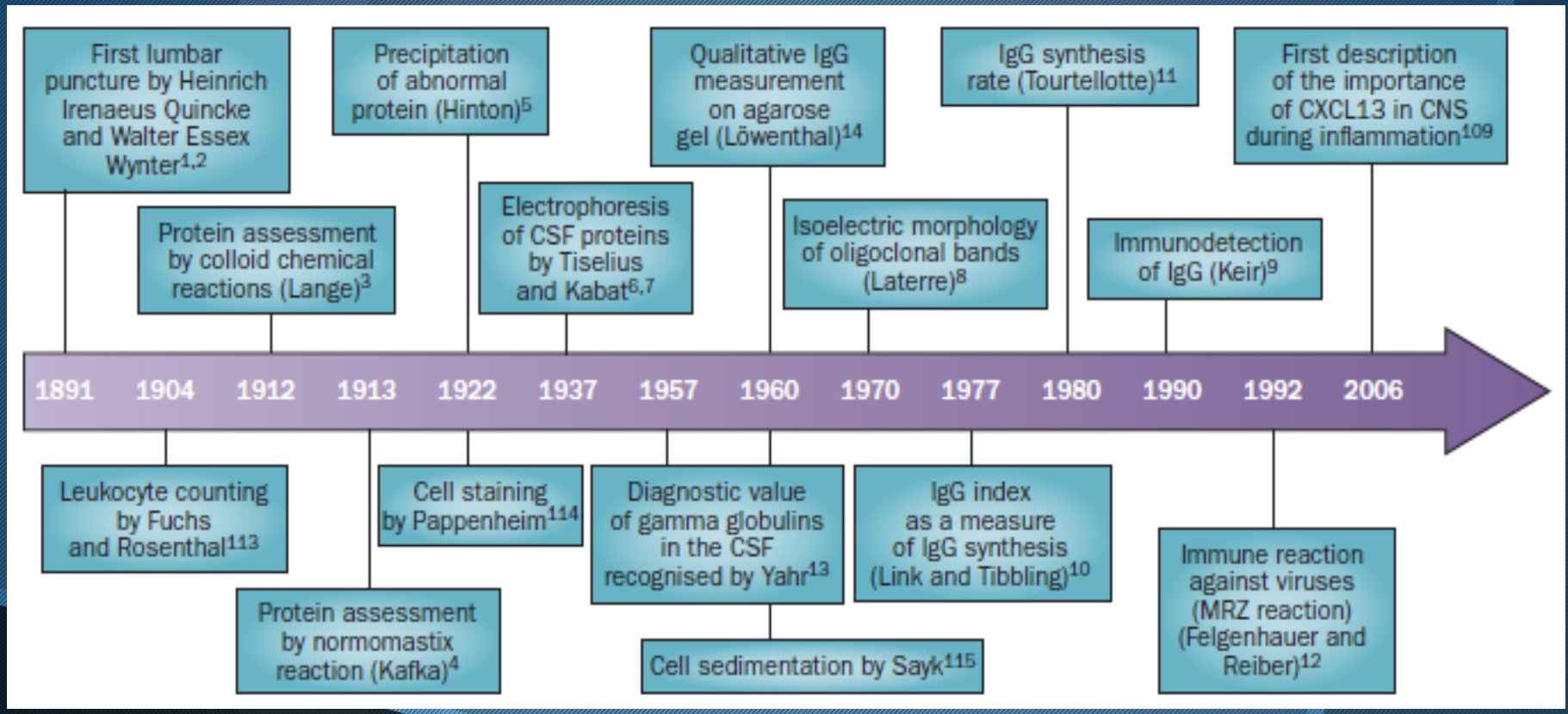
MS Tanısında BOS İncelemesi

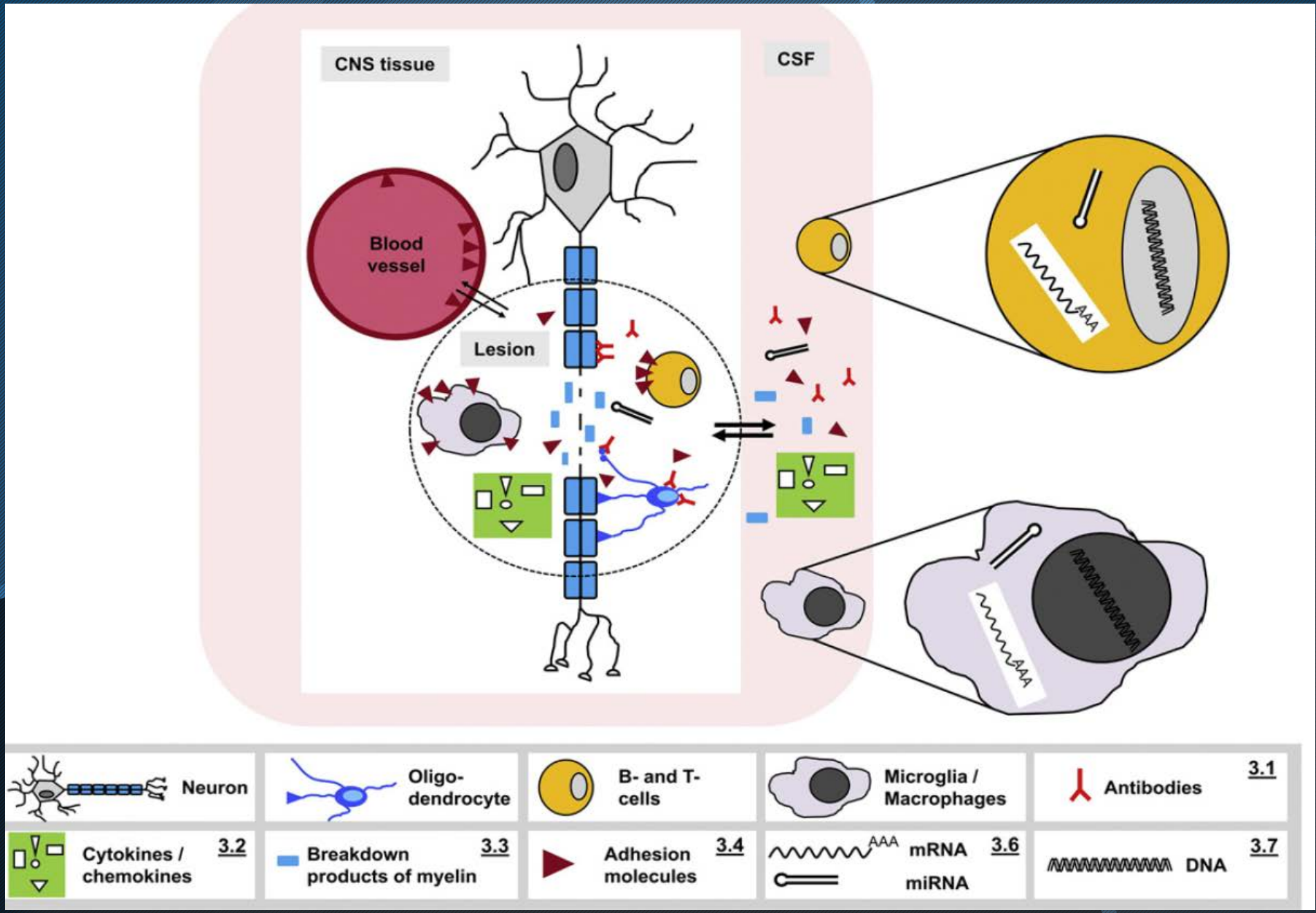
Dr. Murat Terzi

Ondokuz Mayıs Üniversitesi Tıp Fakültesi Nöroloji AD.

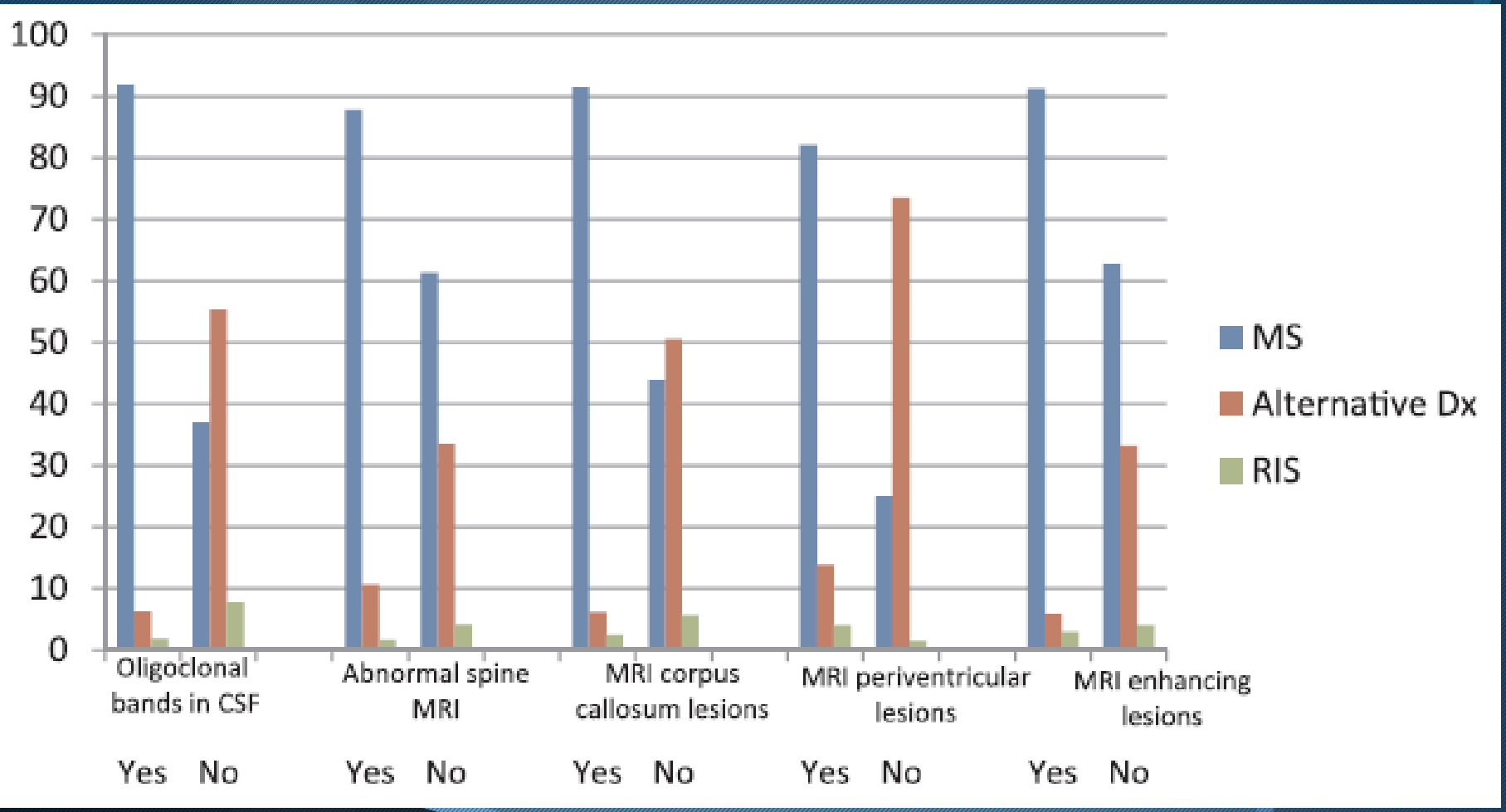
14.02.2019 - Ankara



Nat. Rev. Neurol. 9, 267–276 (2013)



Autoimmunity Reviews 14 (2015) 903–913



Multiple Sclerosis and Related Disorders 18 (2017) 85–89

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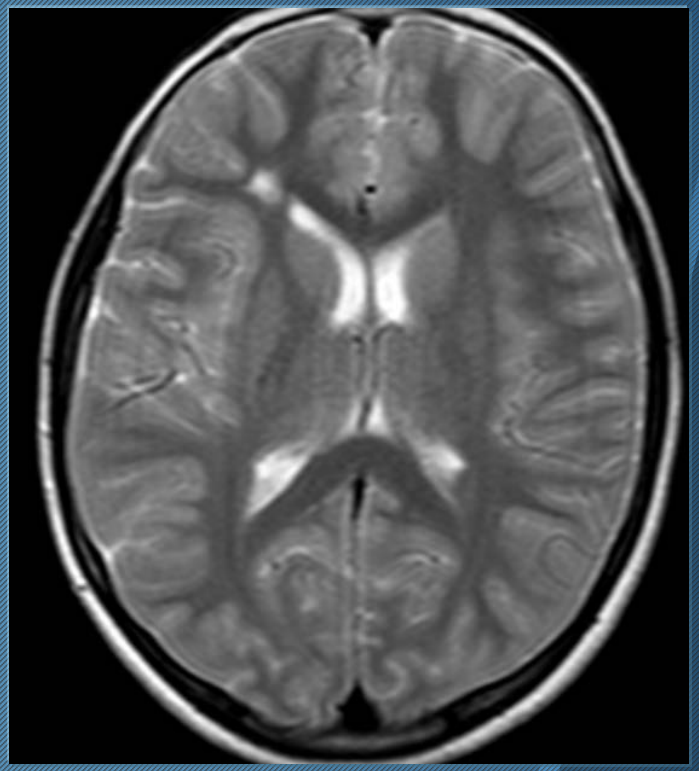

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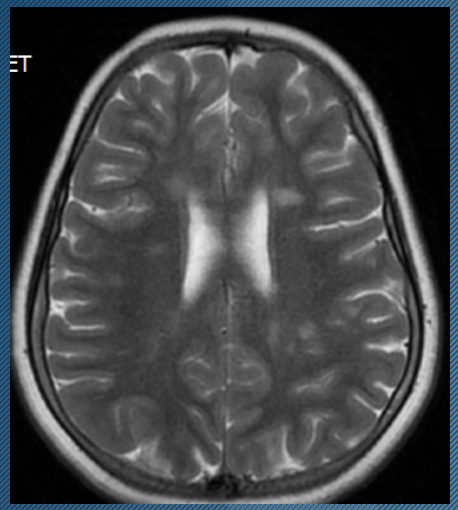

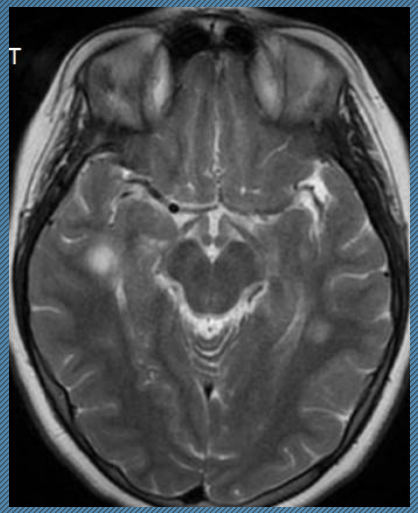

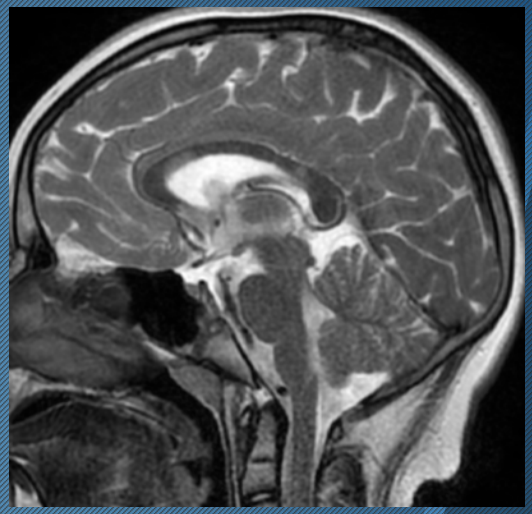

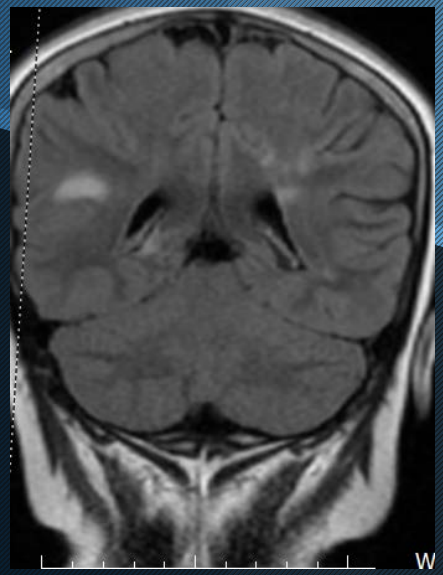

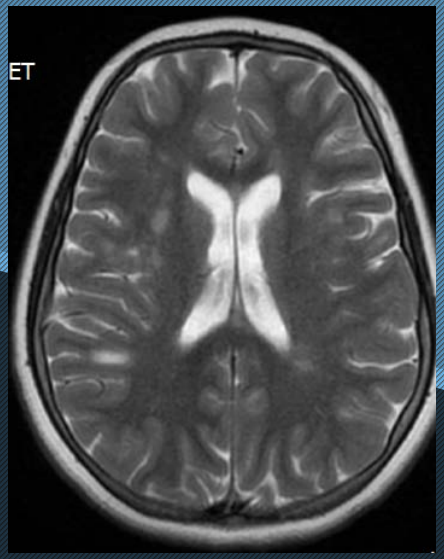

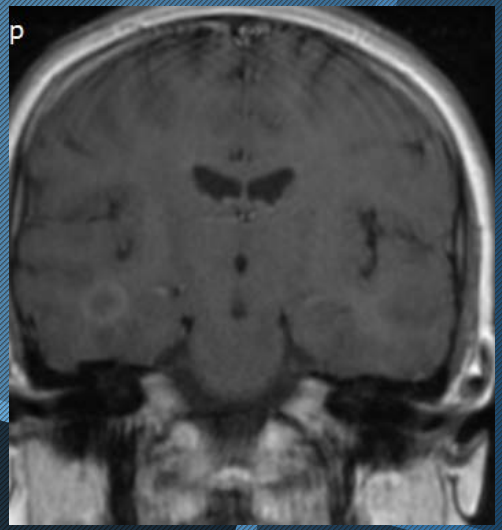

	All patients	Onset at <12 Yr	Onset at 12–18 Yr	P
MRI characteristics				
Supratentorial white matter, n = 191	187 (97.9)	44 (97.8)	143 (97.9)	0.662
Periventricular white matter, n = 181	174 (96.1)	41 (97.6)	133 (95.7)	0.488
Cortical/Juxtacortical, n = 176	113 (64.2)	30 (75.0)	83 (61.0)	0.105
Brainstem, n = 187	118 (63.1)	33 (75.0)	85 (59.4)	0.061
Cerebellar, n = 183	94 (51.4)	28 (62.2)	66 (47.8)	0.093
Spinal cord, n = 185	124 (67.0)	28 (65.1)	96 (67.6)	0.761
VEP latency abnormalities, n = 156	81 (51.9)	20 (64.5)	61 (48.8)	0.117
Patients with a history of ON, n = 66	52 (78.8)	12 (63.2)	40 (72.7)	0.896
Patients without a history of ON, n = 90	29 (32.2)	8 (30.8)	21 (22.6)	0.093
Cerebrospinal fluid				
OCB present in CSF, n = 169	115 (68.0)	25 (67.6)	90 (68.2)	0.944
Elevated IgG index, n = 154	96 (62.3)	20 (54.1)	76 (65.0)	0.233
Positive OCB and/or elevated IgG index, n = 169	132 (78.1)	28 (75.7)	104 (78.8)	0.686
Serum				
Low serum levels of 25-hydroxyvitaminD, n = 111	76 (68.5)	17 (68.0)	59 (68.6)	0.954

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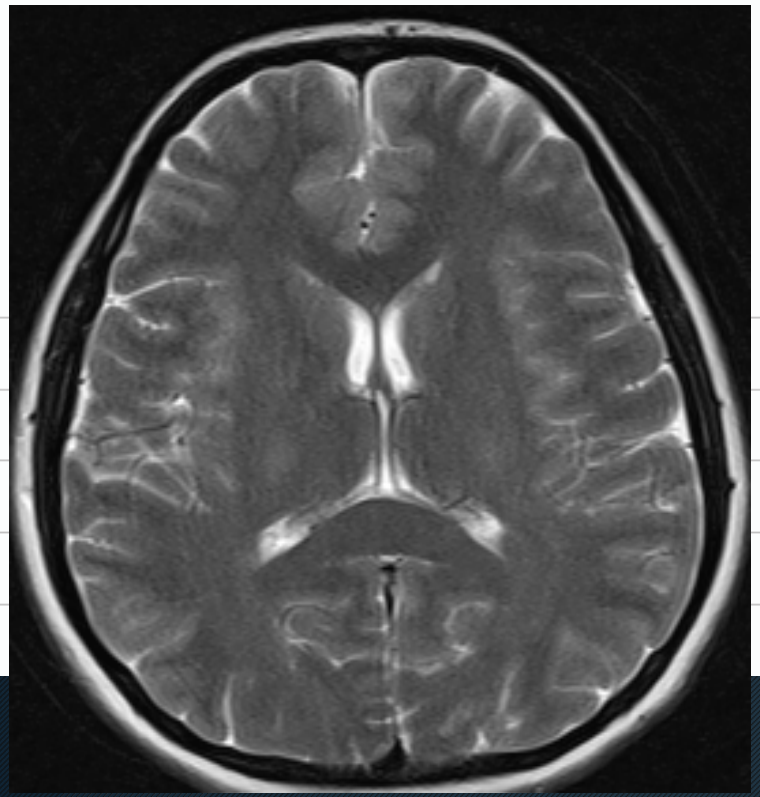


