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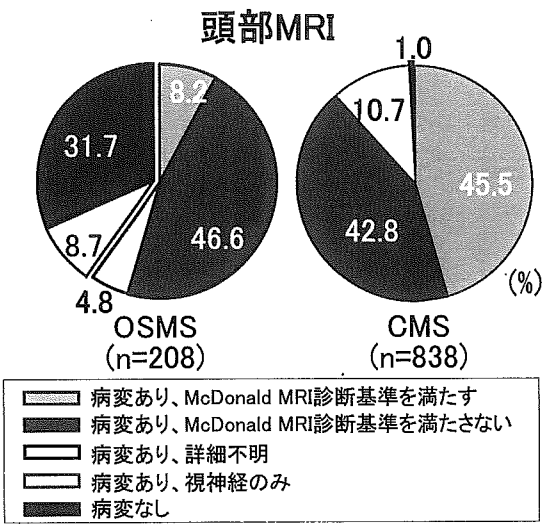
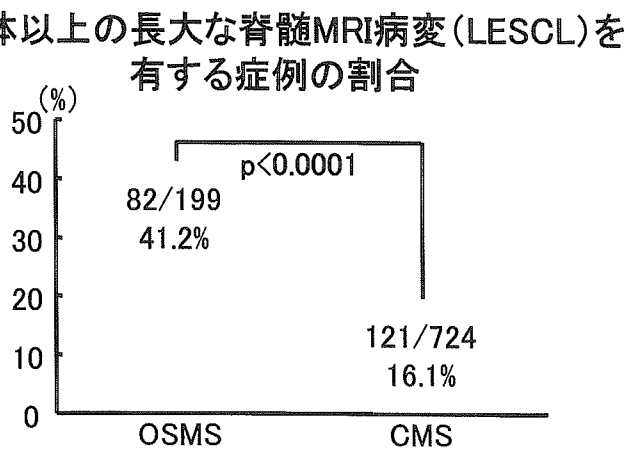
Ⅳ. イラスト

MS2004年全国臨床疫学調査結果第2報：MRI所見からみたMS病像の差異





OSMSにおける病像の差異

	LESCL(+) (n=82)	LESCL(−) (n=89)	p値
発症時年齢(歳)	38.0±13.0 ↑	32.6±12.3	0.0091
罹病期間(年)	11.4±8.9	10.7±8.9	n.s.
男女比(男: 女)	12: 70 (1: 5.83)	17: 72 (1: 4.24)	n.s.
EDSS	5.3±2.4 ↑	3.3±2.5	<0.0001
経過中に両側視力低下が出現した割合	52/82 (63.4%) ↑	36/89 (40.4%)	0.0027
経過中に対麻痺が出現した割合	59/80 (73.8%) ↑	41/86 (47.7%)	0.0006
経過中に横断性脊髄炎徴候が出現した割合	51/80 (63.8%) ↑	33/87 (37.9%)	0.0009
最終時に高度以上の視力障害をきたす割合	44/82 (53.7%) ↑	23/88 (26.1%)	0.0002
最終時に中等度以上の脊髄障害をきたす割合	45/82 (54.9%) ↑	20/88 (22.7%)	<0.0001
髄液細胞数50/mm^3以上を示す割合	9/69 (12.3%) ↑	1/77 (1.2%)	0.0133
McDonaldのMRI診断基準を満たす割合	4/80 (5.0%)	9/87 (10.3%)	n.s.
頭部MRIが正常な症例の割合	47/80 (58.7%) ↑	31/87 (35.6%)	0.0028

解　説

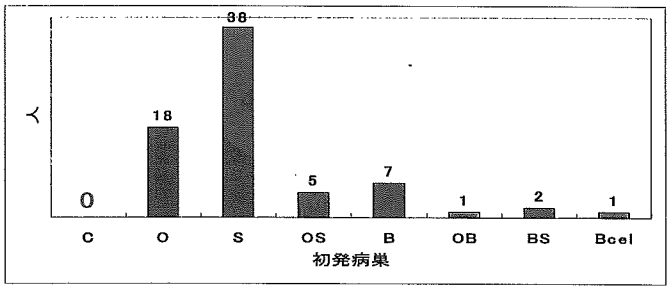
1. McDonaldのMRI診断基準を満たす例がCMSで有意に多かった(45.5% vs. 8.2%、p<0.0001)。

