

# 第34回神経放射線ワークショップ 症例検討2-3

2014.6.20 @グランドプリンスホテル京都  
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# 症例：65歳，女性

- 20XX/2/26 numbness, pain and edema of the left forearm, hand and fingers
- 3/5 unsteadiness in walking
- 3/19 gaze nystagmus → CT: normal
- 3/23 right resistant sensorineural hearing loss → MRI: normal
- 6/ pain, paresthesia and edema of bottom of the bilateral foot
- 6/20 ~ muscle weakness of the four limbs → inability to walk
- 7/ hearing loss of the left ear

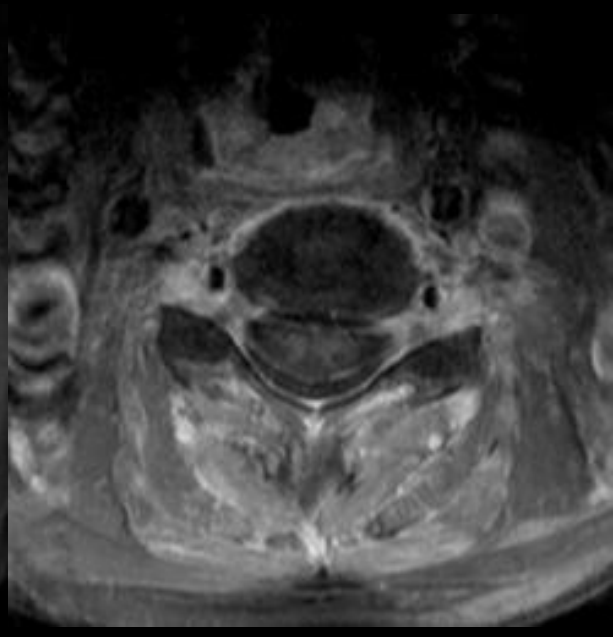