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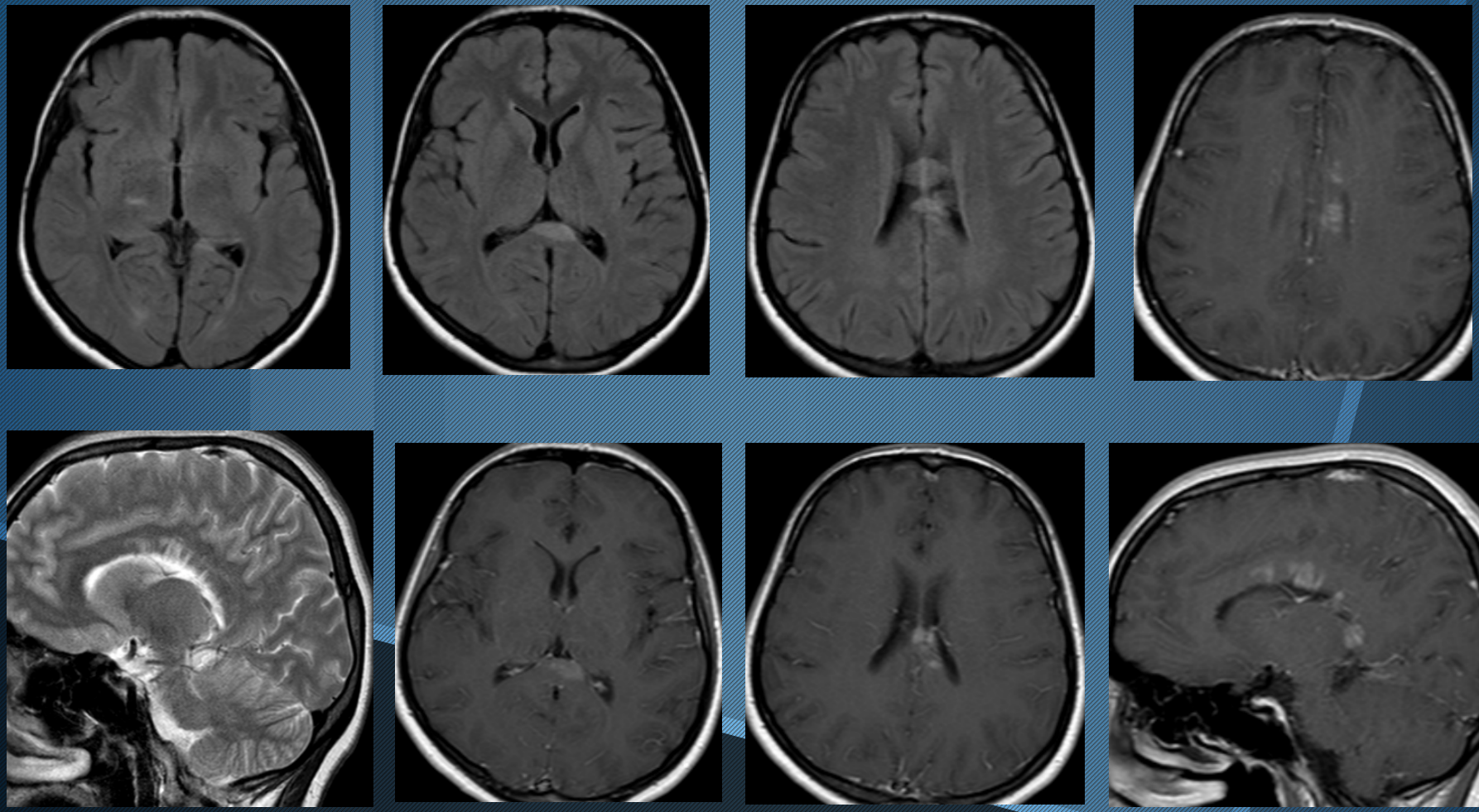

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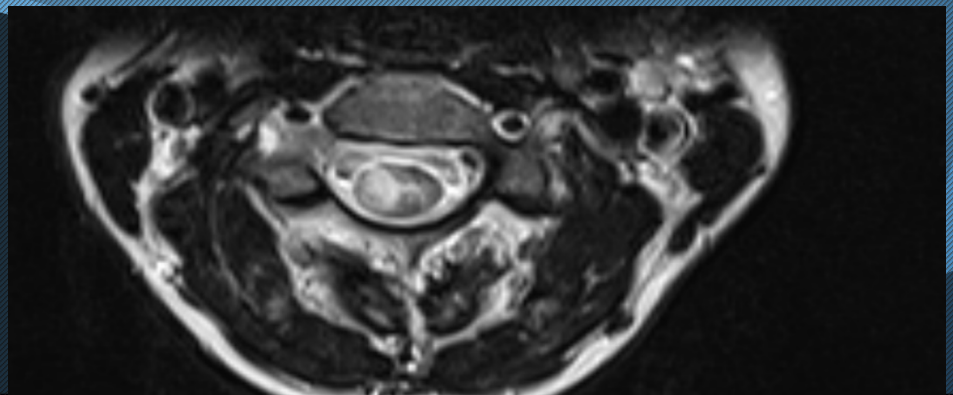

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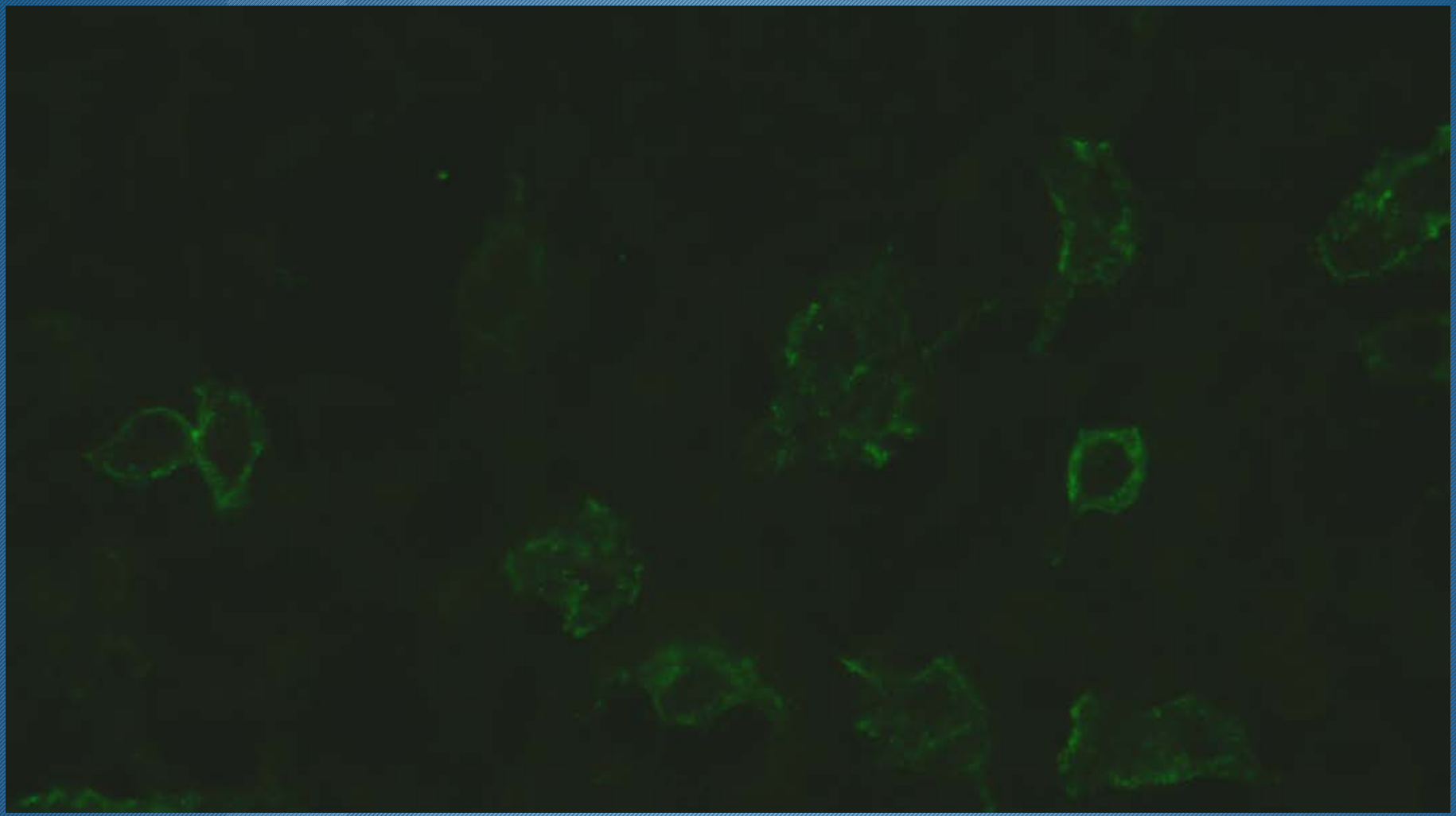


Pencere Ayarı


LPH

	NMOSD ($n = 35$)	MS ($n = 34$)	P values
EDSS	4.67 ± 2.44	2.51 ± 2.01	<0.001***
BBB permeability (10^{-3})	7.37 ± 4.37	4.71 ± 1.34	0.003**
CSF WBC (10^6/L)	24.55 ± 35.58	8.81 ± 9.12	0.023*
CSF protein (g/L)	0.63 ± 0.39	0.40 ± 0.11	0.004**
CSF chlorine (mmol/L)	125.14 ± 5.42	126.92 ± 3.14	NS
CSF glucose (mmol/L)	3.71 ± 0.90	3.46 ± 0.44	NS
CSF polymorphonuclear cells (%)	21.00 ± 18.32	17.33 ± 25.81	NS
CSF mononuclear cells (%)	74.05 ± 24.63	60.00 ± 31.67	NS
CSF IgG (mg/L)	64.28 ± 77.49	48.63 ± 20.43	NS
IgG index	0.85 ± 0.69	0.89 ± 0.59	NS
Serum CRP (mg/L)	4.05 ± 7.38	5.18 ± 10.44	NS

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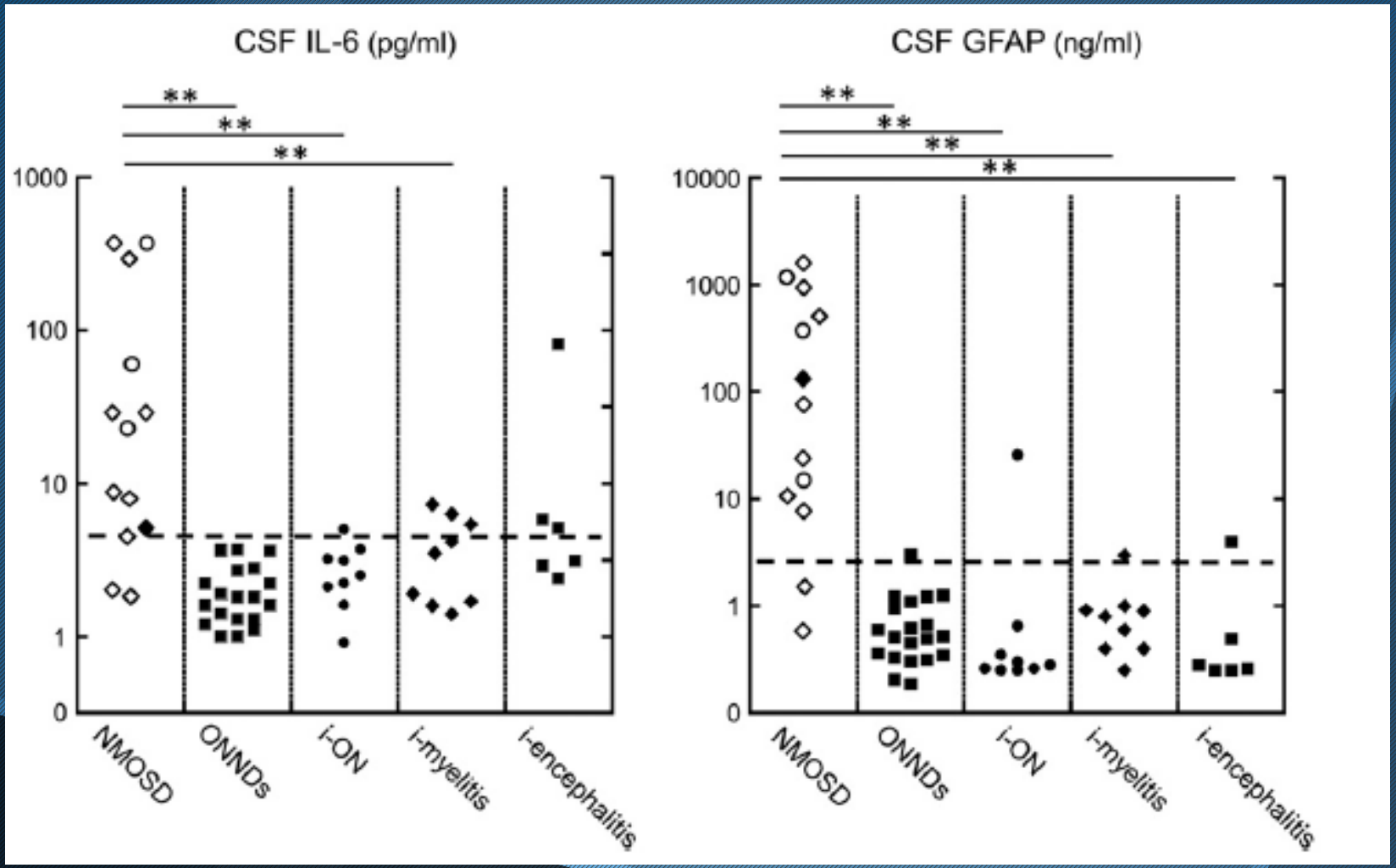
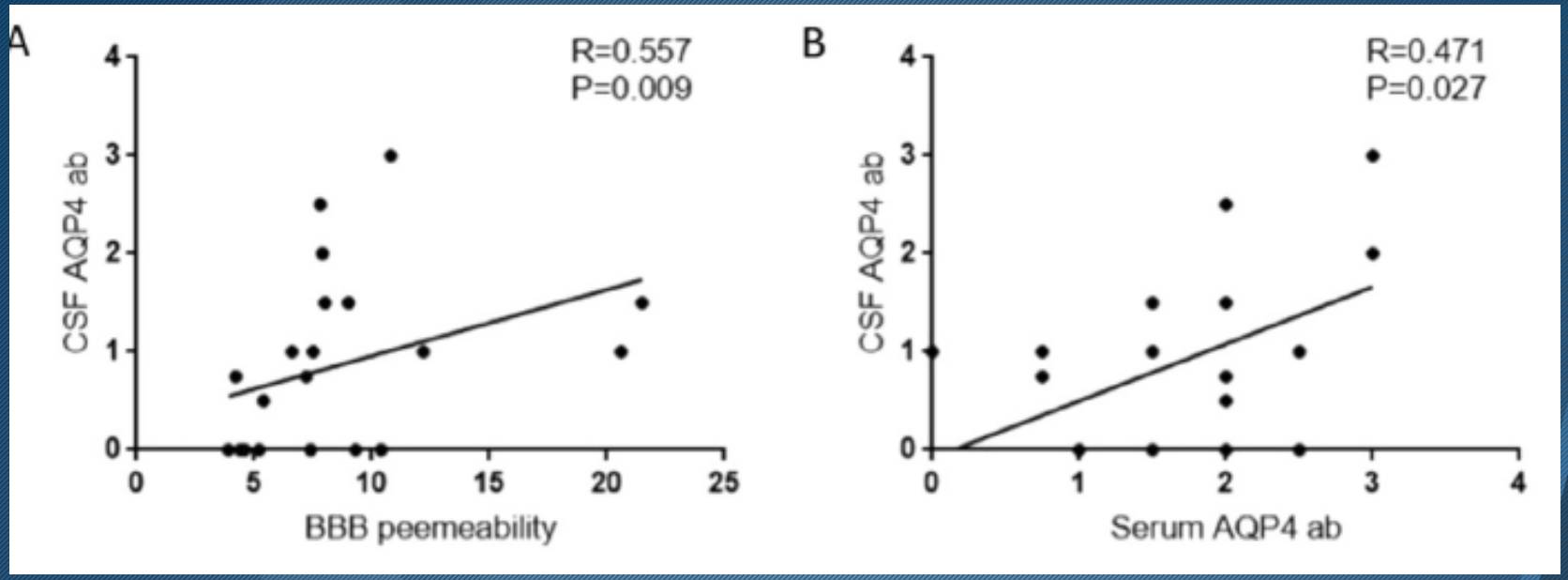
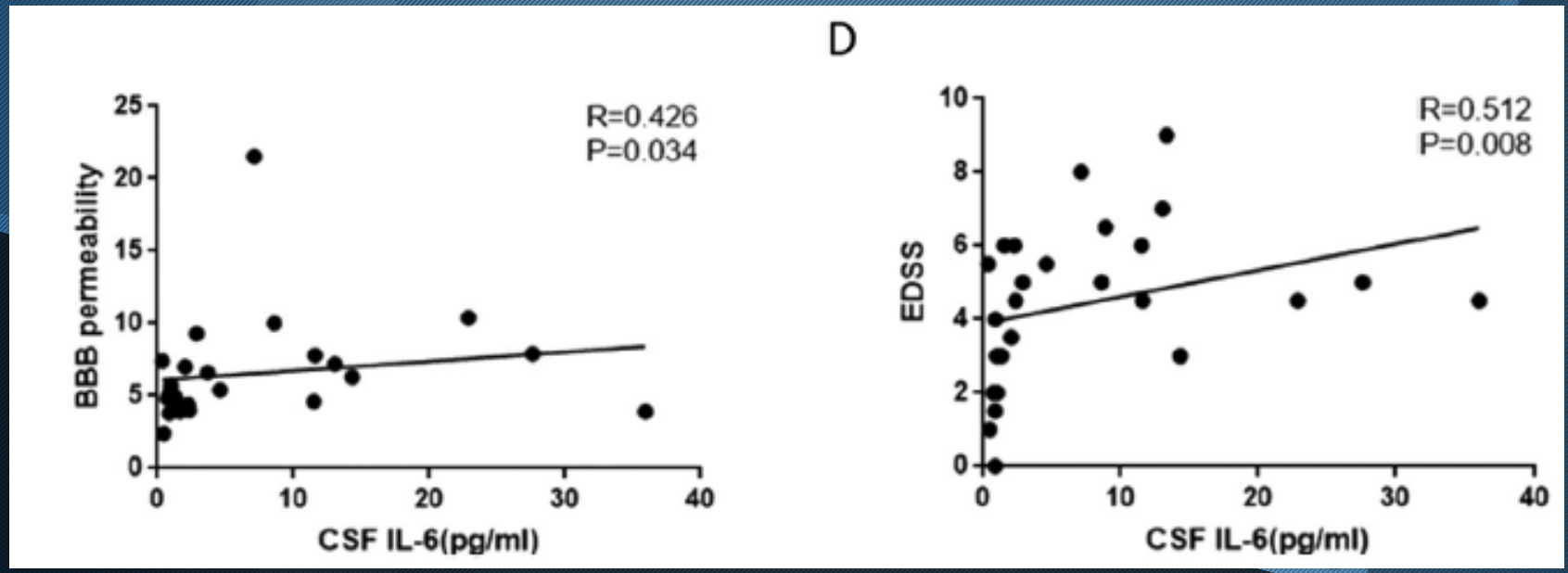


A. Uzawa et al. / Clinica Chimica Acta 421 (2013) 181–183





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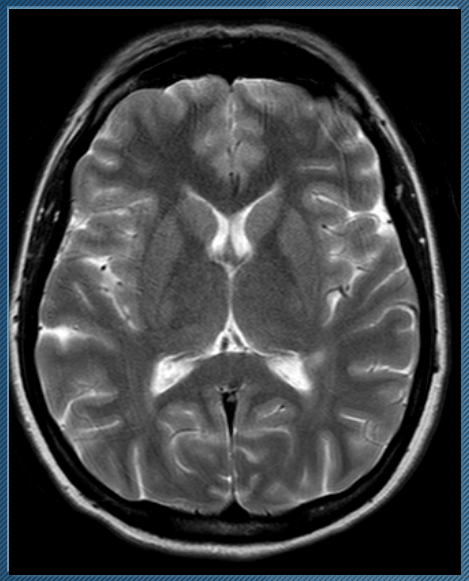
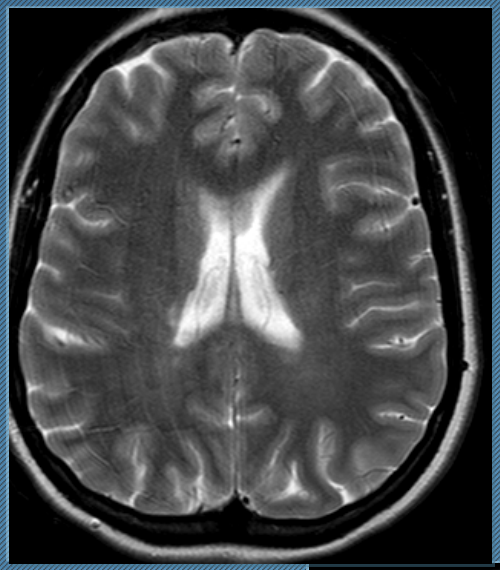
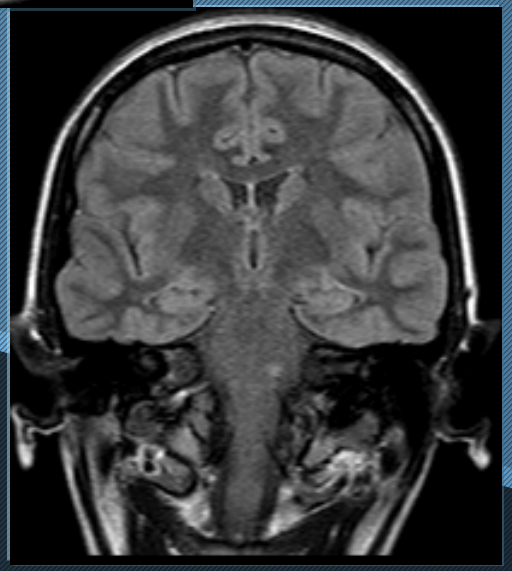
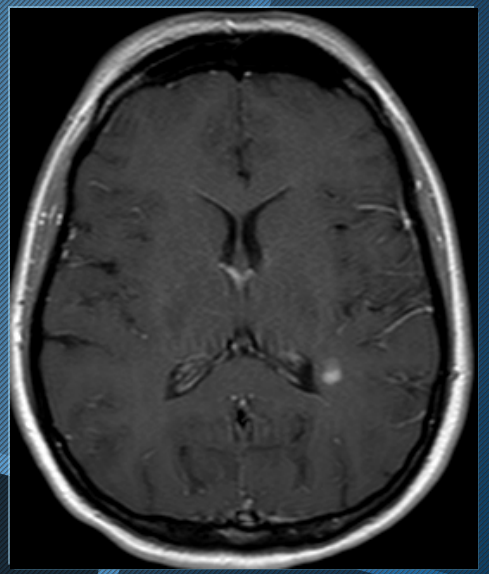
Clinical	AQP4-ab positive (*N*=69)	MOG-ab positive (*N*=14)	Double positive (*N*=10)	*P* value
NMO/ NMOSD-LETM/ NMOSD-ON, *n*	57/8/4	8/6/0	9/ 1/ 0	0.0438
Female sex, *n* (%)	56 (81%)	10 (71%)	10 (100%)	0.1975
Age at first attack, median (range), years	43 (20–63)	32 (15–56)	32 (15–60)	0.1925
Disease duration (time from disease onset to serum drawl), median (range), years	4 (1–22)	3 (1–5)	4 (2–6)	0.1296
Patients with a single attack, *n* (%)	3 (4%)	6 (43%)	0 (0%)	<0.0001
Simultaneous ON+myelitis attacks (any time)	17 (24%)	6 (43%)	3 (30%)	0.3788
Number of attacks, median (range)	3 (1–17)	2 (1–6)	6 (3–10)	0.0697
Brain MRI at attack				
Normal, *n*(%)	43 (62%)	6 (43%)	0 (0%)	0.0008
MS-like (lesion were too few to satisfy the Barkhof criteria for MS), *n*(%)	0(0%)	5 (36%)	0 (0%)	<0.0001
MS-like (satisfy Barkhof criteria), *n* (%)	0 (0%)	0 (0%)	7 (70%)	<0.0001
NMO-like, *n* (%)	17 (25%)	0 (0%)	0 (0%)	0.0268
ADEM-like with lesion enhancement, *n* (%)	0 (0%)	3 (21%)	1 (10%)	0.0010
ADEM-like without lesion enhancement, *n* (%)	6 (9%)	0 (0%)	2 (20%)	0.2264
Nonspecific, *n* (%)	3 (4%)	0 (0%)	0 (0%)	0.5833
Spinal MRI at attack				
Multiple spinal cord lesions, *n* (%)	0 (0%)	14 (100%)	10(100%)	<0.0001
Moderate cord edema, *n* (%)	0 (0%)	14 (100%)	0 (0%)	<0.0001
Serious cord edema, *n* (%)	65 (94%)	0 (0%)	10(100%)	<0.0001
CSF analysis at attack				
Cell count, median (range)	16 (0–276)	4 (0–14)	17 (0–128)	0.5165
Protein, median (range) mg/dl	39 (20–89)	50 (29–86)	44 (29–45)	0.3504
Oligoclonal bands positivity, *n* (%)	4(6%)	3 (21%)	1 (10%)	0.1616
Other serum autoantibodies	13 (19%)	2 (14%)	1 (10%)	0.5778

