–S45 Pohl et al

Diagnosi differenziale Patologie demielinizzanti idiopatiche: Nuovi elementi

- Riscontro di AB specifici per NMO
- Nuove sequenze MRI
  - DIR e PSIR per identificare **lesioni corticali**, specifiche per SM, non presenti in NMO o emicrania
  - Susceptibility weighted imaging SWI per identificare la **distribuzione perivenulare** delle lesioni in SM, non presente in NMO, emicrania, patologie vascolari
- Riscontro di **IgG specifiche – MRZ** (morbillo-rosolia-varicella-zoster) in pazienti con SM
- Riduzione di spessore delle **fibre retiniche nervose** (valutabile con OCT) nei pazienti con SM→ utile per DD con NMO e S di Susac

- MOG-IgG sono stati riscontrati anche in pazienti con ADEM e con neuriti ottiche ricorrenti→ in futuro potrebbe essere identificata un'identità neurologica distinta?

→ Ulteriori modificazioni dei criteri diagnostici sono attesi anche in futuro

Diagnosis of multiple sclerosis: progress and challenges

Wallace J Brownlee, Todd A Hardy, Franz Fazekas, David H Miller

Lancet 2017; 389: 1336–46

GRAZIE PER L'ATTENZIONE