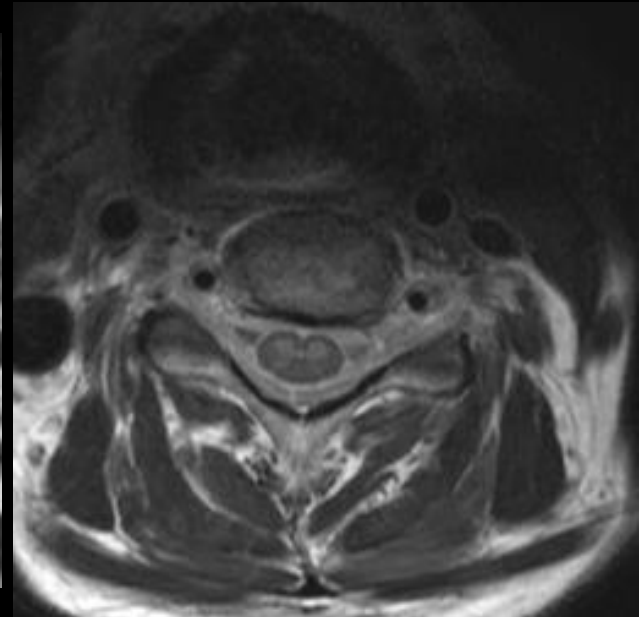
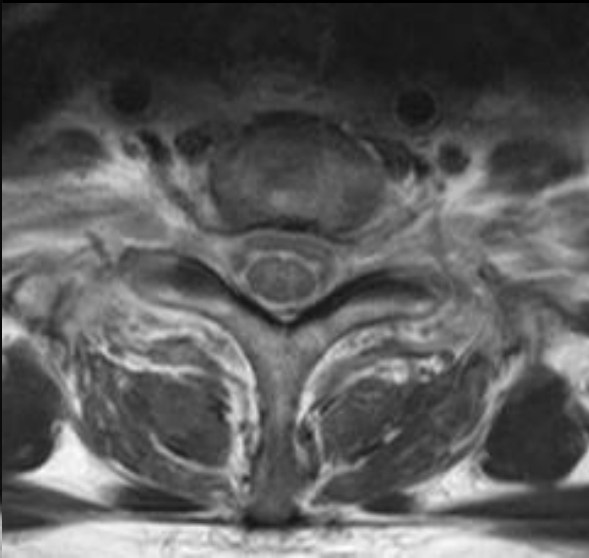
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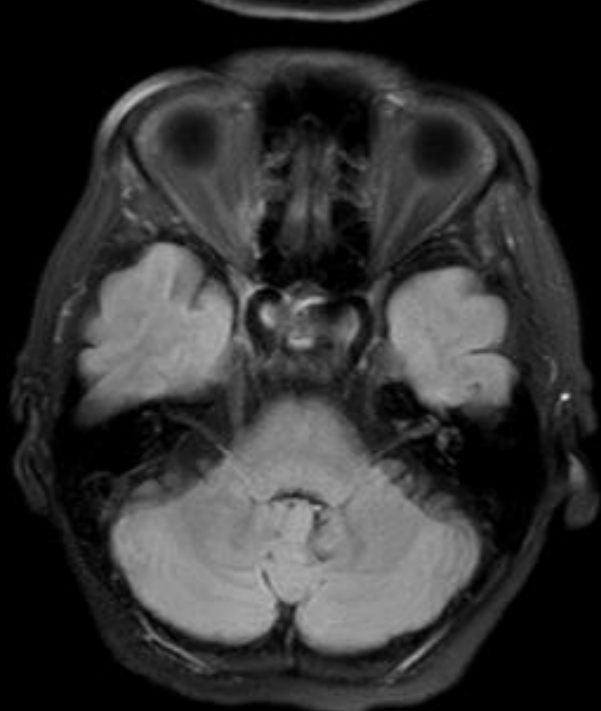
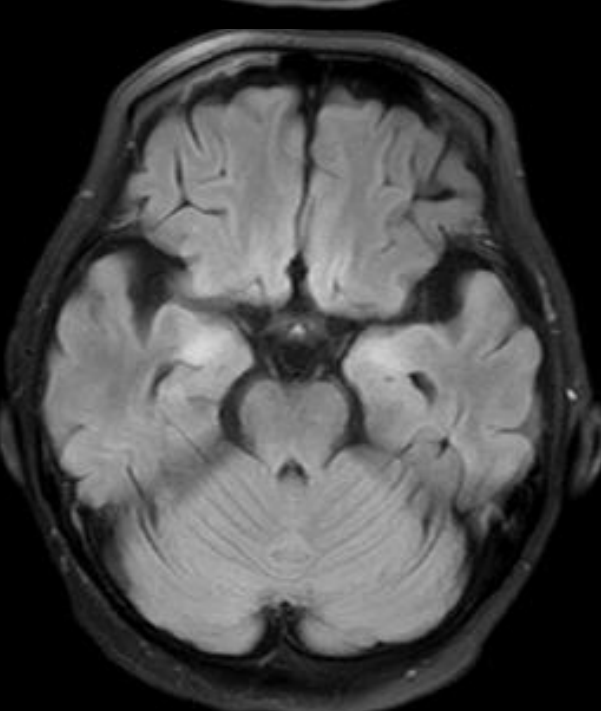
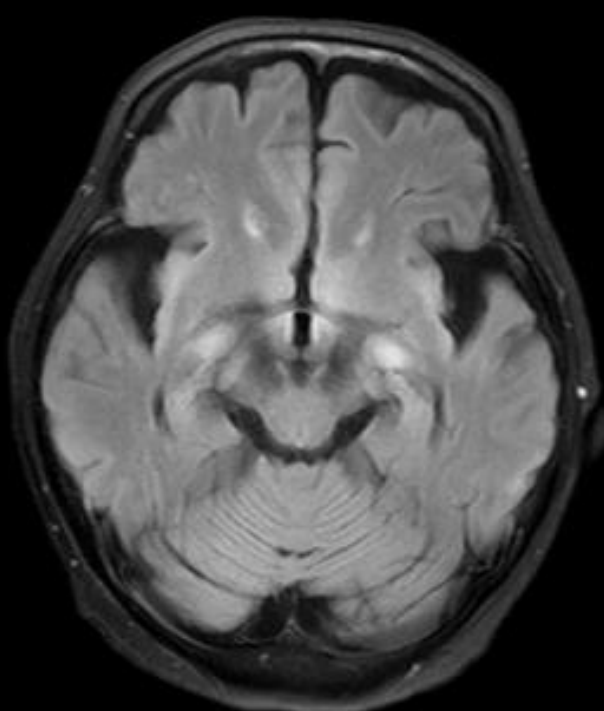
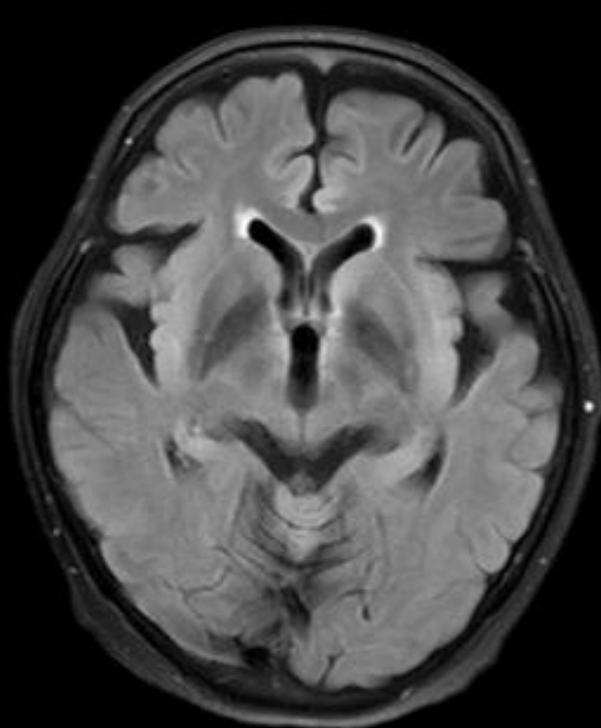