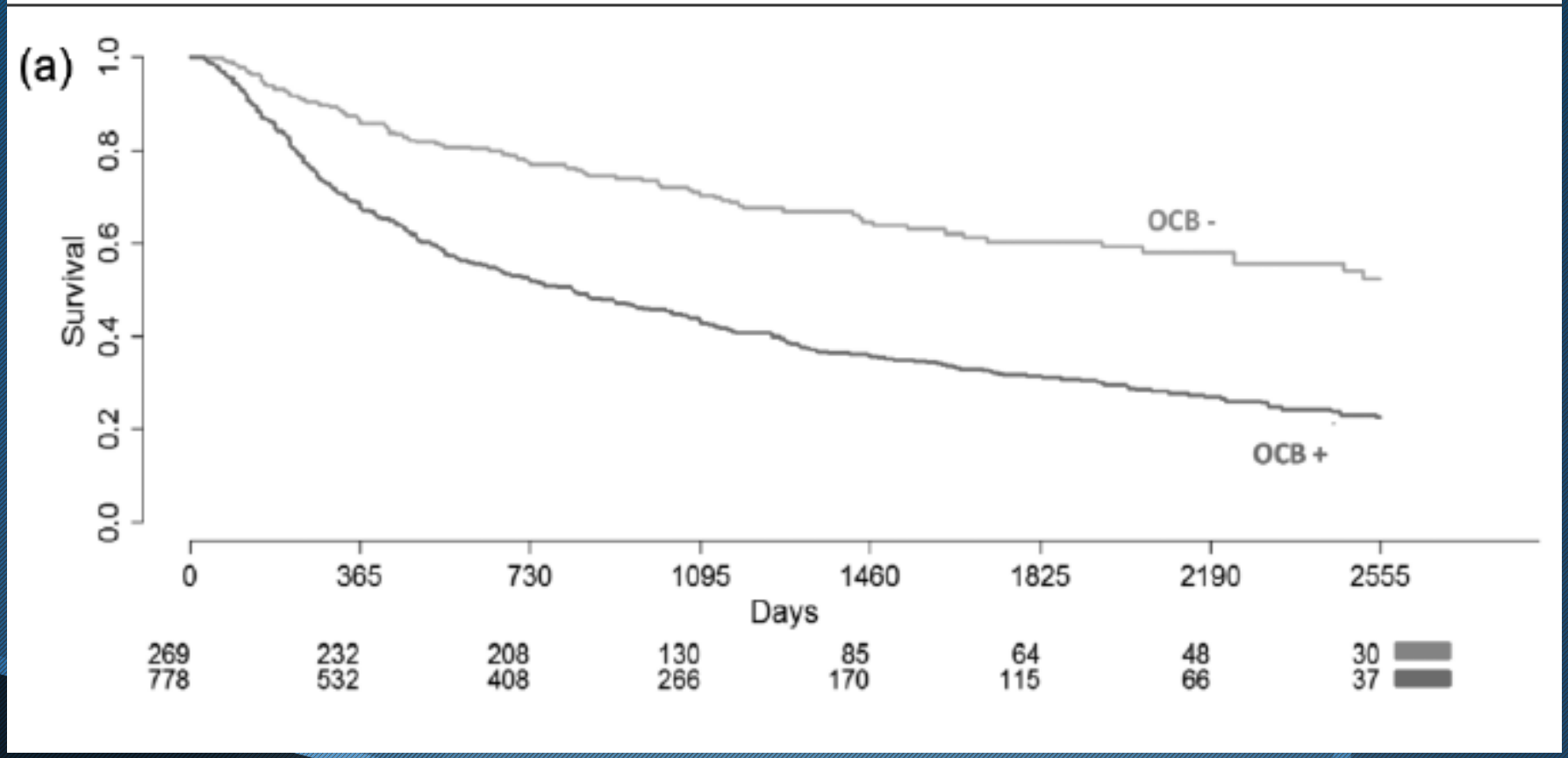
23 Y, K, ekim 2016 sağ ON











Multiple Sclerosis Journal 2015, Vol. 21(8) 1013–1024

Characteristic	Patients who did not develop CDMS	Patients who developed CDMS
No. of subjects	124	95
Age at onset (years)	32.67 ± 9.40	21.73 ± 8.64
Females — %	75 (60.5)	66 (69.5)
Multifocal type of onset — %	20 (16.1)	15 (15.8)
Type of CIS — %		
Optic neuritis syndrome	37 (29.8)	25 (26.3)
Brainstem syndrome	28 (22.6)	30 (31.6)
Spinal cord syndrome	39 (31.5)	25 (26.3)
Other	20 (16.1)	15 (15.8)
CSF findings		
CSF cells	4.18 ± 6.60	5.43 ± 6.71
CSF proteins	35.02 ± 13.93	33.35 ± 11.63
Number of CSF oligoclonal bands	6.73 ± 7.28	8.84 ± 7.01
Blood–brain barrier damage index	0.50 ± 0.25	0.54 ± 0.21
MRI findings		
T2 lesions	5.66 ± 6.02	8.97 ± 5.58
Gd-enhancing lesions	0.51 ± 0.95	0.74 ± 1.17

Journal of Neuroimmunology 289 (2015) 62–67

	CSF IgG oligoclonal bands			
	0	1–7	8–12	≥ 13
No. of subjects	55	55	55	54
Age at onset (years)	32.93 ± 0.88	30.86 ± 0.98	31.77 ± 0.87	31.84 ± 0.89
Females – %	33 (60.0)	37 (67.3)	35 (63.6)	36 (66.7)
Multifocal type of onset – %	11 (20.0)	8 (14.5)	7 (12.7)	9 (16.7)
Type of CIS – %				
Optic neuritis syndrome	16 (29.1)	15 (27.3)	18 (32.7)	13 (24.1)
Brainstem syndrome	10 (18.2)	17 (30.9)	10 (18.2)	21 (38.9)
Spinal cord syndrome	13 (23.6)	16 (29.1)	22 (40.0)	13 (24.1)
Other	11 (20.0)	8 (14.5)	7 (12.7)	9 (16.7)
CSF findings				
CSF cells	2.77 ± 3.93	4.88 ± 5.54	7.32 ± 9.47	3.91 ± 5.71
CSF proteins	33.0 ± 12.13	34.84 ± 13.71	36.13 ± 13.58	32.44 ± 12.49
Blood–brain barrier damage index	0.53 ± 0.24	0.52 ± 0.24	0.55 ± 0.22	0.49 ± 0.24
MRI findings				
T2 lesions	4.58 ± 3.93	4.78 ± 4.76	7.02 ± 5.04	12.11 ± 6.93
Gd-enhancing lesions	0.55 ± 1.14	0.75 ± 1.10	0.54 ± 0.93	0.60 ± 1.05

Journal of Neuroimmunology 289 (2015) 62–67

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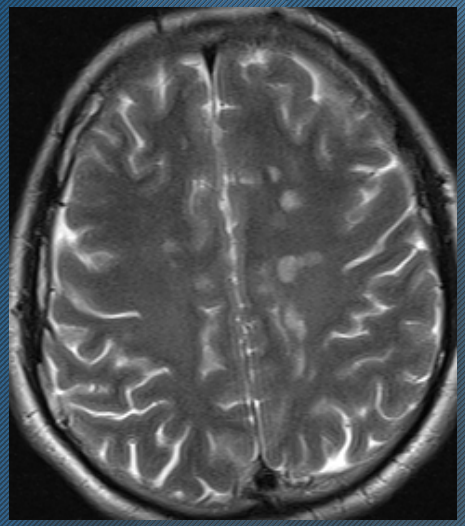
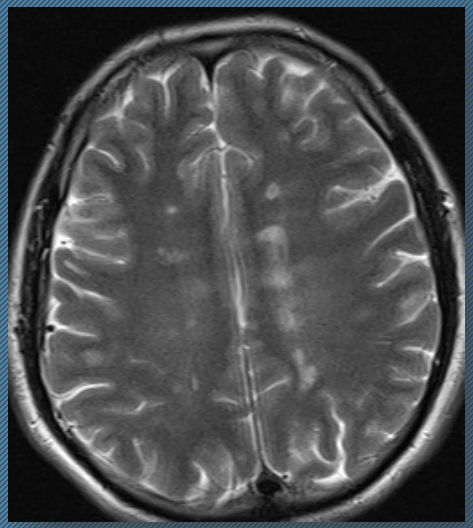
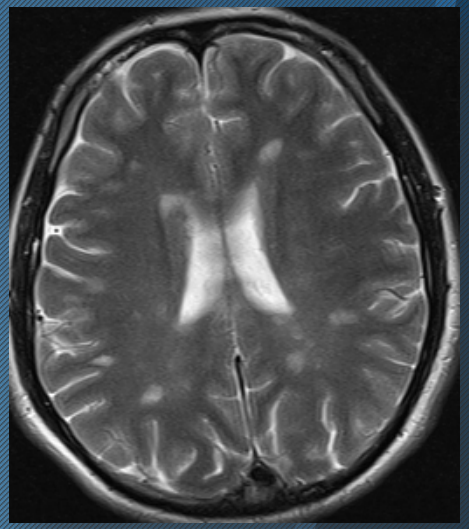
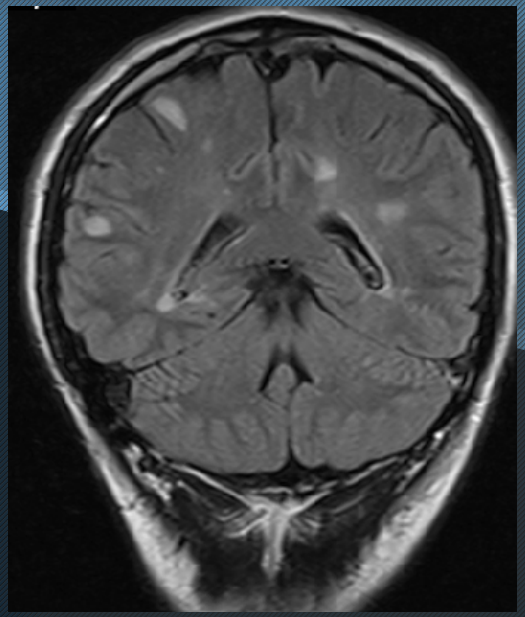
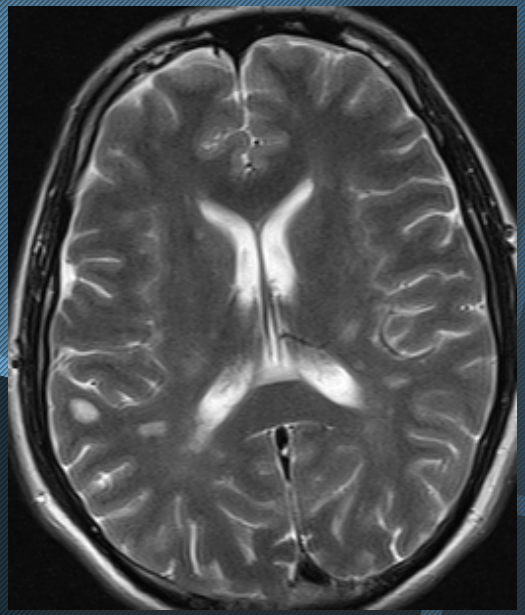
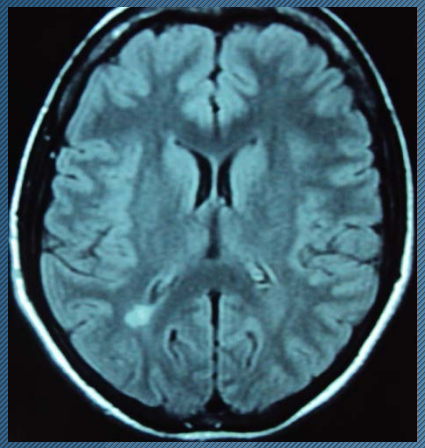
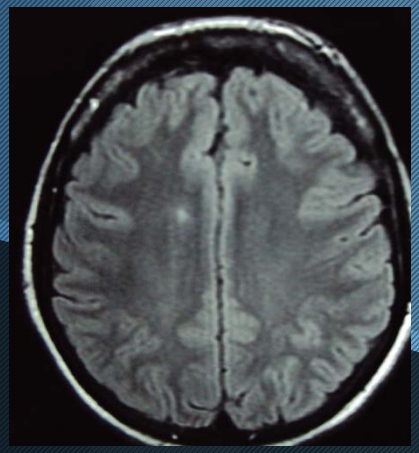






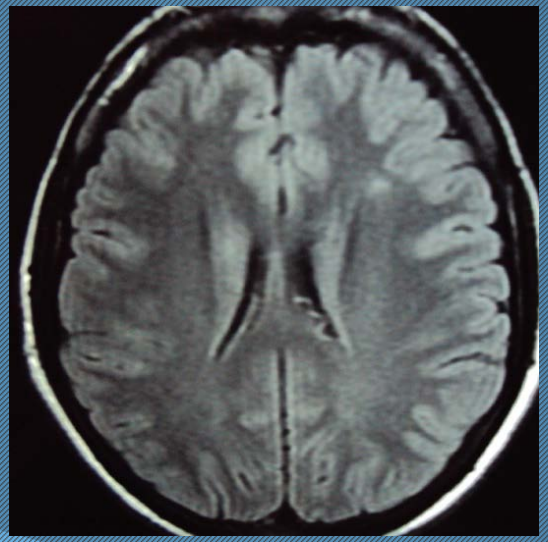
PPMS

42 Y, K, 1.5 yıldır olan ve zamanla artan sağ bacak güçsüzlüğü ve uyuşma

NM; Sağ alt ekstremite 3+/5 kas gücü, DTR'ler altta canlı, Sağda 3-4 atımlık achil klonusu, PY sağda ekstansör, vibrasyon duyusu alt ekstremitelerde azalmış







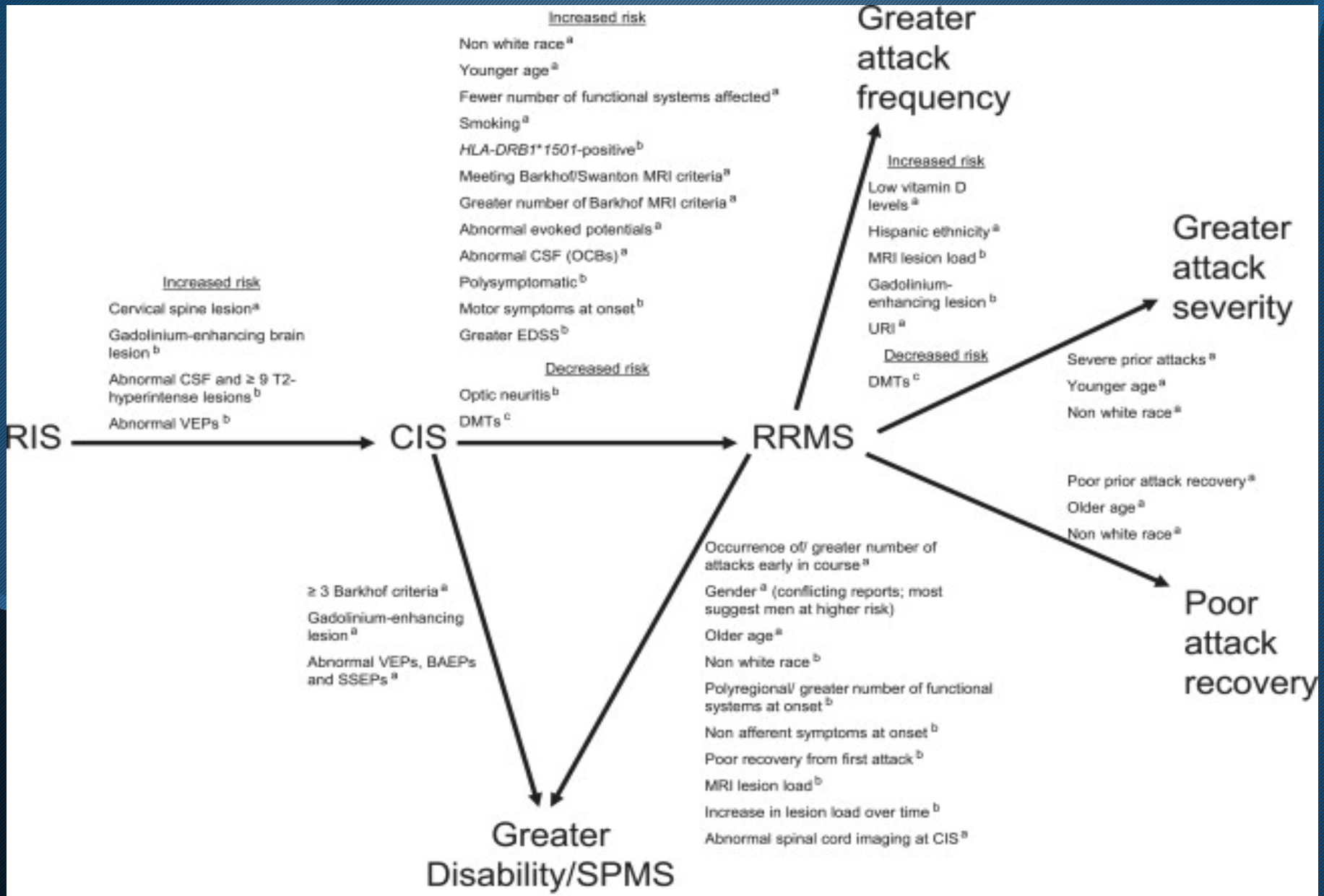
VEP P100 latansı sağda 137, solda 117

BOS Ig G indeksi 1.3

BOS OKB +

	PPMS (n = 103)	RRMS (n = 100)	Comparison statistics
Total CSF cell count in/µl (range; SD)	4.1 (1–43; 5.9)	8.9 (1–47; 10.3)	$p < 0.001$
Intrathecal IgG synthesis in % (range; SD)	19.8 (0–75.4; 21.8)	21.6 (0–84.3; 25.0)	n.s.
Intrathecal IgA synthesis in % (range; SD)	3.8 (0–54.9; 12.6)	2.1 (0–47.4; 7.5)	n.s.
Intrathecal IgM synthesis in % (range; SD)	5.0 (0–92.4; 17.0)	6.1 (0–88.3; 16.8)	n.s.
IgG index (range; SD)	0.93 (0.45–2.83; 0.42)	1.02 (0.23–4.0; 0.65)	n.s.
QIgG $\times 10^{-3}$ (range; SD)	5.3 (2.0–16.9; 3.1)	5.2 (1.0–15.8; 3.3)	n.s.
IgG concentration in CSF in mg/l (range; SD)	60.7 (19.4–217.0; 42.4)	55.9 (9.1–206.0; 39.8)	n.s.