2. 3椎体以上の長さを有する脊髄病巣はOSMSで有意に多かった(41.2% vs. 16.1%、p<0.0001)。

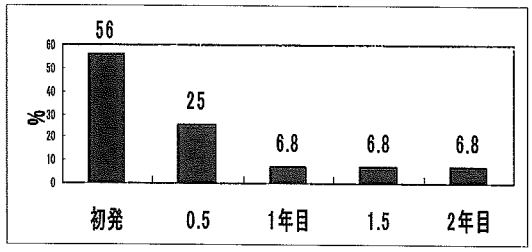
3. OSMSの中でも3椎体以上の長大な脊髄病巣を有する例は、有さない例に比し、より典型的なOSMSの特徴を示していた。OSMSのみでなく、CMSにおいても3椎体以上の長大な脊髄病巣を有する症例では、より重症で、女性に多く、高度の視力障害や脊髄障害をきたしていた。

3椎体以上の長い脊髄病変を有する多発性硬化症の臨床的特徴

初発症状の病巣部位



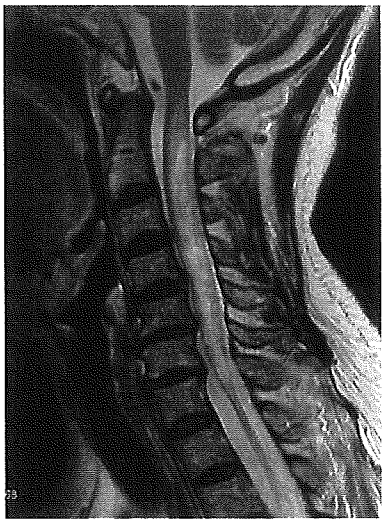
脊髄病変の出現時期

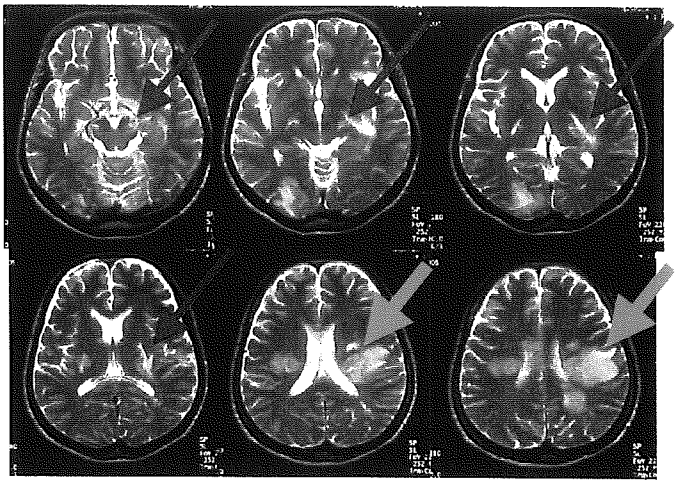


解　説

1). 大脳症状で初発することはない。
2). 脊髄病変は初発から平均0.4年で出現する。
3). 72%で脊髄症状出現時に長い病変が形成される。
4). 39%で初発から6.2年後に脳症状が出現する。
5). 大脳症状を呈した患者の50%が意識障害を呈する。
6). 脳幹症状を呈した患者の14%が中枢性呼吸障害を呈し、人工呼吸器装着を必要とした。
7). 平均罹病期間11.6年の時点でのEDSSは6.9。