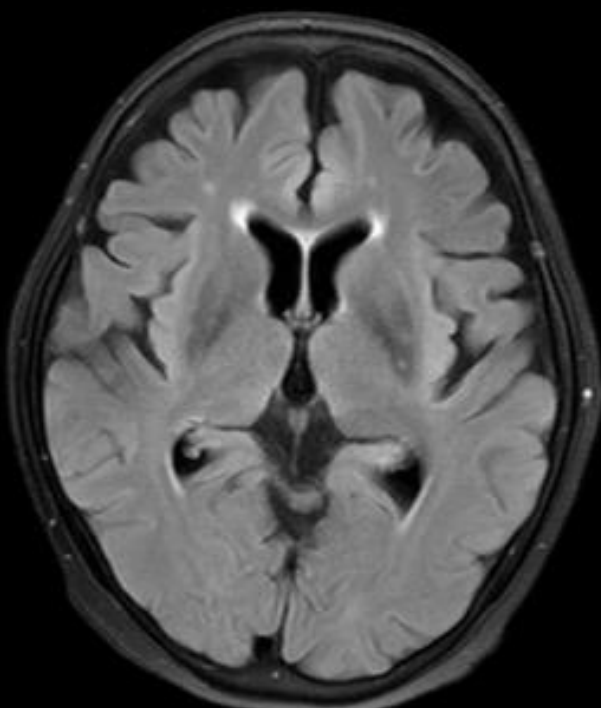
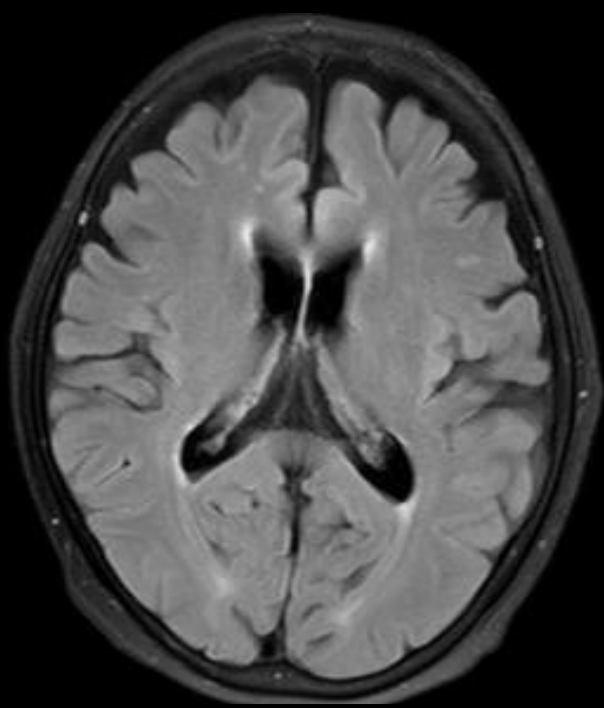
- 【blood test】 **WBC: 10000/μl ↑**, CRP: normal, VB1: 652.8ng/ml ↑, VB12: 88300pg/ml ↑, **sIL2-R 537U/ml ↑**
- **CEA 32.8 ↑** (reference value: under 5) ng/ml, **CA125 489 ↑** (reference value: under 35) U/ml