Hottenrott *et al. Fluids Barriers CNS (2017) 14:2*



Predictors of the Early and Intermediate Course of MS

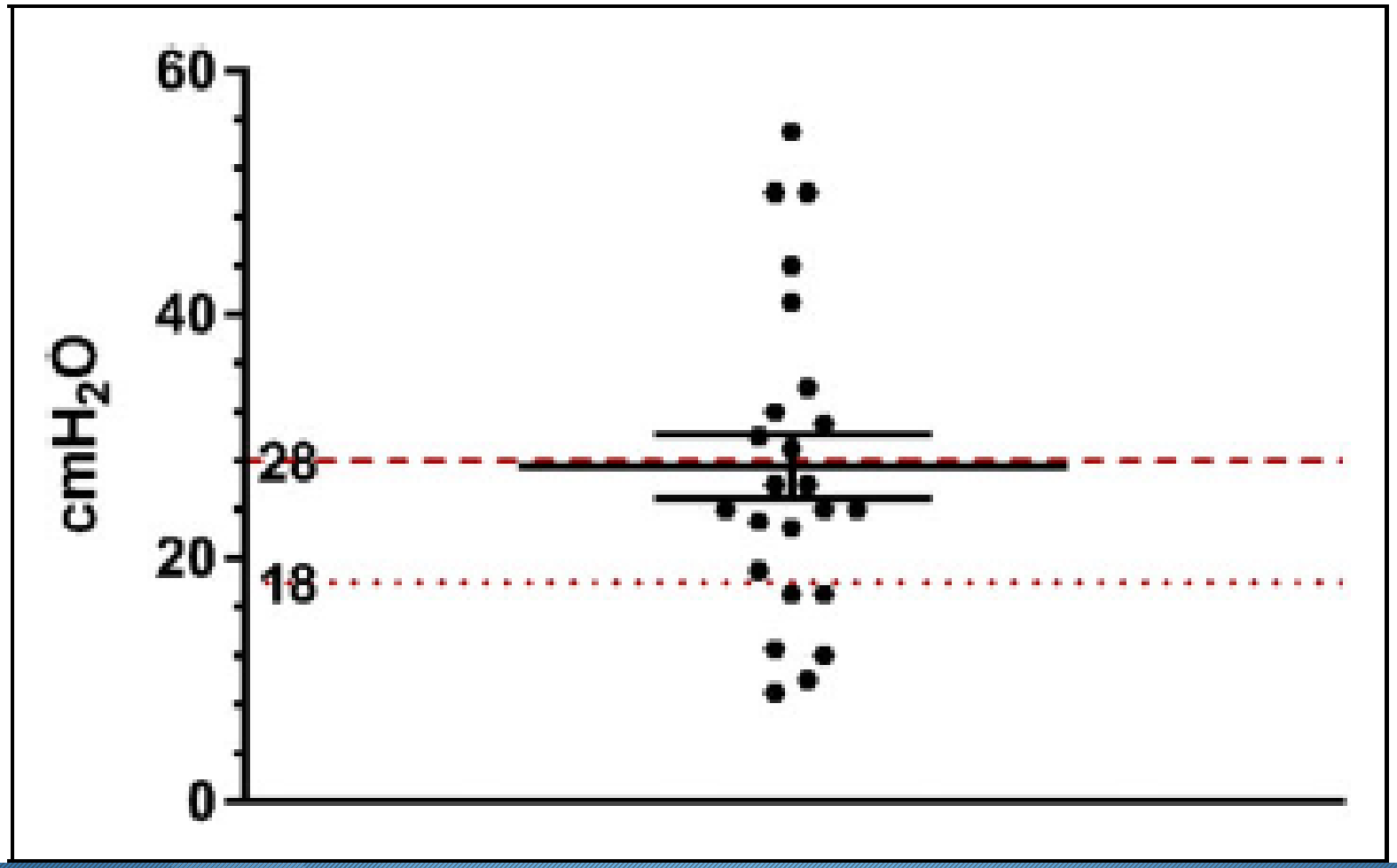
Marker	Detection method	Normal range	MS range	Prevalence in patients with MS (%)
Oligoclonal IgG bands	Isoelectric focusing and immunoblot	≤1 band	Unique in CSF, >1 band	90–100
Albumin CSF:serum ratio	Nephelometry	Age-dependent $<5–10\times10^{-3}$	$<10\times10^{-3}$	85–90
Activated B lymphocytes or plasma cells	Cytochemical staining	<0.1%	IgG type predominant	80
IgG index (linear formula) IgG synthesis rate (linear formula) IgG local synthesis (nonlinear formula)	Nephelometry and calculation	≤0.7 <3.5 mg per day 0.0 g/l	>0.7 >6.0 mg per day >0.0 g/l	50–75
Leukocyte count	Fuchs–Rosenthal chamber, panoptical staining and light microscopy	<5.0 cells per µl	5.0–50.0 cells per µl	50–60
MRZ reaction (optional)	Quantitative immunoassay and antibody index	Antibody index <1.5	Antibody index >1.4 for two or more virus-specific antibodies	70–90

Nat. Rev. Neurol. 9, 267–276 (2013)

Biomarker	Intended clinical purpose	Novel information (obtained 2012–2015)	Level of evidence	Pros and cons
Cerebrospinal fluid biomarkers				
IgG-OCBs	Support for diagnosis of MS	Confirmation[8,9] of numerous previous studies[2]	+++	Clinically implemented; high sensitivity but low specificity when other inflammatory diseases of CNS are considered
	Identification of CIS converters	Confirmation[6] of previous studies[11]	+++	Clinically implemented; high predictive value for identification of CIS converters
IgM-OCBs	Identification of CIS converters	Confirmation[13] of a previous study[12]	++	Replication in additional cohorts needed
MRZ-specific IgG	Support for diagnosis of MS	Confirmation[19,20,23] of previous studies[18]	+++	Technically challenging Replication in additional cohorts needed
κ free light chains (κFLC)	Support for diagnosis of MS	Two confirmatory studies[26,30] of previous[24–29] studies	++	Automatized analysis possible Replication in larger cohorts needed
C–X–C motif chemokine 13 (CXCL13)	Identification of CIS converters	One confirmatory study[41] of a previous study[43]	++	Replication in additional cohorts needed
Chitinase-3-like protein 1 (CHI3L1)	Identification of CIS converters	Two confirmatory studies[48,51,104] of a previous study[50]	+++	Ready for preparations for clinical implementation
Neurofilament light chain (NfL)	Identification of CIS converters	Confirmation[63–65] of previous studies[58,61]	+	Replication in larger cohorts needed

NEDA status[25] • NEDA 1–3 • NEDA 4 • NEDA 5 • NEDA 6 • NEDA 7 • NEDA 8	Clinical event, EDSS, MRI Brain atrophy Cognitive impairment CSF neurofilament level Patients related outcome Oligoclonal bands
BIOMARKERS[7,8] Related to cells, structures, metabolic pathways, and inflammatory and degenerative cascades.	OCB, NAA, Glutamate, IL-12, IL-23, Enolase, NfL, CXCL13, IL-8, ATP break down products, GFAP, MMP9, MMP3, Th17, Th1/Th17, Chitinase 3, IFN-ϒ, TNF-α, Fetuin-A, Osteopontin, PET (microglia), non-conventional MRI. Others.

F1000Research 2017, 6:566 Last updated: 20 JUN 2017



Journal of Child Neurology1-5 The Author(s) 2018

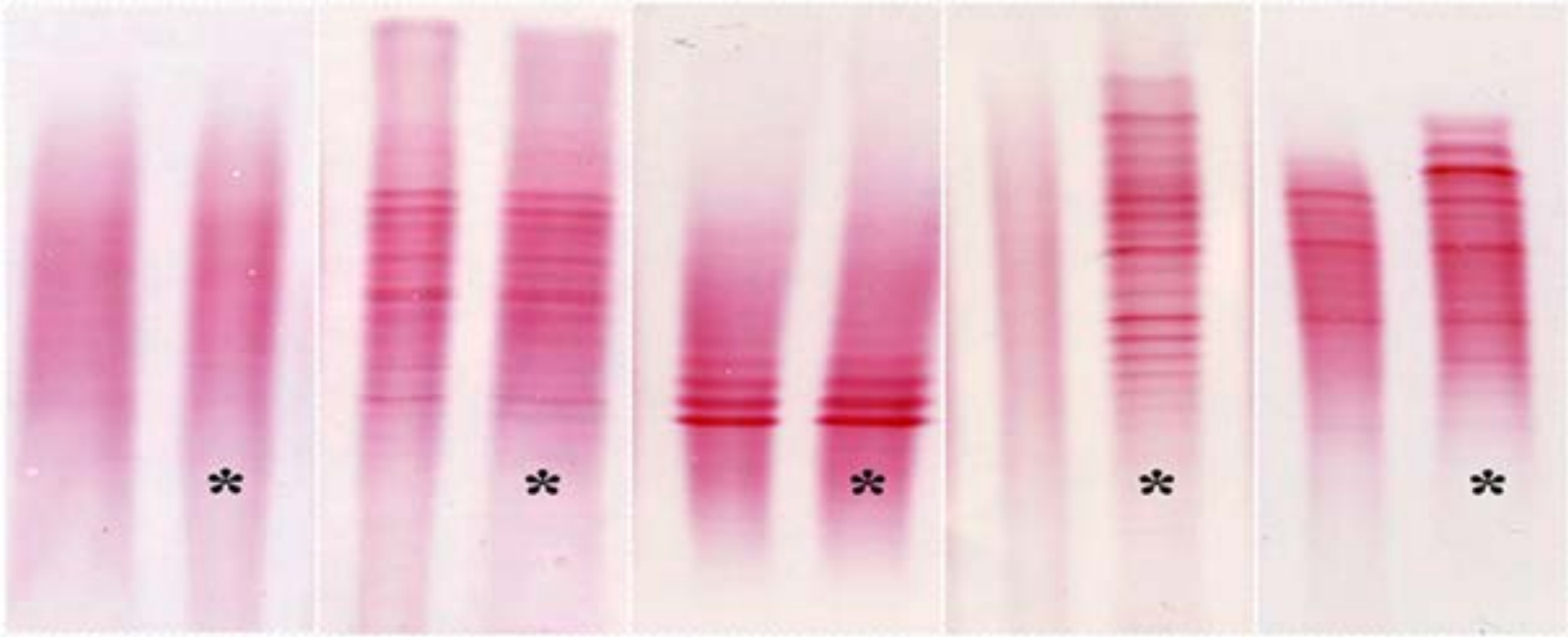
*Eş zamanlı alınan kan ve BOS örneğinde çalışılır
*Kan tercihen 3-4 saat önce alınır

$$\textbf{BOS IgG indeksi} = \frac{\text{IgG (BOS) X Albumin (serum)}}{\text{IgG(serum) X Albumin (BOS)}}$$

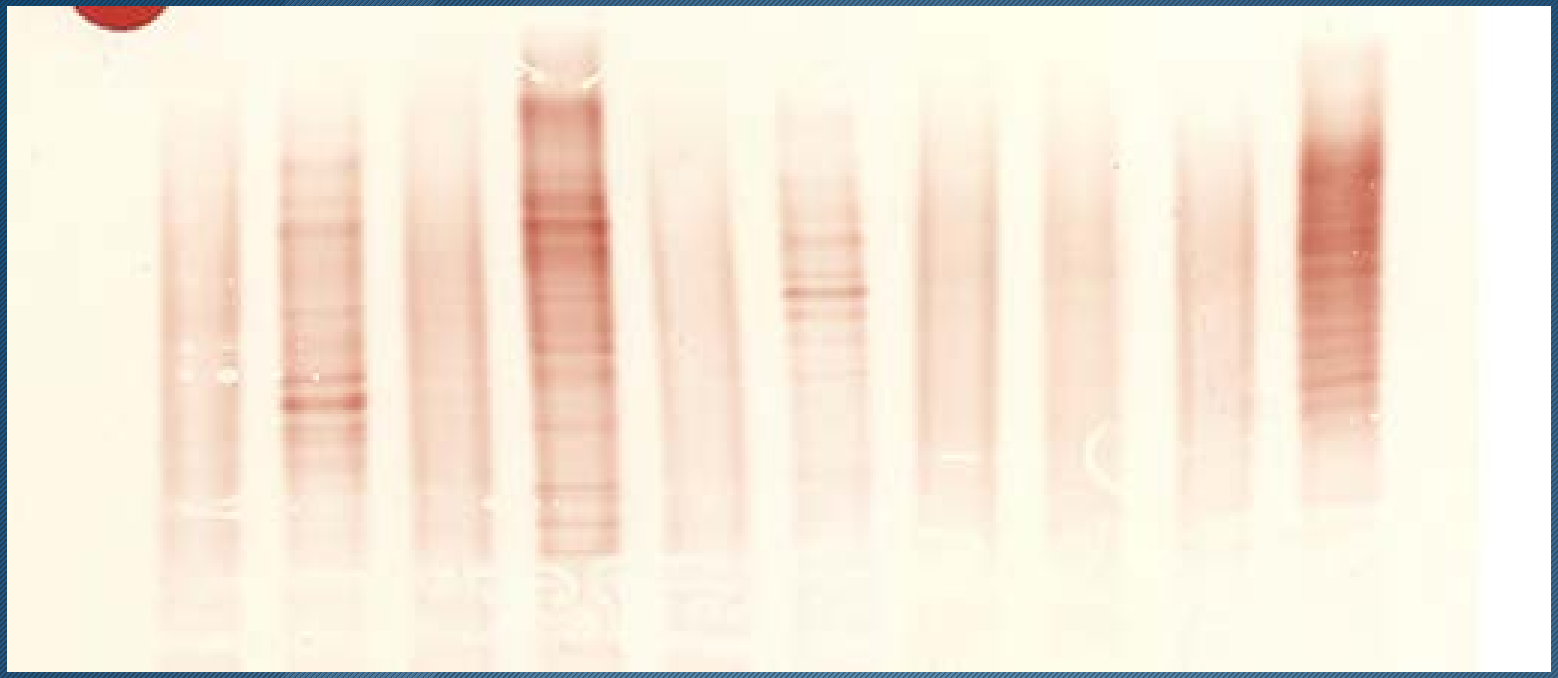
Reference range 0.3 – 0.7
> 0.7 = SSS kaynaklı
< 0.3 = telafi edilemez BBB bozukluğu

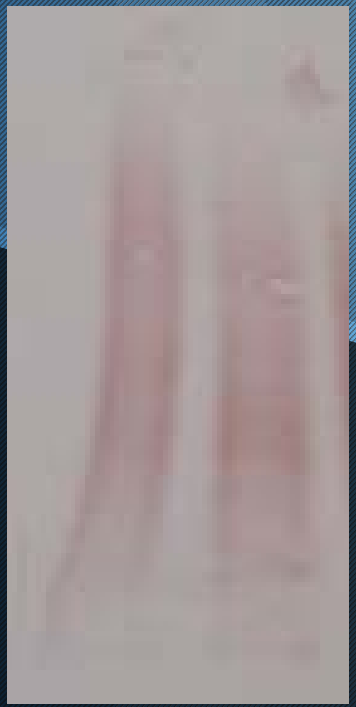
Reibergram : Grafiksel değerlendirme sağlar, referans aralığa göre daha değerli değerlendirme imkanı sunar

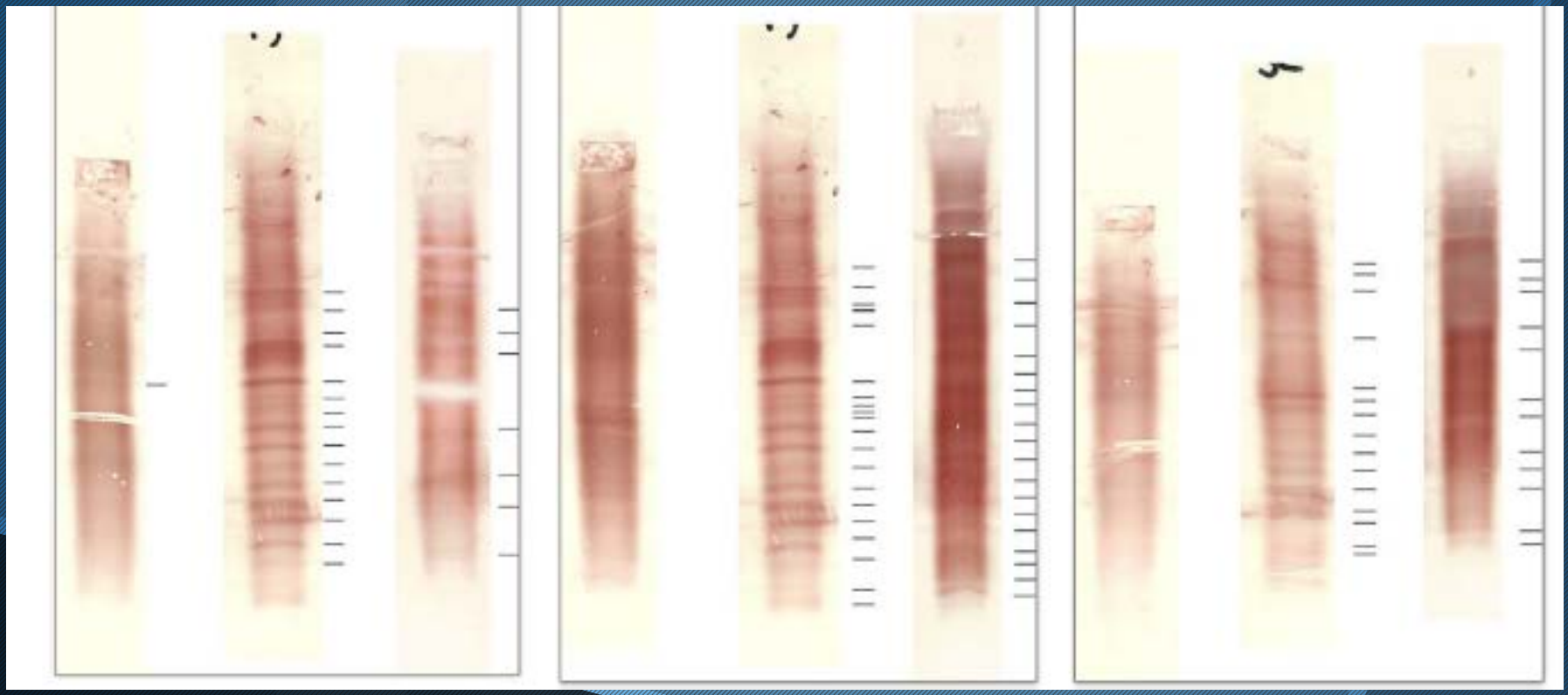
Oligoclonal Band pattern



Pattern: No bands	Pattern: Identical pattern	Pattern: Identical pattern	Pattern: CSF pattern.	Pattern: extra CSF bands.
Normal	**Infection/inflammation**	**Monoclonal protein**	**Seen MS**	**Also seen in MS**
Tip 1	Tip 4	Tip 5	Tip 2	Tip 3







RIS patients ($n = 45$)	OCB positive in tears ($n = 21$)	OCB negative in tears ($n = 21$)
Gender F/M	17/4	15/6
Age (mean; min–max)	33 (19–45)	33 (25–48)
MRI motives		
Headaches	13	14
Trauma	4	1
Endocrinopathy	1	3
Familial MS	1	1
Atypical mood disorders	1	1
Neuro-oncological follow-up	1	1
Brain MRI		
>9T2 lesions	18	18
Peri-ventricular	21	22
Juxta-cortical	19	18
Infra-tentorial	8	5
Gadolinium enhancement	9	5
Spinal cord MRI lesions	9	6
Gadolinium enhancement	1	0
VEP positive	11	5
CSF analysis		
OCB positive	21	1
Increased IgG index	18	1

	Tears−[a]	Tears+[b] (%)	Total (%)
CSF−[a]	25	0	25
CSF+[b]	15	29	44 (63.8%)
Total	40	29 (42%)	69

Multiple Sclerosis 16(1) 87–92 The Author(s), 2010.

	OB (+) MS	OB (−) MS	p
n	67	30	–
Male	24.2%	41.4%	0.105
Onset age	29.6 ± 8.9	31.7 ± 10.4	0.380
Present age	38.9 ± 9.2	42.5 ± 12.3	0.139
Disease duration [yrs]	8.7 ± 5.1	10.6 ± 8.5	0.697
Latest EDSS[a]	2.0 (0.0–8.5)	3.0 (0.0–7.5)	0.269
MSSS	3.90 ± 2.79	4.16 ± 2.48	0.669
Total relapses	3.4 ± 3.2	3.3 ± 2.8	0.871
Relapses per year	0.51 ± 0.45	0.47 ± 0.53	0.732
Serum-CSF-paired study at the onset			
n	36	15	–
CSF-CC	5 (0−12)	3 (0−13)	0.506
CSF-total protein	27.0 ± 9.9	33.1 ± 12.8	0.0795
Q_{Alb}	0.0048 ± 0.0024	0.0059 ± 0.0020	0.067
(Serum-albumin)	(4.22 ± 0.32)	(4.09 ± 0.45)	(0.324)
(CSF-albumin)	(18.5 ± 7.6)	(23.1 ± 8.9)	(0.135)
Q_{IgG}[a]	0.0034 (0.0015–0.0184)	0.0033 (0.0014–0.0047)	0.658
(Serum-IgG)	(1255 ± 350)	(1245 ± 203)	(0.933)
(CSF-IgG[a])	(3.3 [1.5–19.7])	(4.4 [1.8–5.5])	(0.571)
Q_{LDH}	0.094 ± 0.038	0.122 ± 0.073	0.291
Q_{CI}	1.212 ± 0.044	1.205 ± 0.029	0.639
IgG-index[a]	0.78 (0.50–3.23)	0.59 (0.41–0.69)	0.00016

	OB (+) MS	OB (−) MS	p
Barkhof criteria in the latest Gd-contrasted MRI			
n	61	25	–
Gd-enhancement (+) or ≥9 T2-high lesions	67.2%	48.0%	0.0962
(≥9 T2-high lesions)	(67.2%)	(32.0%)	(0.0027)
≥3 PVLs	80.3%	44.0%	0.00088
Number of PVLs[a]	6.0 (3.0, 11.0)	3.0 (1.0, 7.0)	0.0121
≥1 infratentorial lesions	31.1%	28.0%	1.00
≥1 juxtacortical lesions	68.9%	50.0%	0.0693
Fulfillment of Barkhof criteria	62.3%	36.0%	0.0261
Brain volumetry in 2016			
n	30	19	–
Disease duration at volumetry [yrs]	9.5 ± 5.6	10.4 ± 8.3	0.633
Whole brain volume [cc]	1427 ± 84	1441 ± 70	0.568
Grey matter volume [cc]	869 ± 47	865 ± 55	0.798
Age-corrected grey matter atrophy [cc]	68.2 ± 38.9	65.1 ± 35.3	0.781
White matter volume [cc]	559 ± 50	576 ± 38	0.207
Age-corrected white matter atrophy [cc]	53.6 ± 51.0	32.9 ± 34.7	0.126
FLAIR lesion volume [cc]	16.5 ± 12.0	7.6 ± 5.2	0.0039