3椎体以上の長い脊髄病変を有する多発性硬化症の頭部MRIの特徴





解　説

1). 20 mm以上の長さに及ぶ脳幹から頭頂部にかけての長い病変を示す(赤矢印: 95%)。

2). Cavityを示す(80%)。

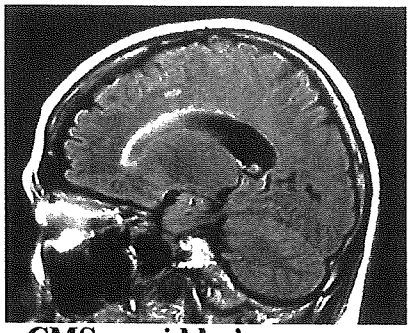
3). 長径が30 mm以上の大きさの脳病変を示す(緑矢印: 68%)。

多発性硬化症自験108例の脳脊髄MRI所見からみた日本人における特徴
:periventricular lesionの画像・病理所見に着目して

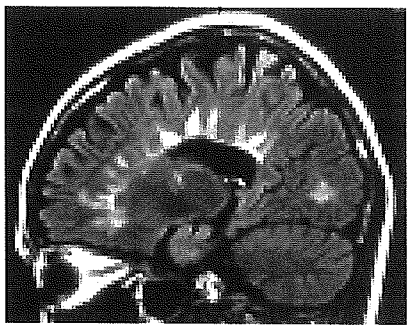
OSMSとCMSのMRI所見の比較

	OSMS (%)	CMS (%)
McDonald/Barkhof診断基準	23.7*	65.4*
Gd増強または9個以上T2病巣	31.6*	69.2*
Gd増強病巣	11.1*	32.7*
9個以上T2病巣	23.7*	61.5*
傍皮質下に1個以上T2病巣	47.4	63.5
テント下に１個以上T2病巣	26.3*	67.3*
側脳室周囲に3個以上T2病巣	26.3*	71.2*
脳病巣なし	21.1*	0.0*
脳病巣3個以下	63.2*	13.5*
側脳室前角周囲にrim様病巣	65.2*	30.0*
Ovoid lesion	52.2*	96.7*
3椎体以上の長大な脊髄病巣	57.9*	25.0*