- ProGRP • NSE • SCC • CYFRA • AFP • PIVKA-II: normal
- **ANA(FA) 1280-folds ↑**, **Anti SS-A antibody(+)**
- anti SS-B antibody • anti ds-DNA antibody • anti Sm antibody • P-ANCA • C-ANCA(-)
- Anti HBs antibody • anti HBc antibody(+)
- 【CSF】 **cell 6 ↑** (lymphocyte 4, monocyte 2), **protein 66 mg/dl ↑**, GLU 65mg/dl, Cl 122mmol/l, LDH 14IU/l

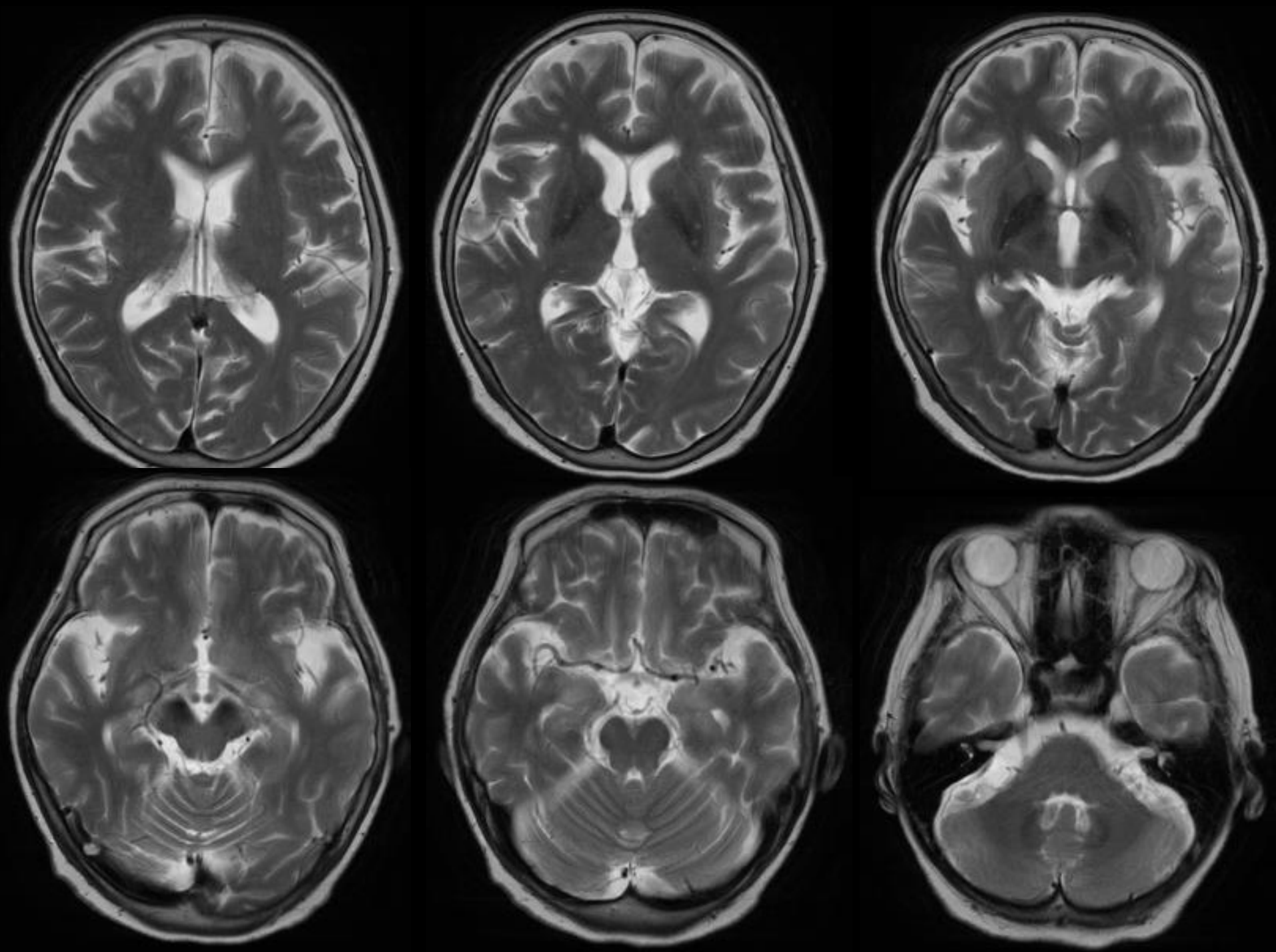
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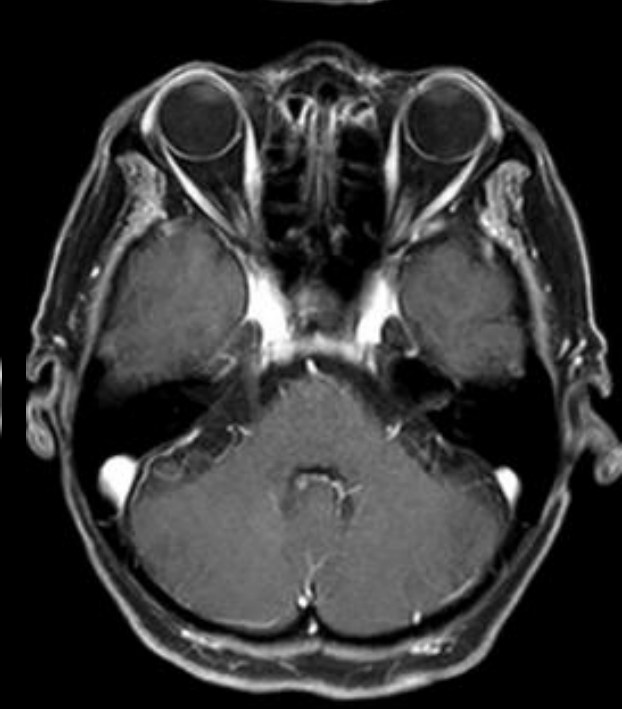
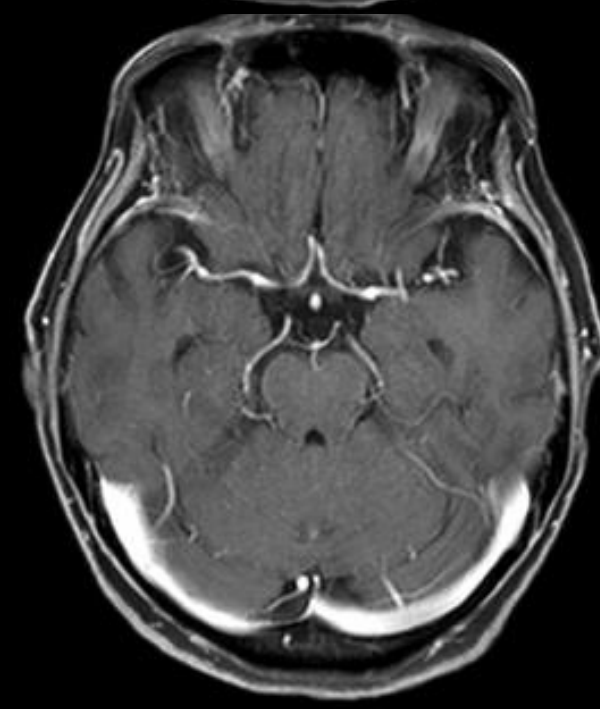