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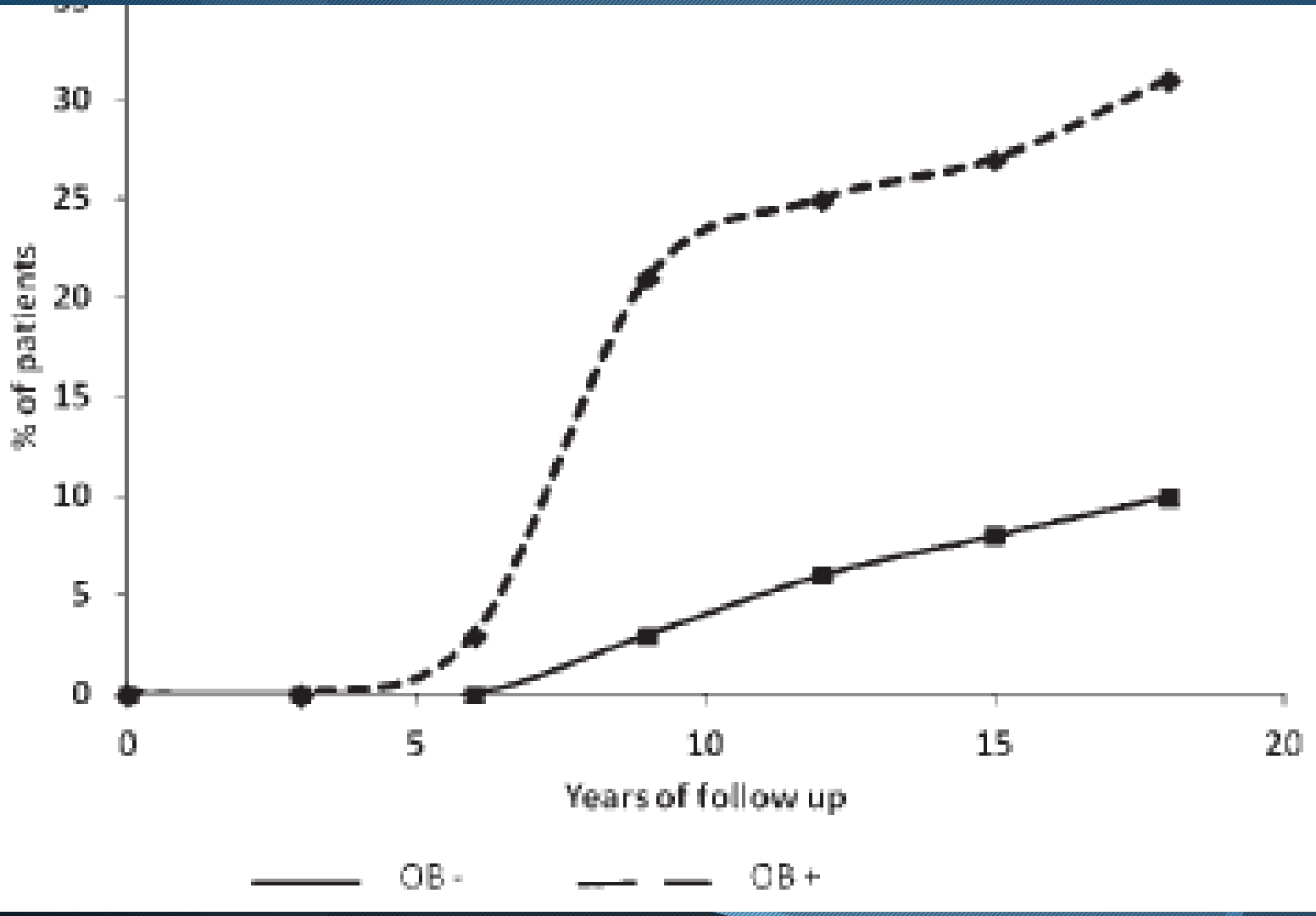
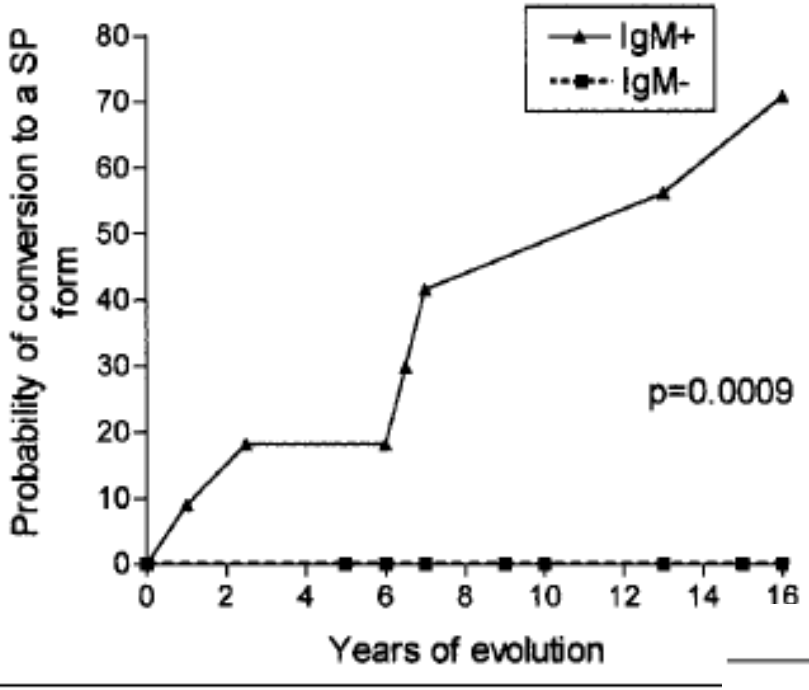
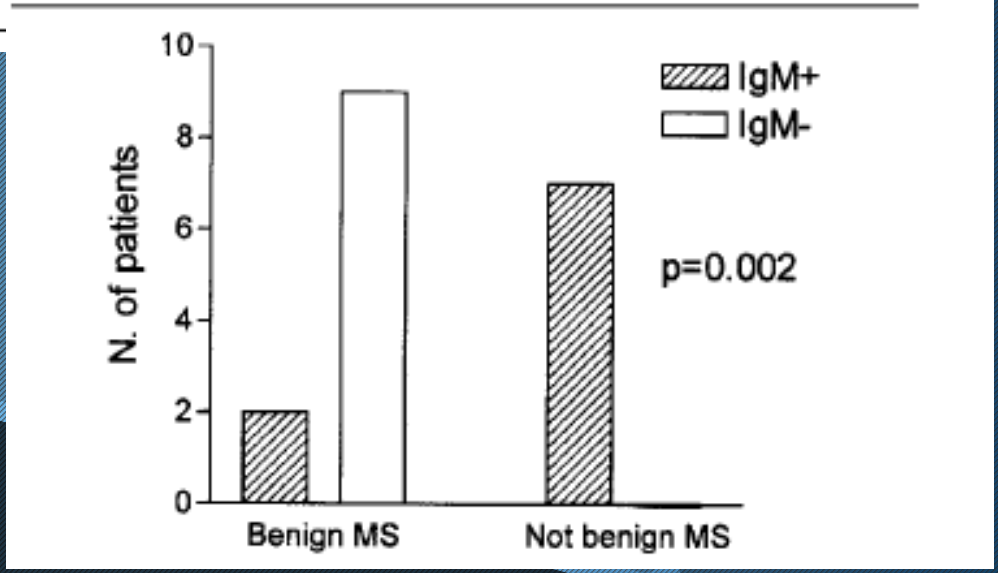


Neurological Research 2012 VOL. 34 NO. 9 889

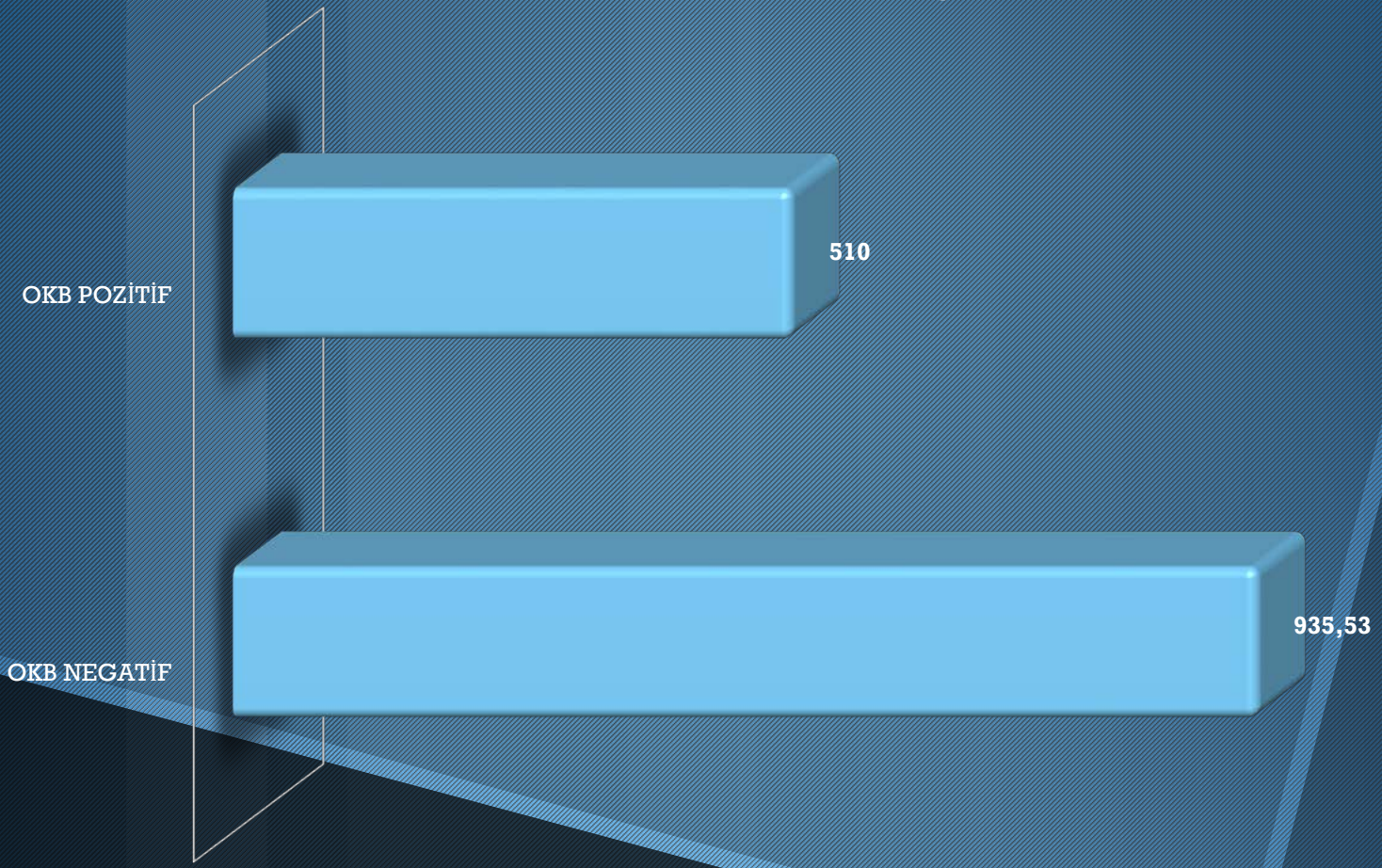


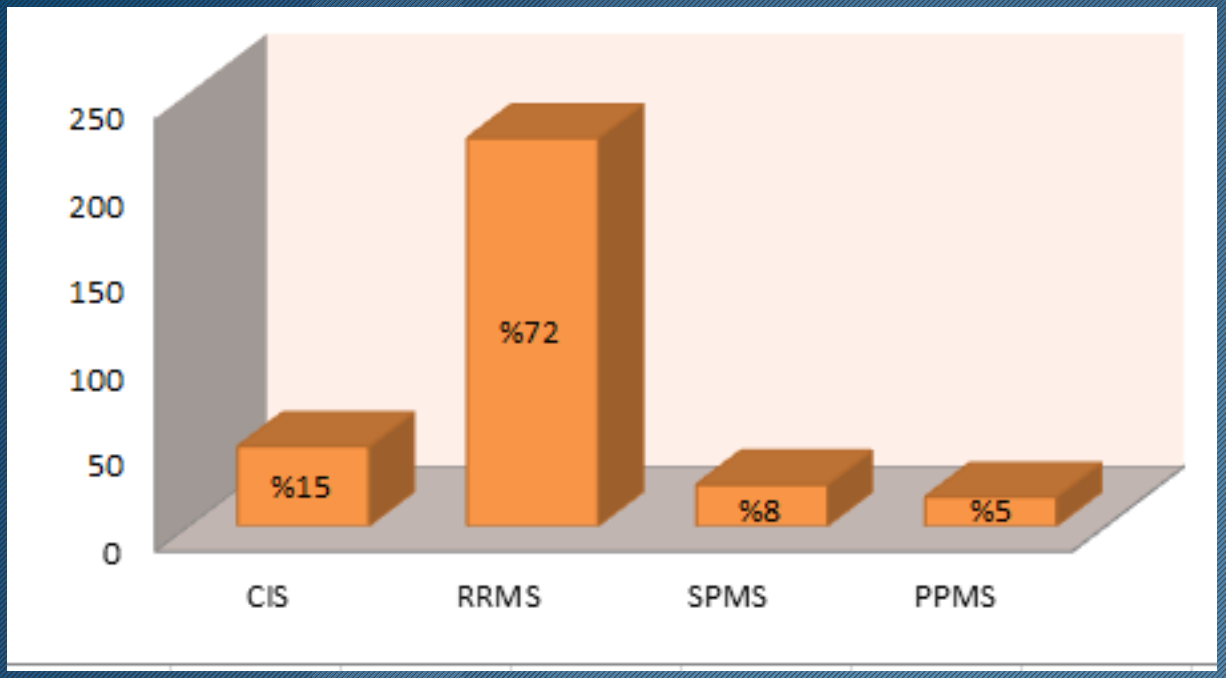


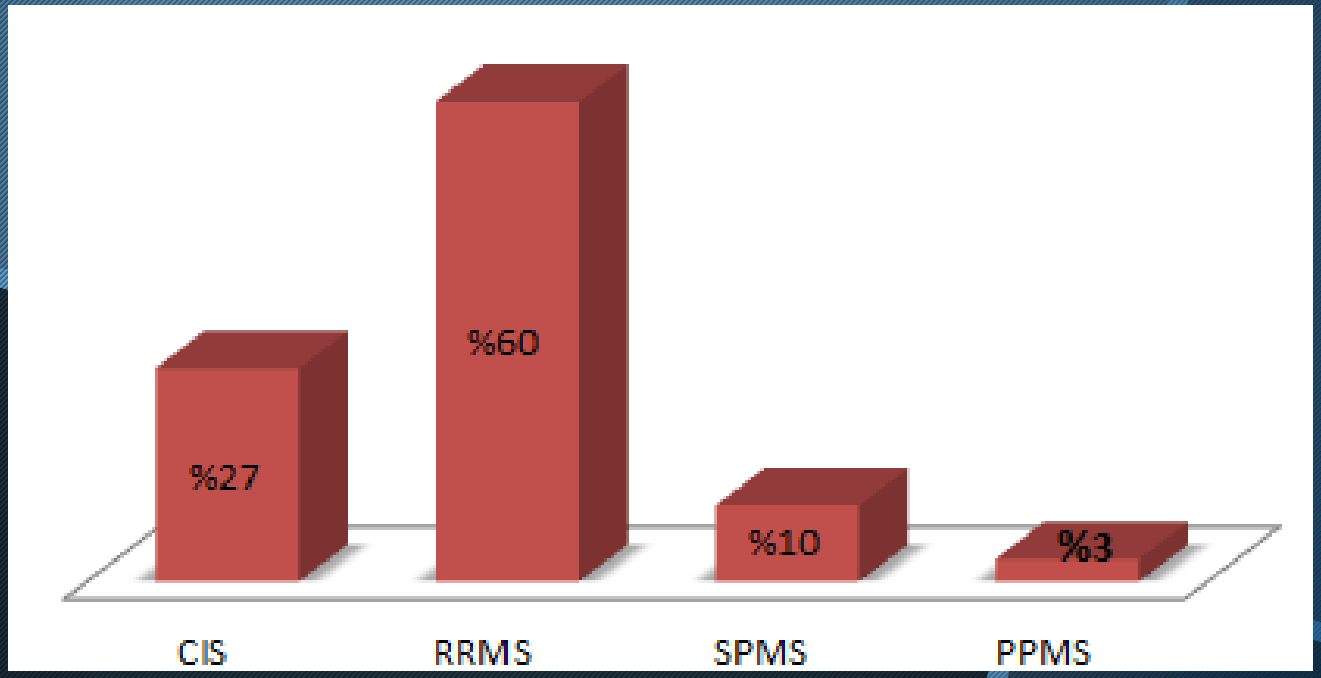
Ann Neurol 2003;53:222–226

	OKB (+) (n=311)	OKB (-) (n=104)	P
YAŞ ORTALAMALARI	42,29 (17-62)	42,48 (17-70)	P>0,05
KADIN/ERKEK ORANI	1,74 209/102	1,97 69/35	P>0,05
ORTALAMA EDSS	1,96	1,68	P>0,05
YILLIK ATAK SAYISI	3,8	3,27	P>0,05
ORTALAMA HASTALIK SÜRESİ	9,4	9,92	P>0,05

İLK ATAK-2. ATAK ARASINDA GEÇEN SÜRE (GÜN)




250
200
150
100
50
0
%15
%72
%8
%5
CIS
RRMS
SPMS
PPMS


%27
%60
%10
%3
CIS
RRMS
SPMS
PPMS

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)
yaş	,002	,013	,033	1	,856	1,002
EDSS	,067	,069	,955	1	,328	1,070
TOPLAMATAK	,132	,057	5,380	1	,020	1,142
Gender	-,054	,249	,047	1	,829	,948
Supratentorial	-,176	,445	,157	1	,692	,838
OpticPathways	-,183	,443	,171	1	,680	,833
BrainstemCerebellum	,204	,445	,211	1	,646	1,227
SpinalCord	,128	,547	,055	1	,815	1,137
ProgressionFromOnset	,849	,686	1,532	1	,216	2,337
hastalıkyaşı	-,036	,024	2,142	1	,143	,965
Constant	,045	2,147	,000	1	,983	1,046

Bağımlı değişken group (-,+)

Hepsi önemsiz.

REIBERGRAM

Q (indeks) =
BOS/ serum oranı

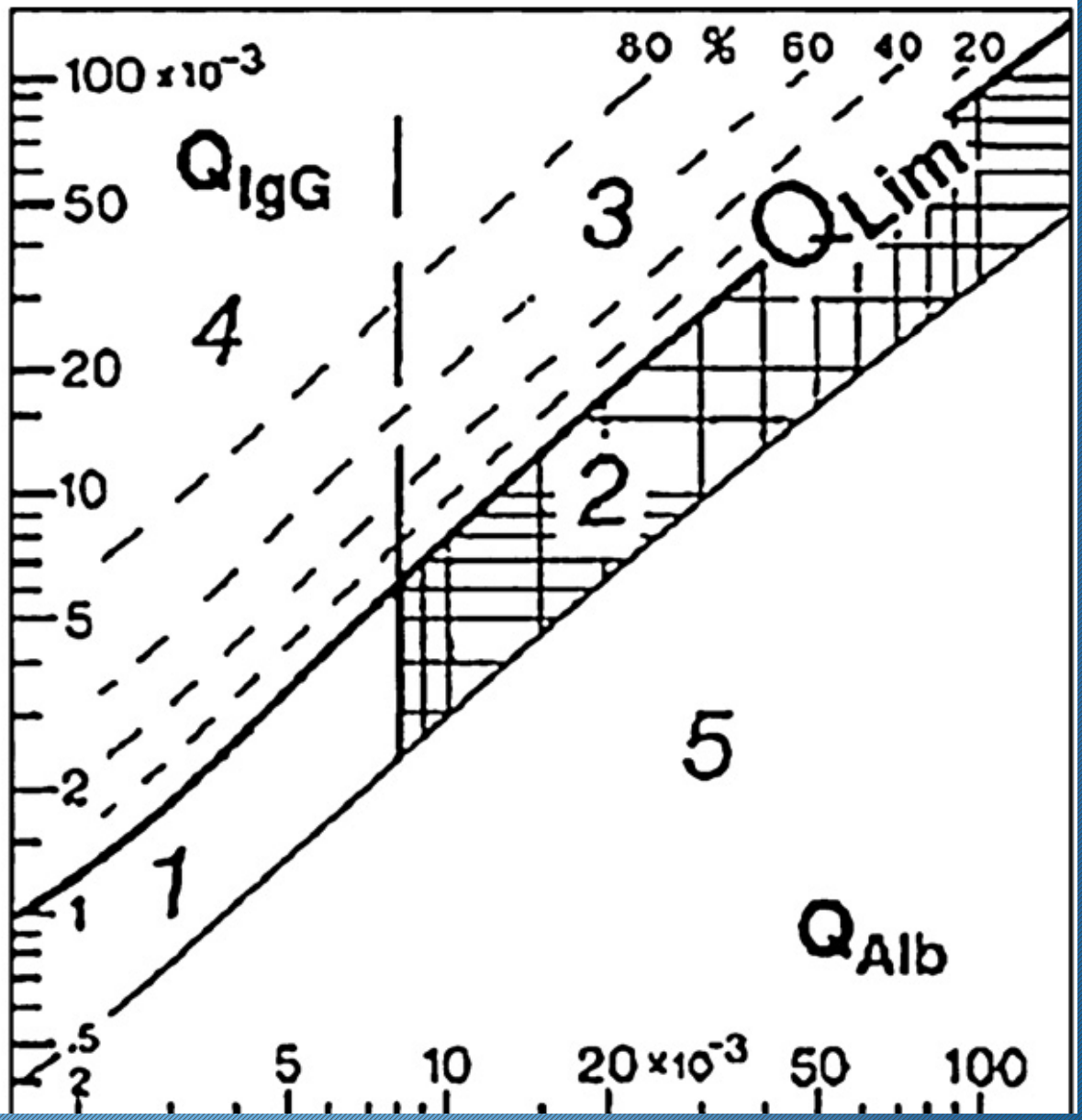
1 : NORMAL

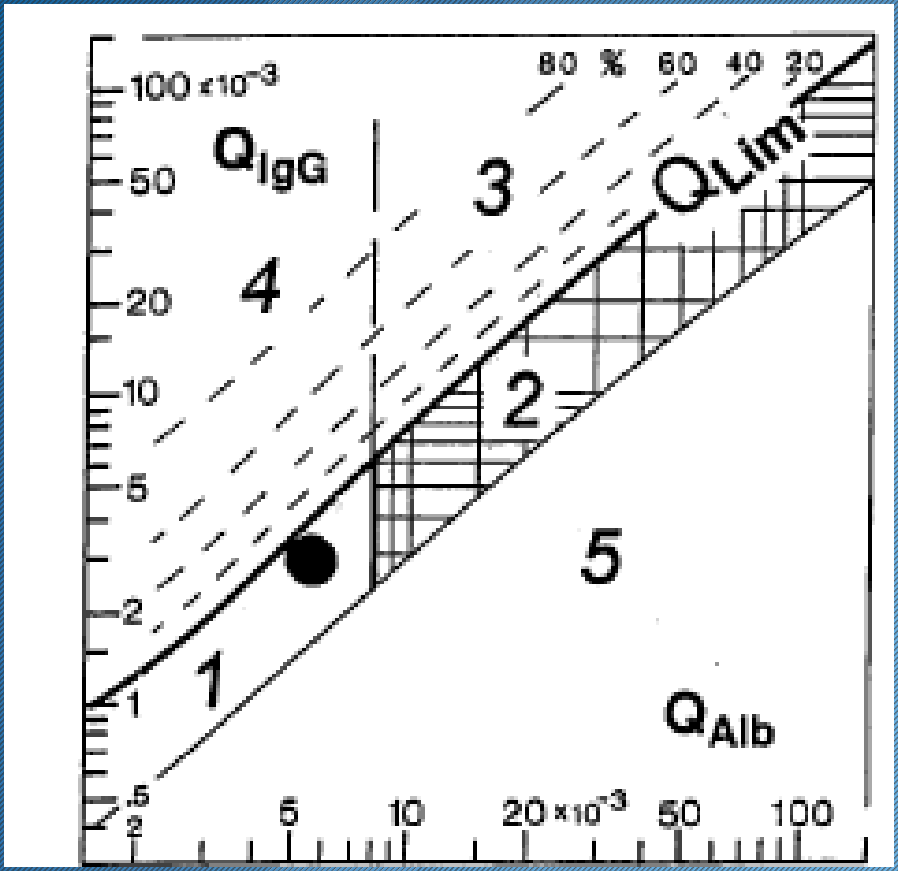
2:Kan-beyin bariyeri disfonksiyonu

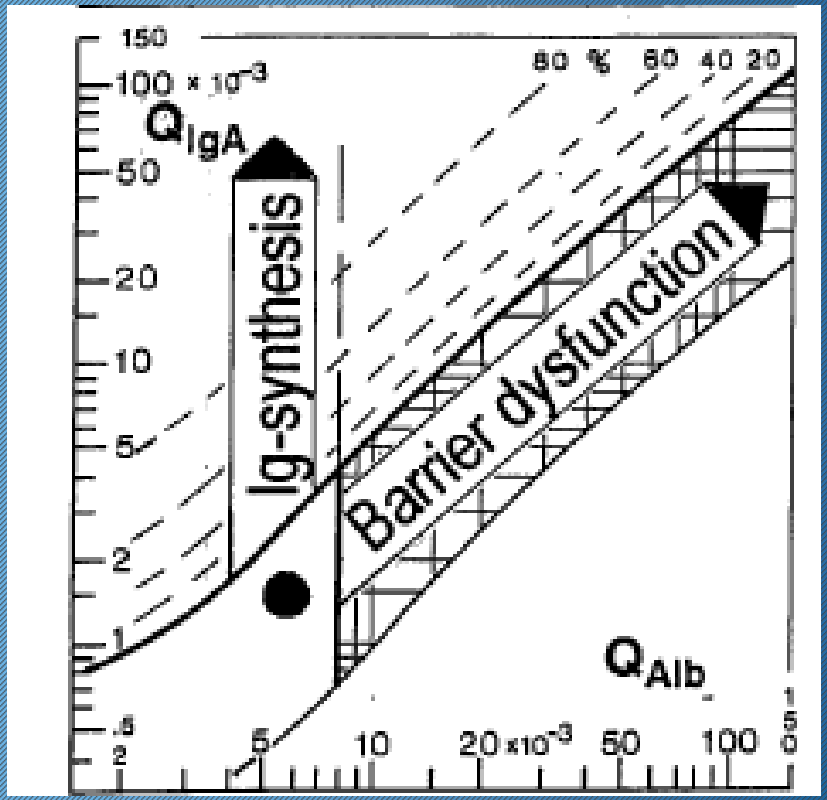
3. Intratekal Ig G sentezi ve kan-beyin bariyeri Disfonksiyonu