OSMS: rim like lesion

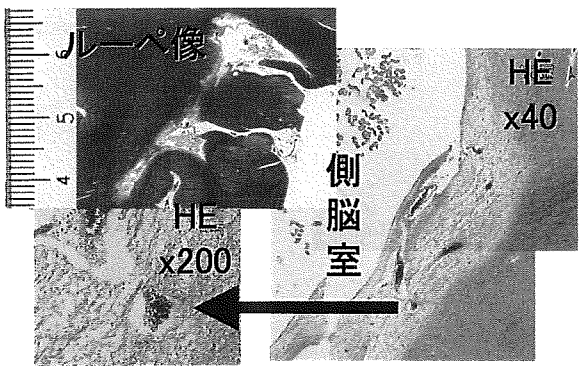


CMS: ovoid lesion

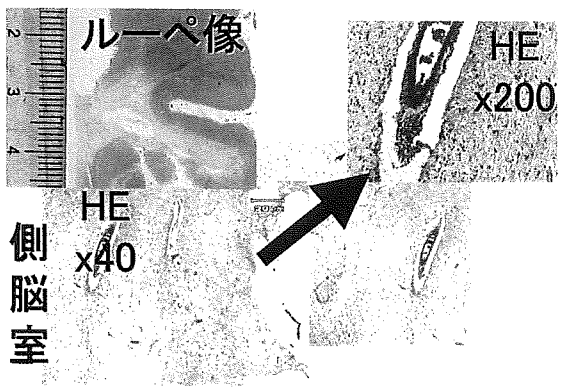


側脳室周囲病理所見

OSMS



CMS



解　説

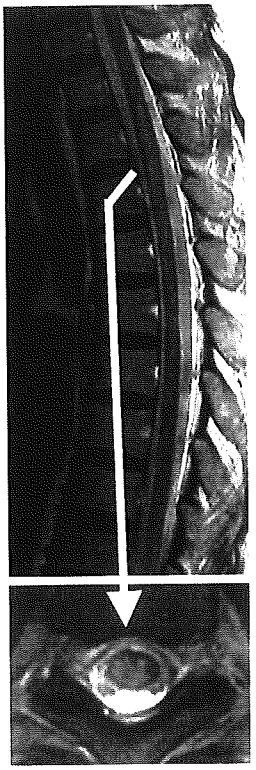
MS患者108例を対象として脳脊髄MRIを調査し，5症例の病理評価を行った．

1．日本人OSMSではMcDonald/BarkhofのMRI診断基準を満たす例は少なく，長い脊髄病巣を有することが特徴として挙げられた．

2．側脳室周囲病巣は，OSMSではMRIおよび病理所見にて側脳室に沿って帯状に分布するのに対し，CMSでは白質深部へ進展するovoid lesionを認めた．

結論として，側脳室周囲の帯状病巣は日本人OSMSの特徴の一つと考えられる．

日本人多発性硬化症におけるlongitudinally extensive spinal cord lesion (LESCL) の形成機序



脊髄病巣の特徴

好発部位	
上部胸髄	頚髄
ガドリニウム造影	
Th3-Th4	頚髄
灰白質病巣	
72.3% ＞	36.6%

LESCLを規定する因子

	脊髄病巣の長さ	EDSS
髄液IL-17	正の相関	相関なし
髄液IL-8	正の相関	正の相関
血清MPO	相関なし	正の相関 (OSMS)
血清VEGF	正の相関	相関なし

解　説

1. LESCLの特徴

a) 日本人MSにおいて、OSMSでは44.9%、CMSでは27.7%に認める

b) 上部胸髄に多く分布し、同部でのGd増強病変の割合も高い

c) 脊髄灰白質へ暴走が及ぶ割合が高い

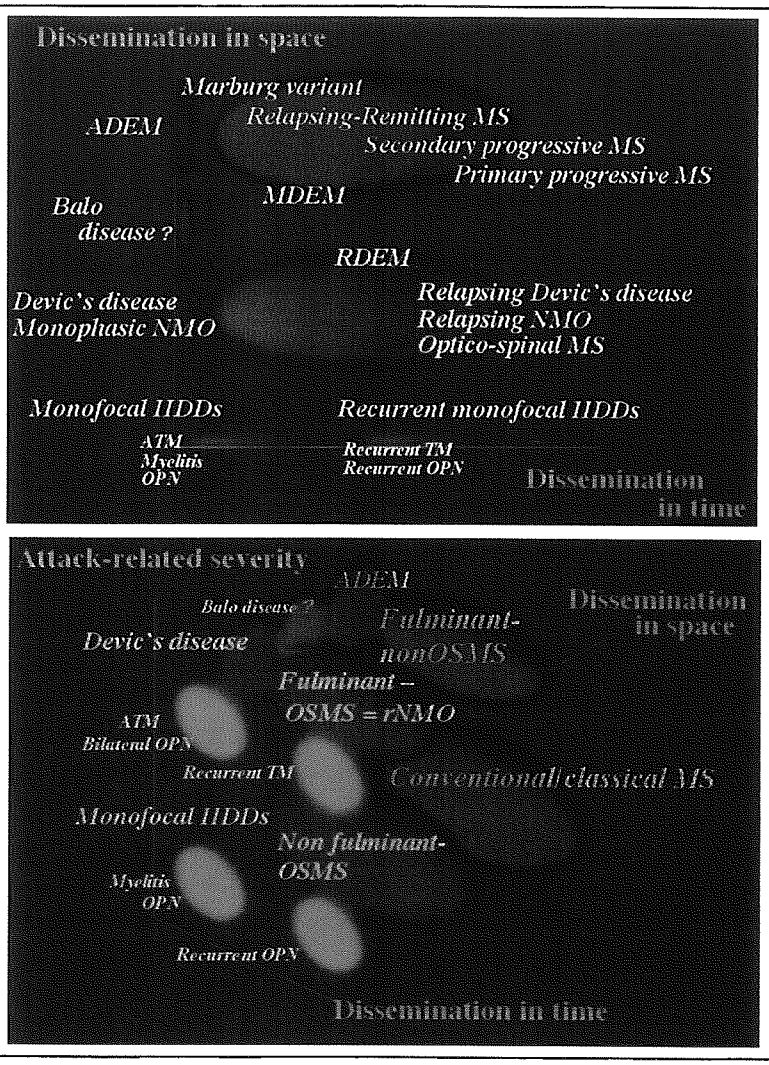
LESCLは通常の脊髄病変とは特徴が異なり、その形成機序が異なることが示唆された