4. Intratekal Ig G sentezi

5.Metot hatası







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Visual Inspection					Hemoglobin				Lactate	Tot. Protein
clear	turbid	xanth	blood	art. blood	0	+	++	+++	6,0 mmol/l	1563 mg/l

CELLS

Cell count 337 / µl Ery 0 / µl

Lymphoc % | Monoc % | N. Granuloc. % | Plasma c. %

Other Cells

PROTEINS	CSF		Serum		Q x 10^3		Intrath. Fract, (IF)	
Albumin	**809**	mg/l	**35,2**	g/l	QAlb =	**23**		
IgG	**189**	mg/l	**13,6**	g/l	QIgG =	**13,9**		%
IgA	**55,7**	mg/l	**2,9**	g/l	QIgA =	**19,2**	**22**	%
IgM	**31,4**	mg/l	**5,9**	g/l	QIgM =	**5,3**		%

Oligoclonal IgG CSF-spec. bands [0] o/+ Type **1**

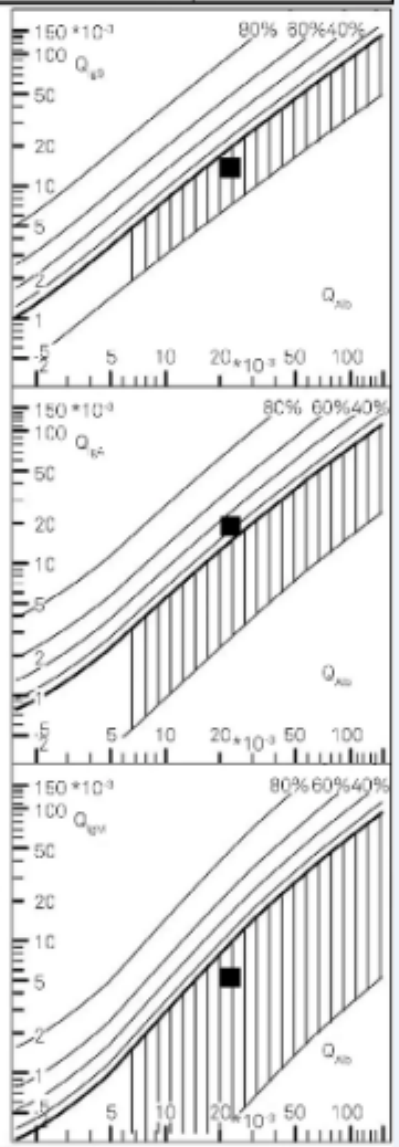
Specific Antibodies Synthesis in CNS : AI≥1.5 , n.d. = not detectable

Measles-AI =	Borr.-AI(IgG) =	TP-AI (IgG) =
Rubella-AI =	Borr.-AI(IgM)=	TP-AI (IgM) =
VZV-AI =	HIV-AI =	
HSV-AI =	Toxopl –AI =	
CMV-AI =	EBV-AI =	

Surrogate marker (Tumor, Dementia, Hemorrhage, Psychiatric diseases)

Interpretation

Normal CSF-Report	☐	Normal proteins	☐
B-CSF barrier dysfunction	☒	Cell count increased	☒
Inflammatory process	☒	Lactate increased	☒
AB-synthesis in CNS	☐	Path. Dementia markers	☐



Comments

The combination of an intrathecal IgA synthesis, pathologically increased lactate (>3.4mmol/l), a severe blood-CSF barrier dysfunction and intermediate increase of the cell count is a typical result found with a very high plausibility for **neurotuberculosis**. A corresponding, specific investigation is adviced

Cells

Cellcount	3	/mm³	RBC		/mm³
Lymphoc.	80 %	Mononucl.c. 20 %	PMNR (n.)	%	Plasmac. few

Other Cells		
Activ. B-Cells		% of Lymphocytes

Proteins

	CSF		Serum		Q(CSF/Ser) · 10³		Intrathec. fraction	
Tot. Prot.	270	mg/L						
Albumin	111	mg/L	41.4	g/L	Q_{Alb} =	2.7		
IgG	56	mg/L	8.8	g/L	Q_{IgG} =	6.3	73	%
IgA	1.9	mg/L	2.2	g/L	Q_{IgA} =	0.9		%
IgM	2.1	mg/L	2.0	g/L	Q_{IgM} =	1.0	56	%

Oligoclonal IgG – Bands in CSF (Type 2)

Specific Antibodies

Measles-AI	= 9.2	HIV-AI	=	Borrel.-AI(IgG)	=
Rubella-AI	= 12.3	CMV-AI	=	Borrel.-AI (IgM)	=
VZV-AI	= 8.1	Toxopl.-AI	=	.....-AI	=
HSV-AI	= 1.0	.....-AI	=	.....-AI	=

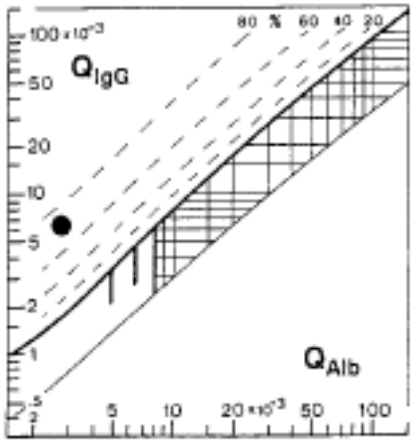
Lactate 1.6 mmol/L CSF

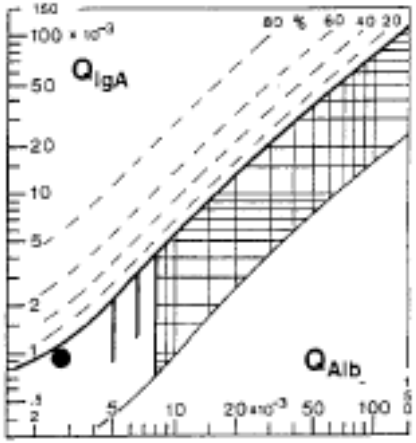
Interpretation

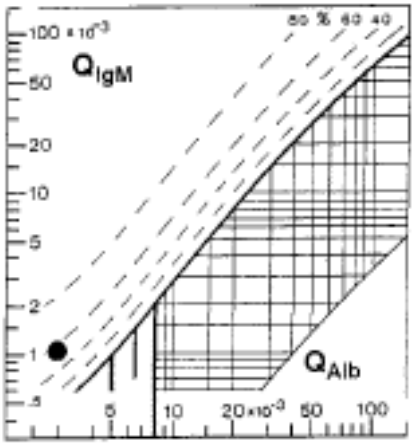
Normal CSF	☐	Normal CSF proteins	☐
B-CSF Barrier dysfunction	☐	Cellcount increased	☐
Inflammatory proc. in CNS	X	Spec. Ab-Synthesis in CNS	X

Comment:

Chronic inflammatory process. DD: Multiple sclerosis or autoimmune disease with involvement of CNS

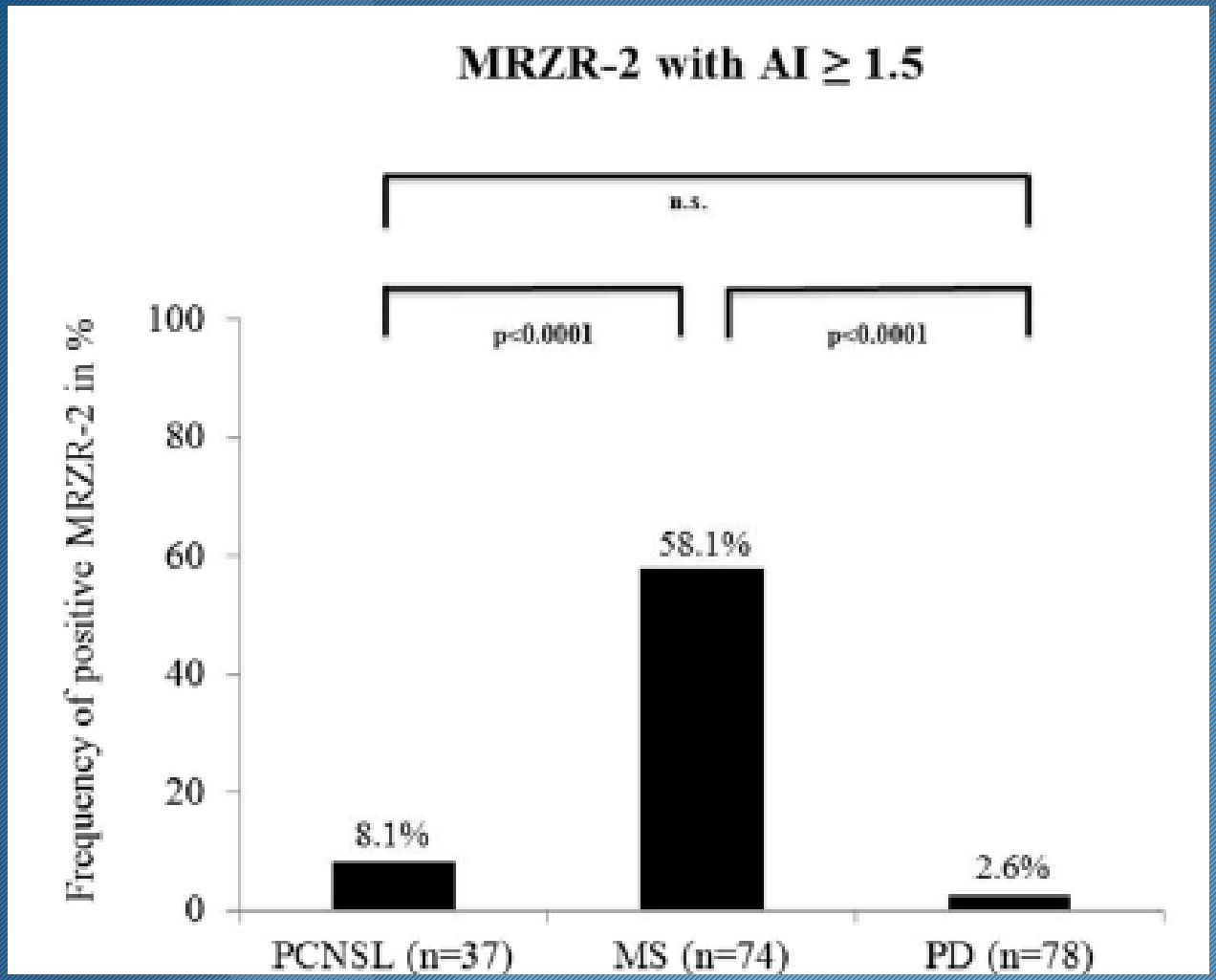




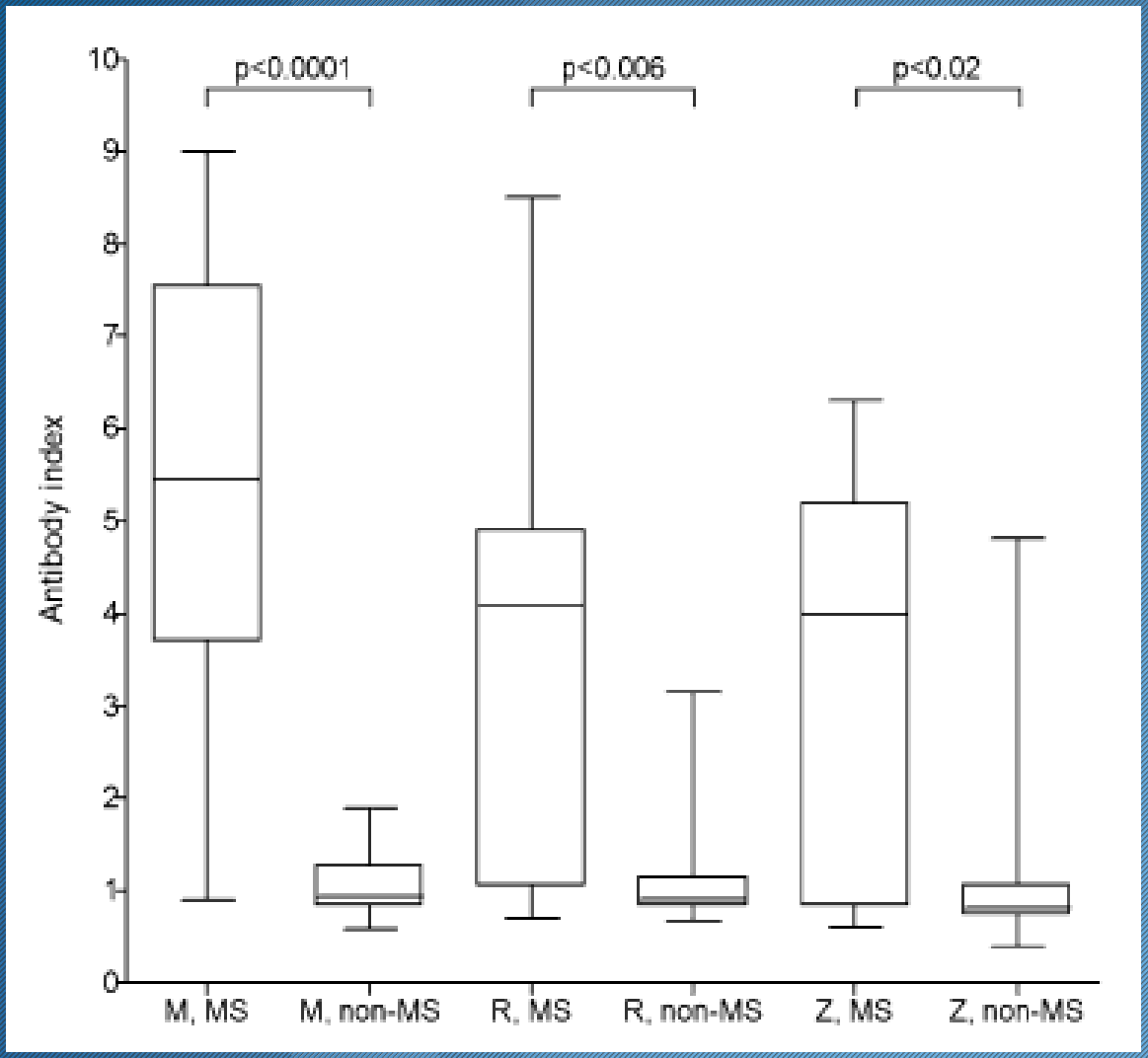


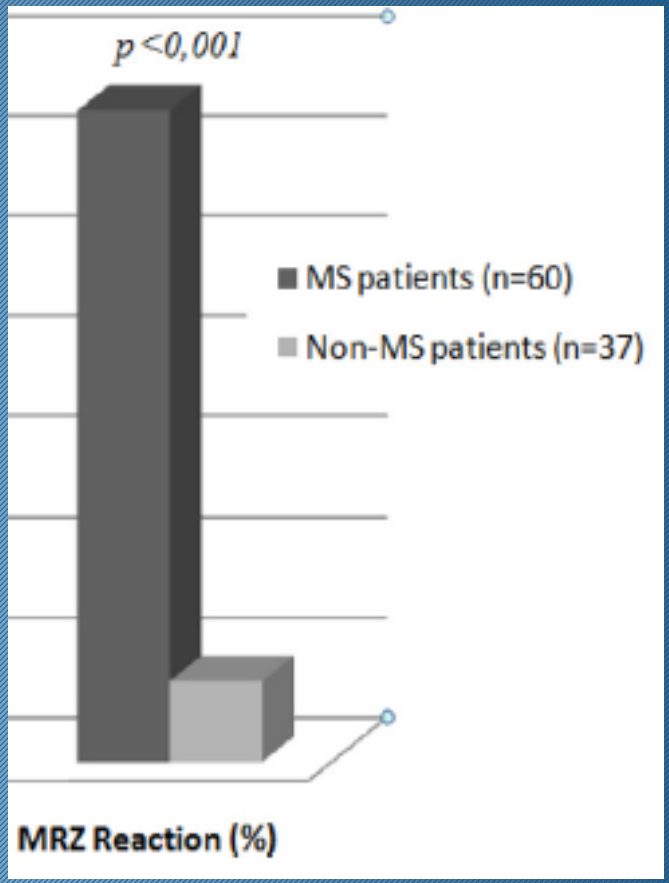
Diagnostic Group	Sensitivity (%)	Specificity (%)
Q_{Alb} (cut-off = 6.24)	79.4	48.2
IgG index (cut-off = 0.59)	69.4	76.7
R4	43.5	92.0
OCB (+)	82.4	83.6
OCB (+ >10)	51.5	92.0
R4 with OCB (+ >10)	37.0	95.0

NSN 2018; 35: 21-28



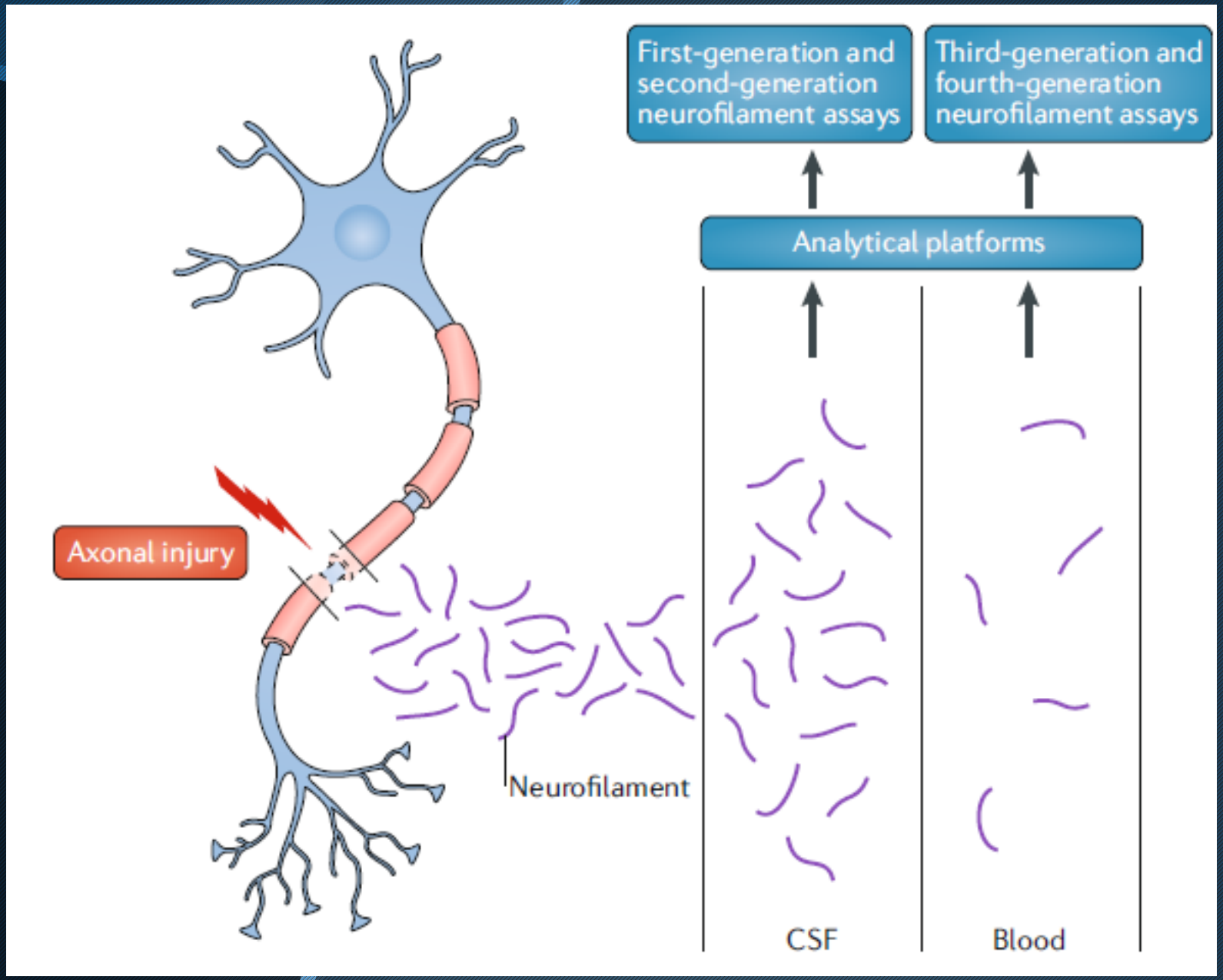
Journal of Neurology (2018) 265:1106–1114