2. LESCLを規定する因子

a) OSMS剖検症例の脊髄病巣では約半数に著明な好中球浸潤が認められること、髄液IL-17/IL-8とLESCLの長さと正の相関が認められることから、LESCLの形成には好中球の関与が示唆される

b) 血清MPOは、LESCLの長さと相関はないものの、重症度との相関が認められた

Attack-related extending cord lesions
多発性硬化症の病態理解における重要性と規定因子の検討
三次元的病態理解の重要性



二次元的理解

OSMSは均一か？

NMOとの相違は？

LESL(+)のCMSの位置づけは？

三次元的理解

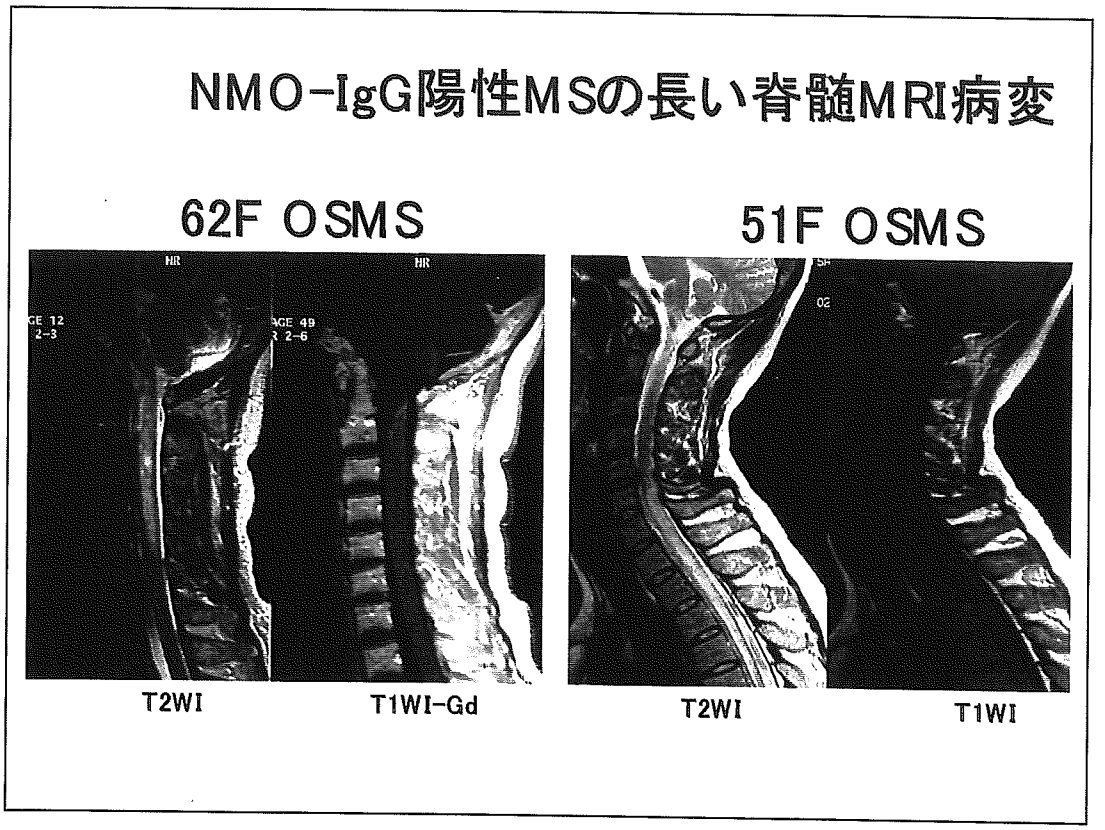
多様性の理解に有用

人種によって Prototype の頻度は異なる！

解　説

1. MS症候群の理解には"attack-related severity (attack-related lesion expansion)"、臨床経過および病変分布の3つの要因(軸)に基づいた三次元的病態把握が重要である。
2. 脊髄縦長病変の有無はattack-related lesion expansionの指標として重要である。
3. 各々の軸を規定している因子の検討が病態把握に重要である。
4. Attack-related severity (attack-related lesion expansion)軸は、少なくも一部、遺伝的に規定されたCTLA4分子によるdown-regulationが関与している可能性がある。
5. 病変分布の特異性はHLA-DP多型が関与している可能性がある。
6. 三次元的病態理解は適切な治療法選択にも重要と思われる

NMO-IgG陽性多発性硬化症の脊髄病変



解　説

NMO-IgG陽性の多発性硬化症では、3椎体以上の長さを持つ脊髄MRI病変が最大の特徴である。