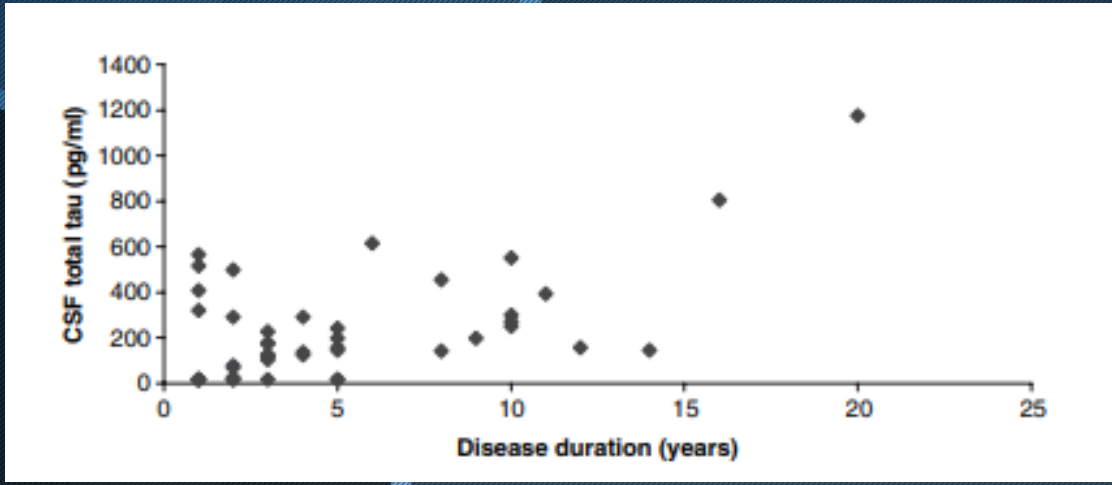
Neurol (2017) 264:453–466

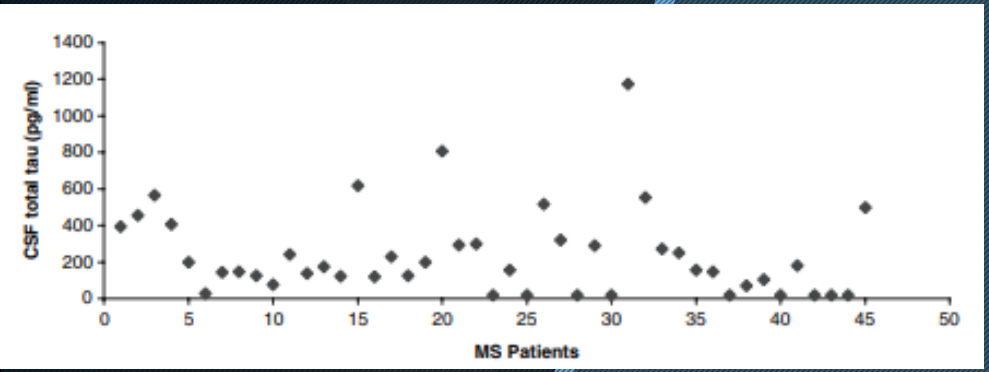
		CIS all	CIS-CIS	CIS-RRMS	S*
n (female/male)		89 (56/33)	40 (22/18)	49 (34/15)	NS
Age [years]	Median (Range)	38.5 (13.1–70.9)	38.4 (16.8–70.9)	39.4 (13.1–63.6)	NS
EDSS	Median (Range)	2 (0–5)	2 (0–5)	3 (0–5)	NS
Measles AI≥1.5	n (%)	37 (42)	11 (33)	26 (59)	NS
Rubella AI ≥1.5	n (%)	32 (36)	9 (24)	23 (49)	p=0.03
Zoster AI ≥1.5	n (%)	32 (36)	12 (32)	20 (42)	NS
MRZR	n (%)	33 (37)	10 (25)	23 (47)	p=0.04
MRZS	n (%)	19 (21)	4 (10)	15 (31)	p=0.018
OCB	n (%)	74 (83)	27 (68)	47 (96)	p=0.001
MRI	n (%)	59 (66)	21 (53)	38 (78)	p=0.02
Barkhof criteria	n (%)	25 (28)	8 (20)	17 (35)	p=0.125

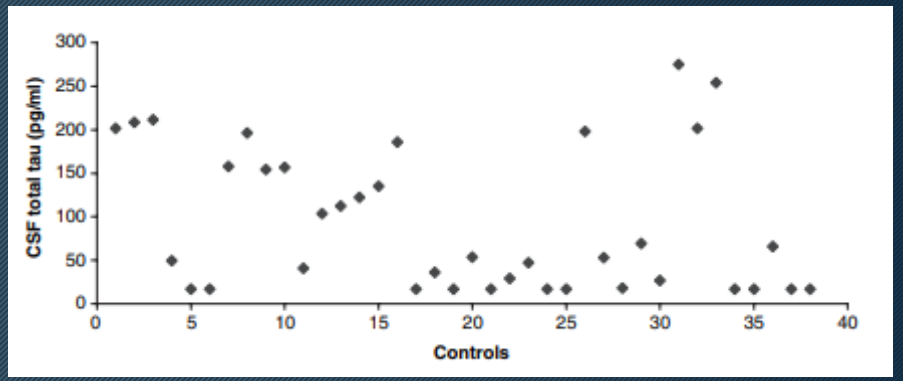

First-generation and second-generation neurofilament assays
Third-generation and fourth-generation neurofilament assays
Analytical platforms
Axonal injury
Neurofilament
CSF
Blood

GFAP	Astrocyte	CSF	↑ (versus MS)	EDSS and length of involved spinal cord
			↑(versus ONNDs)	EDSS and length of involved spinal cord
S100B	Astrocyte	CSF	↑ (versus MS)	EDSS and length of involved spinal cord
			↑(versus ONNDs)	EDSS and length of involved spinal cord
C5a	Complement	CSF	↑ (versus ONNDs)	EDSS [105]
C5b-9	Complement	CSF	↑ (versus MS)	EDSS [106]
			↑ (versus ONNDs)	EDSS [106]
HMGB1	Macrophage	Serum	↑ (versus MS)	
			≅ (versus MS)	
			≅ (versus ONNDs)	
		CSF	↑ (versus MS)	
			↑(versus ONNDs)	
Haptoglobin	Neutrophils, macrophages, astrocytes	CSF	↑ (versus MS)	EDSS [110]
			↑ (versus ONNDs)	
MMP-9	Neutrophils, macrophages	Serum	↑ (versus HC)	EDSS [89]
			↑ (versus MS)	
CCL4	Macrophages	Serum	↑ (versus MS)	
		CSF	↑ (versus ONNDs)	
sICAM-1,	Cell adhesion	Serum	↑ (versus HC)	
		CSF	↑ (versus MS)	
			↑ (versus ONNDs)	
sVCAM-1	Cell adhesion	CSF	↑ (versus MS)	
			↑ (versus ONNDs)	
CXCL8	Neutrophils	CSF	↑ (versus MS)	
			↑ (versus ONNDs)	
CXCL13	B cells	Serum	↑ (versus ONNDs)	
		CSF	↑ (versus MS)	
			≅ (versus MS)	
			↑ (versus ONNDs)	
NFH^{SM135}	Neurofilament	CSF	↑ (versus MS)	
Acetate	Metabolites	Serum	↑ (versus HC)	
			↑ (versus MS)	
Scyllo-inositol	Metabolites		↓ (versus MS)	

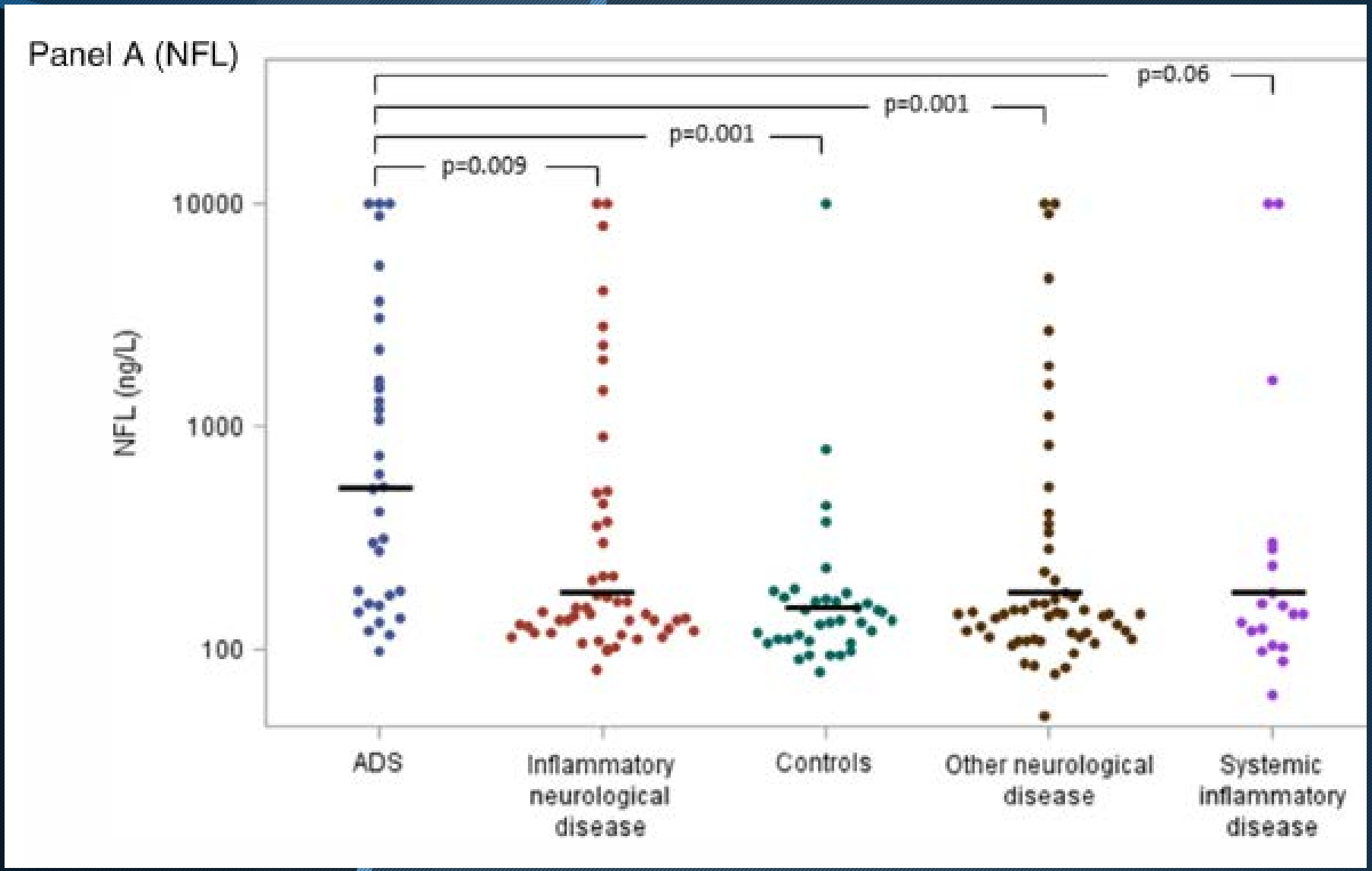
K.-H. Chang et al. / Clinica Chimica Acta 440 (2015) 64–71







Acta Neurol Scand 2007: 115: 325–330



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Author, year	Country	Gender (% male)		Mean age (years)		Disease duration (year)	Sample origin	N		MS (NFL ng/L)		HC (NFL ng/L)	
		MS	HC	MS	HC			MS	HC	Mean	SD	Mean	SD
Novakova et al, 2017[96]	Sweden	29.9	59.5	37	28	NA	CSF	204	42	730	82,807	205	903.7
Haghighi et al, 2004[98]	Sweden	NA	NA	44	33	NA	CSF	47	50	258.7	186.7	128.3	15.8
Norgren et al, 2003[99]	Sweden	NA	NA	NA	NA	NA	CSF	5	11	2,500	3,354	31	76.3
Rosengren et al, 1996[100]	Sweden	NA	NA	35.6	53	8	CSF	5	11	463	402	128	6
Novakova et al, 2017[101]	Sweden	71.4	64.1	37	34	6.6	CSF	7	39	1,900	1,722	364	302.3
Novakova et al, 2017[102]	Sweden	37.2	64.1	39.7	33.6	NA	CSF	43	39	1,183	2,135	364	254
Håkansson et al, 2017[103]	Sweden	22	23	31	32	0.98	CSF	41	22	895	1,304	212	102.2
Novakova et al, 2015[104]	Sweden	35.5	68.8	36	41	8.4	CSF	31	16	2,391	5,274	308	95
Zhang et al, 2007[105]	China	36.5	43.5	39	29	8	CSF	63	46	26	33	10	7
Malmeström et al, 2003[106]	Sweden	47.8	70	32.4	35.4	7.9	CSF	23	50	1,727	1,711	125	152.5
Novakova et al, 2017[96]	Sweden	29.9	59.5	37	28	NA	Serum	204	42	16.9	1,095	10.5	44.4
Disanto et al, 2017[97]	Switzerland	35.2	31.9	37.9	44.3	NA	Serum	142	254	35.9	29.3	22.9	10.8
Disanto et al, 2017[97]	Switzerland	34.1	31.9	42.2	44.3	7.4	Serum	719	254	29.4	18.6	22.9	10.8
Kuhle et al, 2016[107]	Switzerland	35.5	44	32	31	3.6	Serum	31	18	9	17.4	1.3	3.9
Disanto et al, 2016[108]	Switzerland	33	37	30.6	35	0.31	Serum	100	92	24.1	28.4	7.9	8.6

Abbreviations: CSF, cerebrospinal fluid; HC, healthy control; MS, multiple sclerosis; N, number; NA, not available; NFL, neurofilament light chain.

Subkutan cladribin kullanan OKB pozitif 29 MS hastasında % 55 negatifleşme

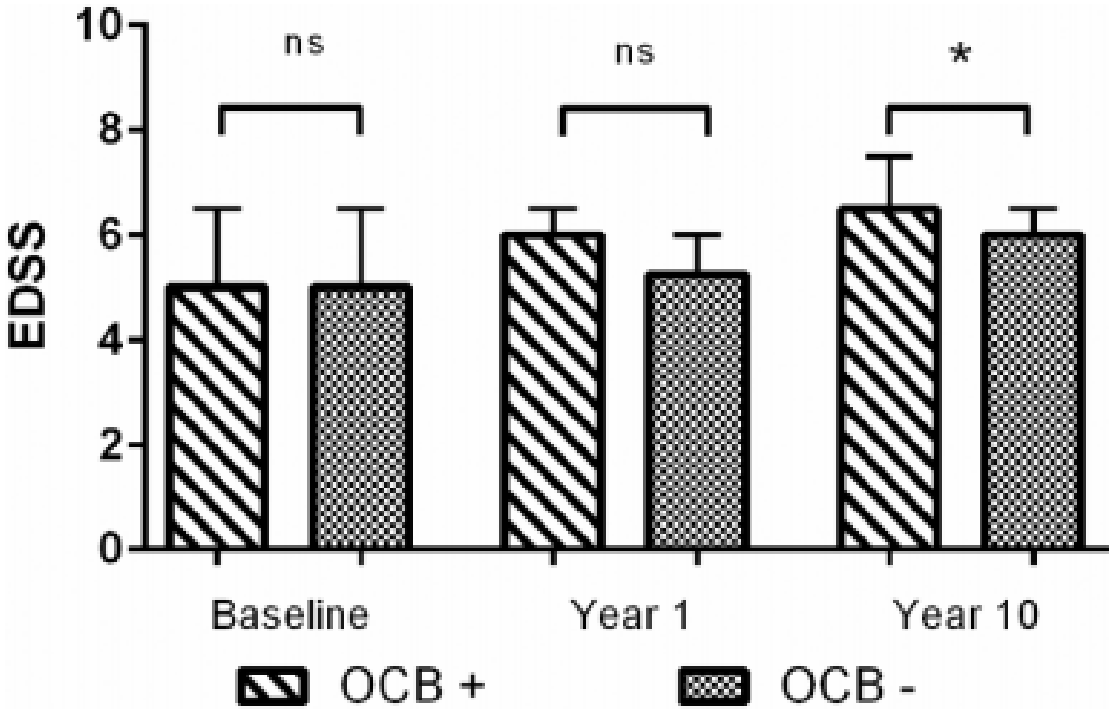

Fig. 1. Comparison of Expanded Disability Status Scale (EDSS) scores between patients with oligoclonal bands (OCB +) versus patients without (OCB −) as assessed at the last follow-up, at different time points: baseline ($p > 0.05$), the end of induction cladribine treatment cycle (Year 1; $p > 0.05$) and at the last follow-up (Year 10; $p = 0.03$). EDSS values are expressed as medians with range.

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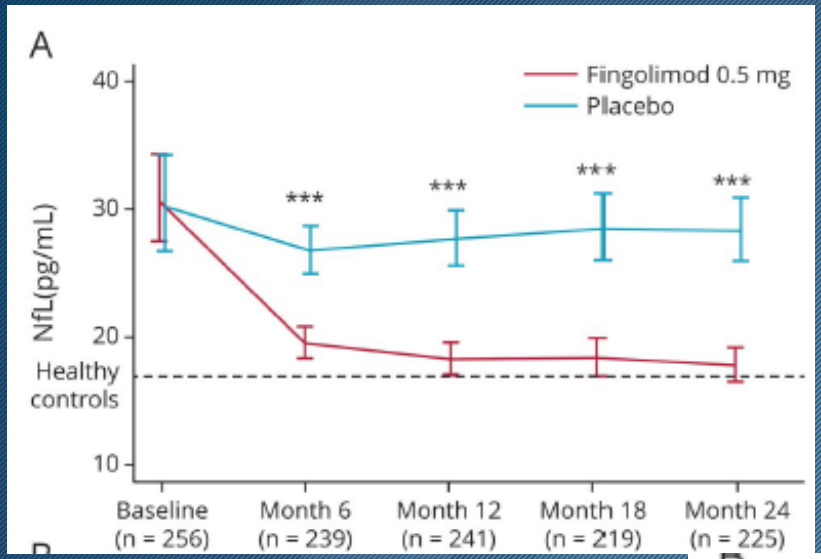

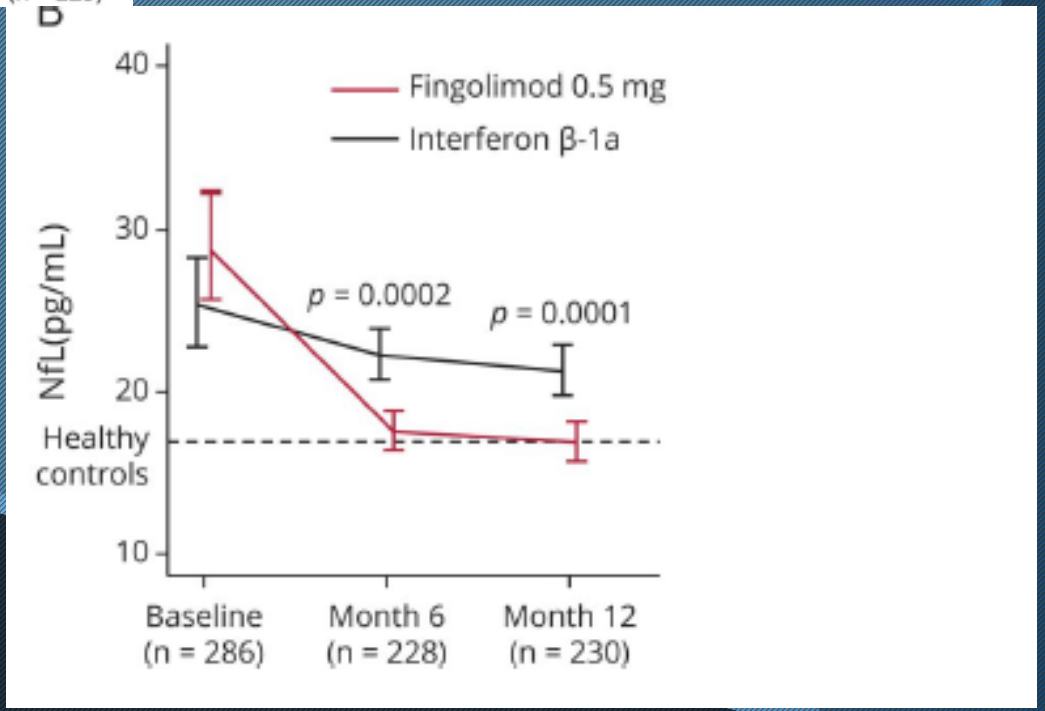

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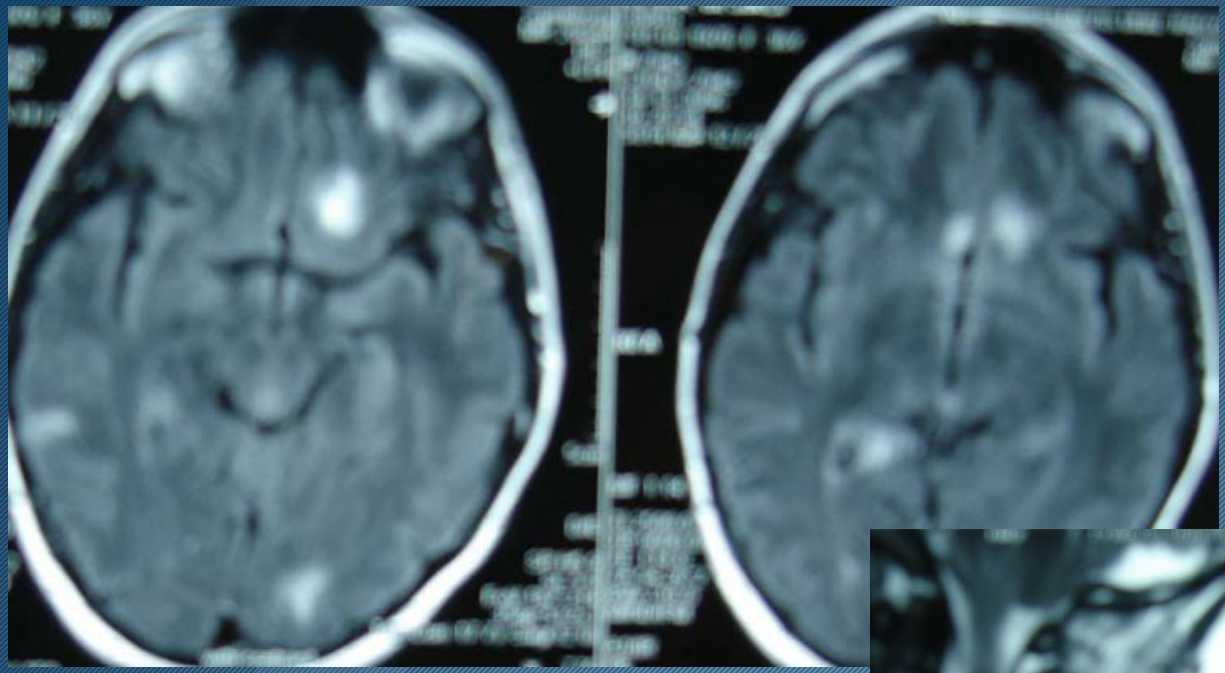

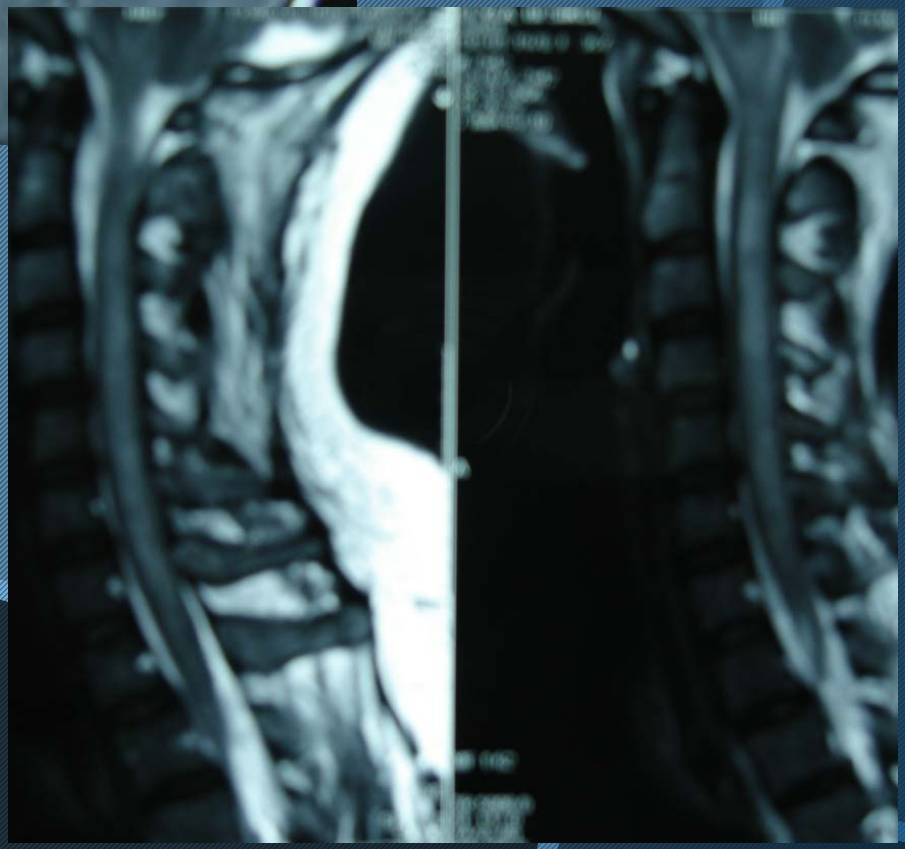

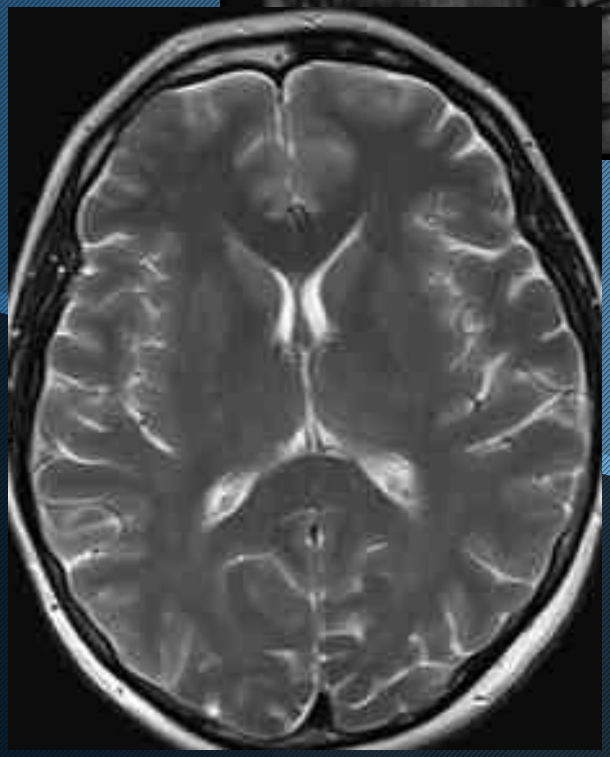

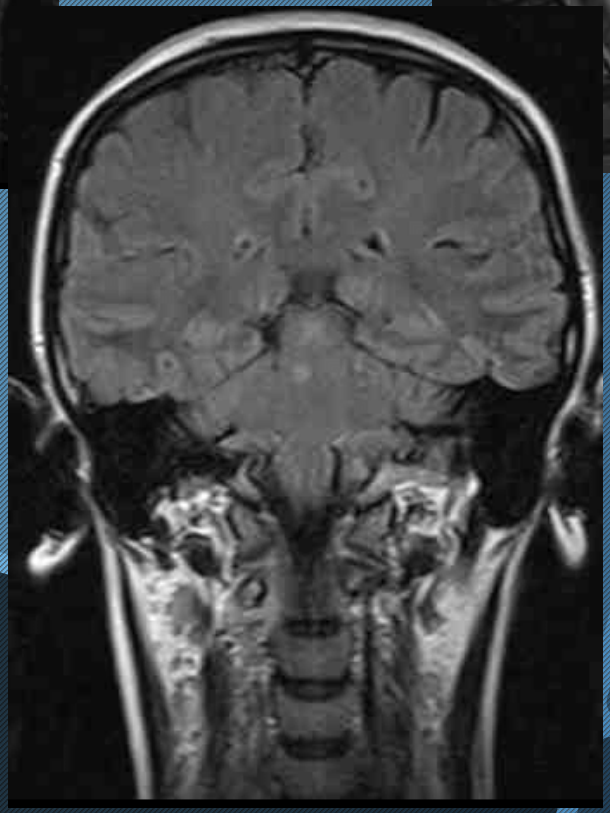

	All children (n = 193)	ADS (n = 33)	Controls (n = 36)	Inflammatory neurological disease (n = 50)	Other neurological disease (n = 55)	Systemic inflammatory disease (n = 19)
Age at onset, y, median (range)	13.8 (1.3–17.9)	15.0 (2.5–17.9)	15.5 (10.8–17.7)	11.3 (1.3–17.8)	13.2 (1.4–17.7)	13.3 (2.0–17.4)
Female, n (%)	108 (56)	16 (48)	24 (67)	28 (56)	29 (53)	11 (58)
OCB positive, n (%)	36 (23)	18 (55)	0	15 (30)	0	3 (16)
IgG index (> 0.67), n/total (%)	26/121 (21)	13/28 (46)	0/28	10/43 (23)	0/34	3/14 (21)
CSF pleocytosis (≥ 5), n/total (%)	50/189 (26)	23/32 (72)	0/35	27/50 (54)	0/54	0/18
Glucose ratio < 0.6 or CSF-glucose < 2.5 mM, n/total (%)	3/185 (2)	1/32 (3)	0/34	1/49 (2)	1/53 (2)	0/17
Albumin ratio > 6.8 or CSF-protein > 0.45, n/total (%)	32/191 (17)	8/32 (25)	6/36 (17)	10/50 (20)	6/54 (11)	2/19 (11)

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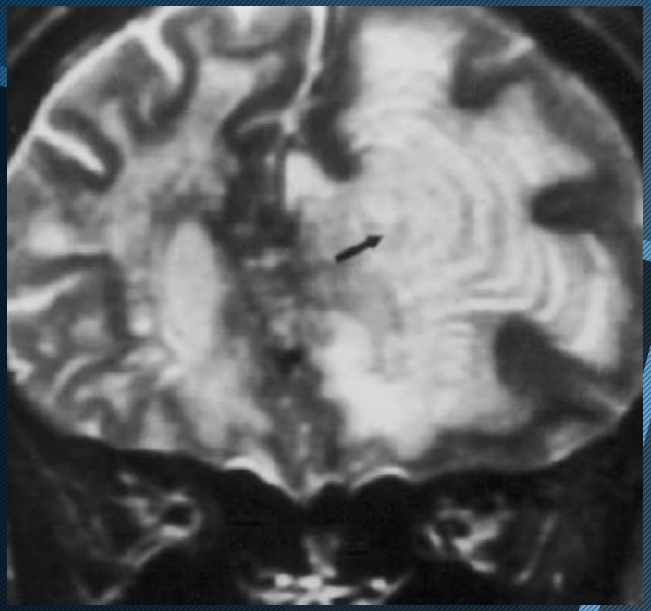
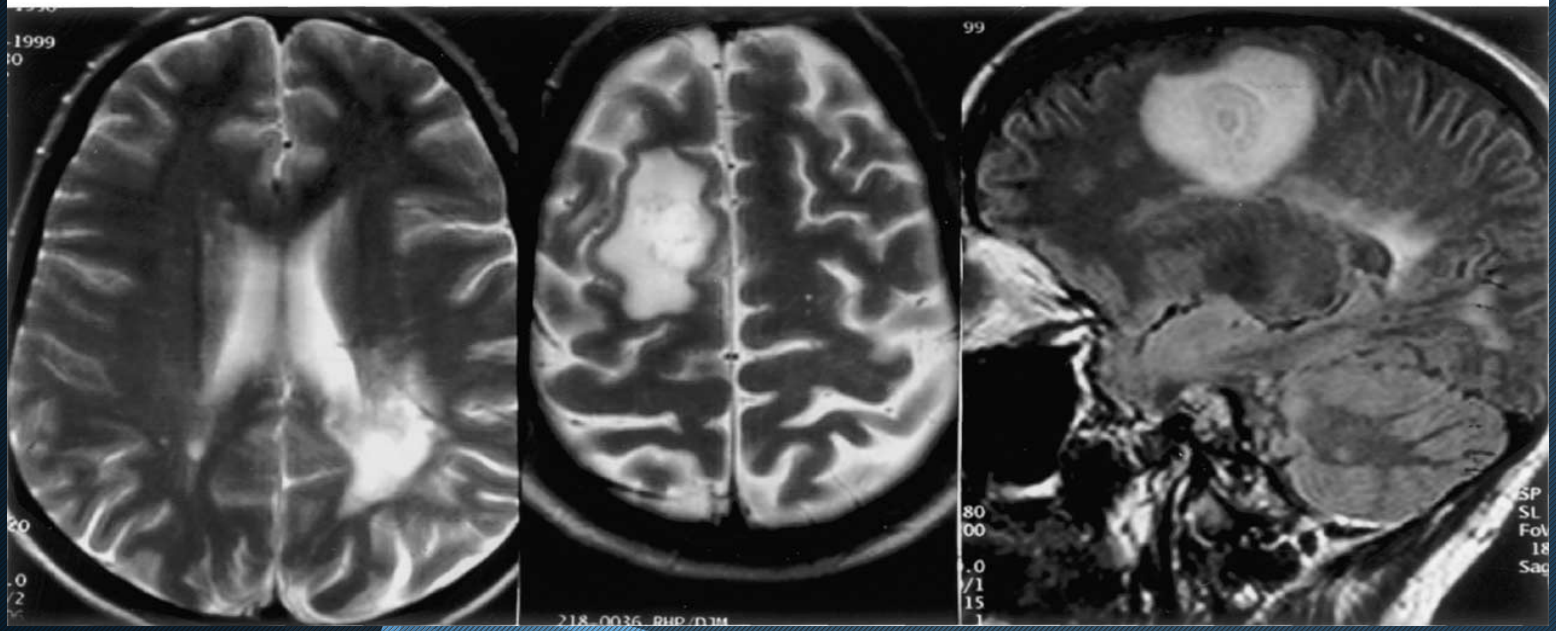
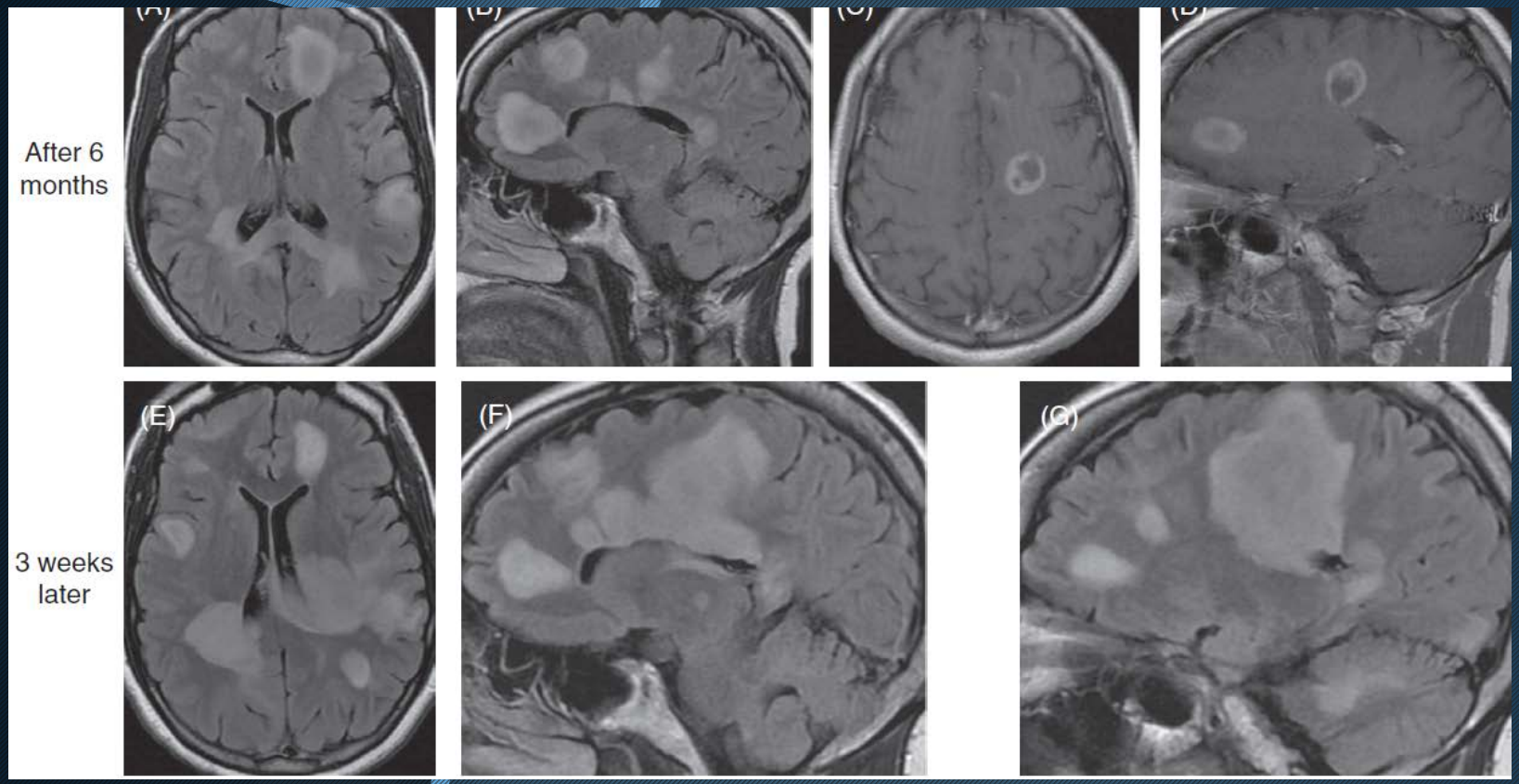
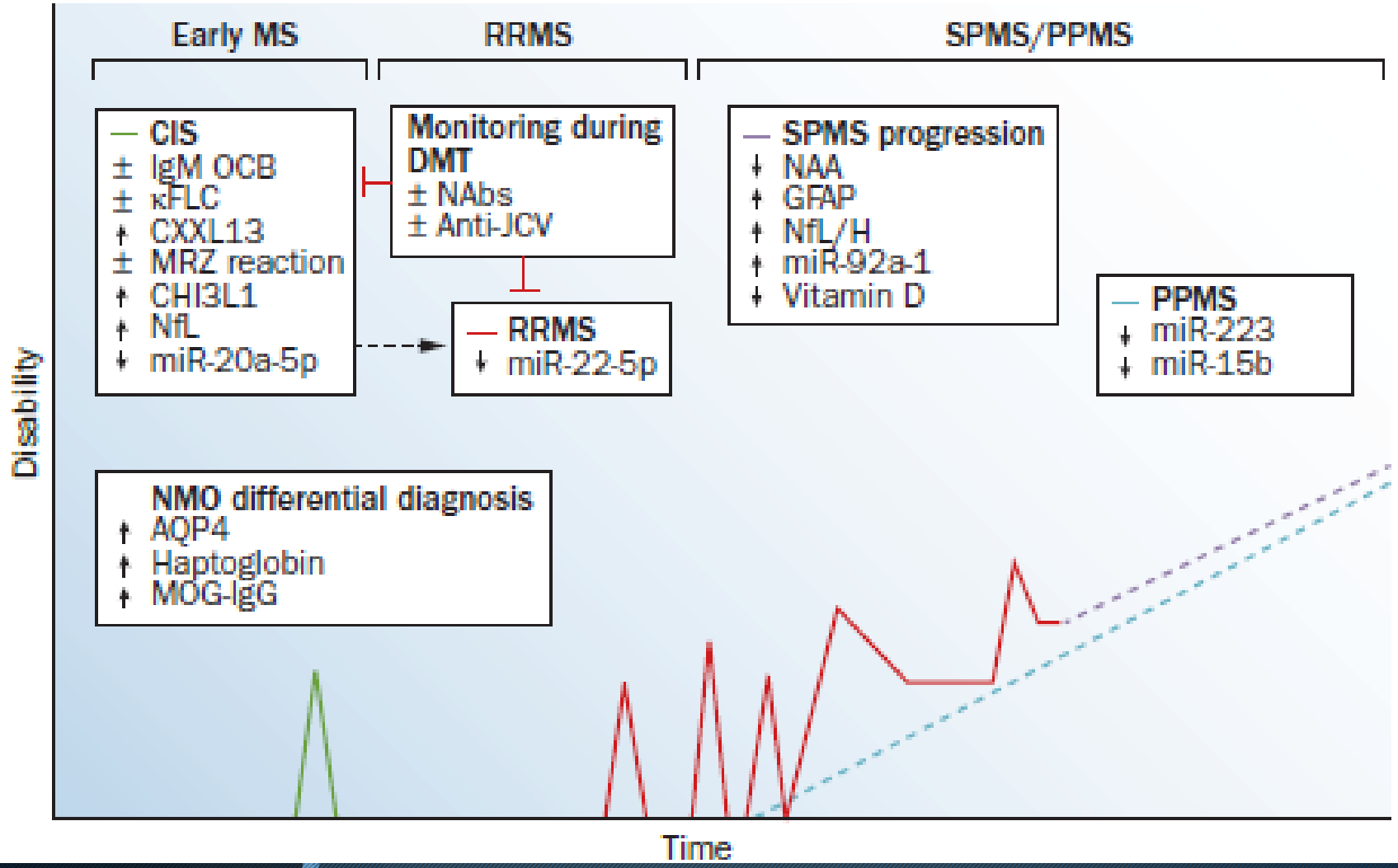


Pseudo-Baló lesion in MS





Multiple Sclerosis Journal 17(12, 2015


Early MS
RRMS
SPMS/PPMS
— CIS
± IgM OCB
± κFLC
↑ CXXL13
± MRZ reaction
↑ CHI3L1
↑ NfL
↓ miR-20a-5p
Monitoring during DMT
± NAbs
± Anti-JCV
— RRMS
↓ miR-22-5p
— SPMS progression
↓ NAA
↑ GFAP
↑ NfL/H
↑ miR-92a-1
↓ Vitamin D
— PPMS
↓ miR-223
↓ miR-15b
NMO differential diagnosis
↑ AQP4
↑ Haptoglobin
↑ MOG-IgG
Disability
Time

Ondokuz Mayıs Üniversitesi Tıp Fakültesi
Nöroimmunoloji Laboratuvarı
Oligoklonal Band İstem Formu

Ad/Soyad: **Yaş:** **Cinsiyet:**

Hastane Adı/Protokol No: **MS Protokol No:**

Doktor Adı-Soyadı/Telefon/E-mail:

Laboratuvar Protokol No:

Alınan Örnek: BOS ( ) Serum ( )

Örnek Alınma Tarihi ve Saati:

Laboratuvara Geliş Tarihi ve Saati:

Tanı: □ MS

RRMS ( ) SPMS ( ) PPMS ( ) Klinik İzole Sendrom ( ) Radyolojik İzole Sendrom ( )
□ NMO □ NMO Spektrum Hastalıkları □ Diğer (Belirtiniz):

Hastanın Kullanmakta Olduğu İlaçlar:

□ Steroid (Süre ve Doz Bilgisi):

Test / Ay		Oligoklonal Band (150 TL)	Anti-NMO (200 TL)	Otoimmun Ensefalit (350 TL)	Paraneoplazi (350 TL)	Anti-MOG (300 TL)	Gangliozid (200 TL)

* Oligoklonal Band Ücreti (150 TL) aşağıdaki banka hesabına yatırılmalı, banka dekontu, bu form ve hasta örnekleri birlikte gönderilmelidir. Dekontun açıklama bölümüne **Hastanın Adı Soyadı, T.C. Kimlik Numarası ve Nöroimmünoloji Laboratuvarı** yazılması gereklidir.
* Oligoklonal Band için IgG indeksine (IgG (serum), IgG (BOS), Albümin (serum) ve Albümin (BOS)) ihtiyaç duyulmaktadır. Eğer hastanenizde IgG indeksi bakılıyor ise oligoklonal band istem formu ile birlikte laboratuvarımıza gönderdiğiniz BOS ve serum ile eş zamanlı alınmış örnekten bu değerlere bakılıp bildirilmesi gerekir. Aksi halde IgG indeksi istemi de yapılmalı ve IgG Indeksi Ücreti (40 TL) de aynı hasaba yatırılmalıdır.

Ondokuz Mayıs Üniversitesi Tıp Fakültesi Hesap Numarası
IBAN: TR 63 0001 0014 7909 7123 9551 11

* Form eksiksiz doldurulmalı ve formda **doktor kaşesi, telefon numarası ve e-mail adresi** mutlaka bulunmalıdır.
* Tüm örnekler **tedavi uygulamasından önce** alınmalıdır.
* Tedavi altındaki hastalarda ayrıntılı tedavi bilgisi doldurulmalıdır.
* **BOS ve Serum eş zamanlı alınmalıdır.**
* BOS 2 **Jelsiz** Biyokimya Tüpü'ne alınmalıdır. Toplamda iki tüpteki BOS miktarı en az 6-8 ml olmalıdır.
* Kan 3 Biyokimya Tüpü'ne alınmalıdır. Her üç tüp de tam dolu olmalıdır. Santrifüj edilerek **Jelsiz**

Ondokuz Mayıs Üniversitesi Tıp Fakültesi Nöroimmünoloji Laboratuvarı

Anasayfa Hakkımızda Test İstem Formları Bize Ulaşın İletişim Sonuç Kontrol

Ondokuz Mayıs Üniversitesi Tıp Fakültesi Nöroimmunoloji Laboratuvarı

Adı	gangliozid_istek_formu.pdf	DOSYAYI İNDİR
Yükleme Tarihi	14/09/2018	
Bilgi	GANGLİOZİD İSTEK FORMU	

Türü	Test İstem Formları	
Adı	mog_istek_formu.pdf	DOSYAYI İNDİR
Yükleme Tarihi	14/09/2018	
Bilgi	MOG İSTEK FORMU	

Türü	Test İstem Formları	
Adı	mog-nmo-istek-formu.pdf	DOSYAYI İNDİR
Yükleme Tarihi	14/09/2018	
Bilgi	MOG-NMO İSTEK FORMU	

Türü	Test İstem Formları	
Adı	nmo_istek_formu.pdf	DOSYAYI İNDİR
Yükleme Tarihi	14/09/2018	
Bilgi	NMO İSTEK FORMU