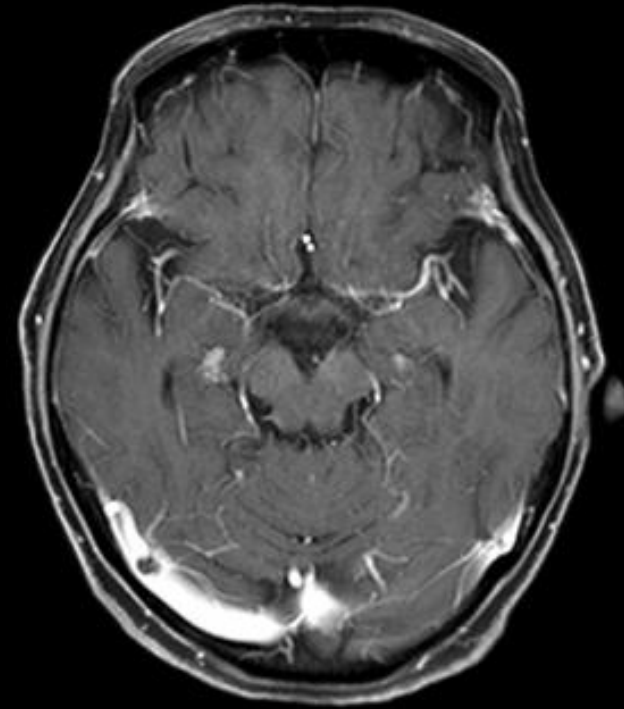
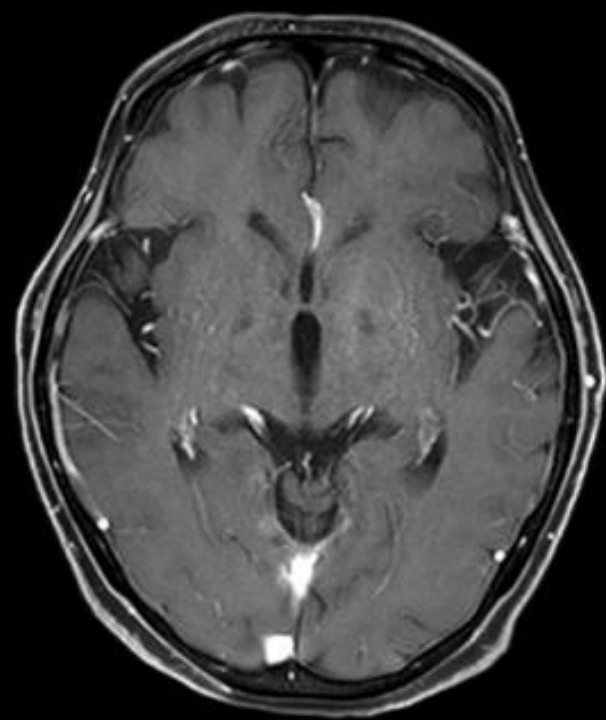
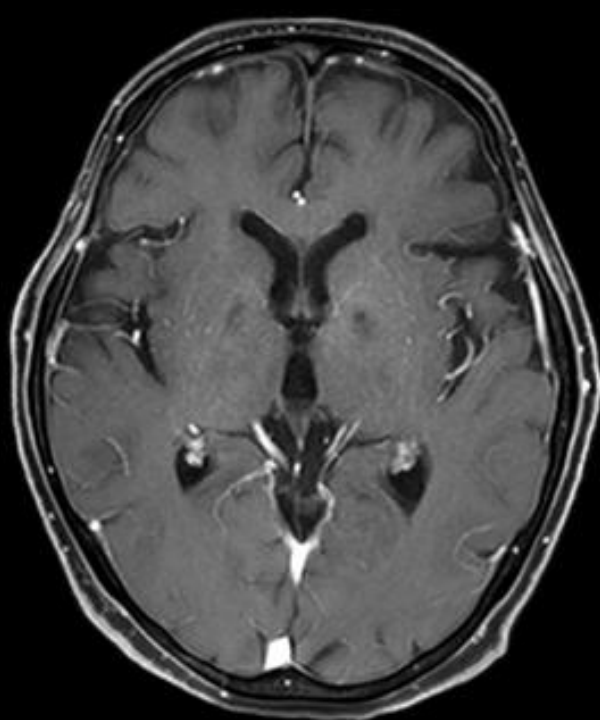
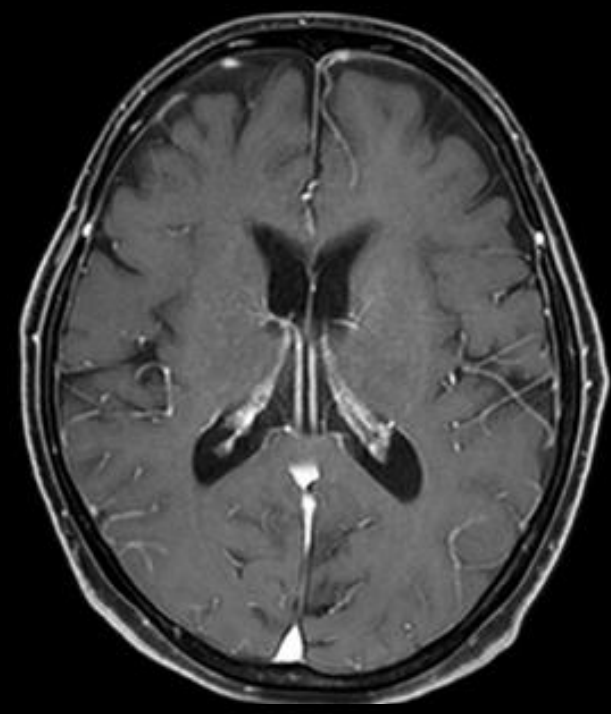
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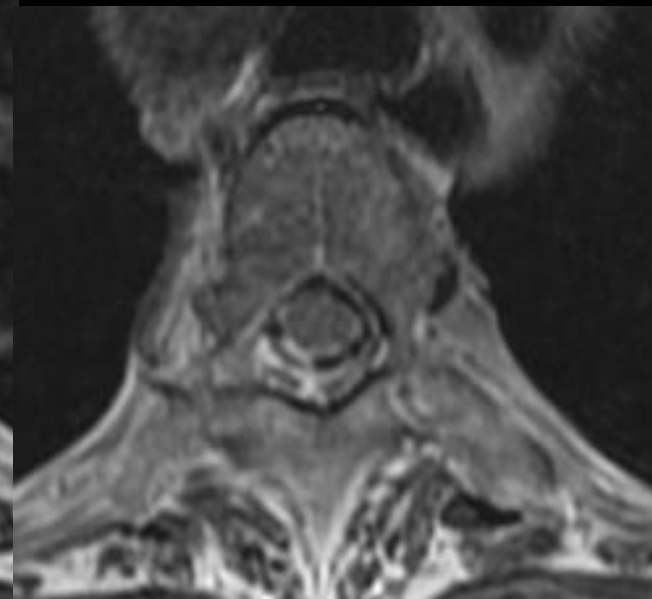
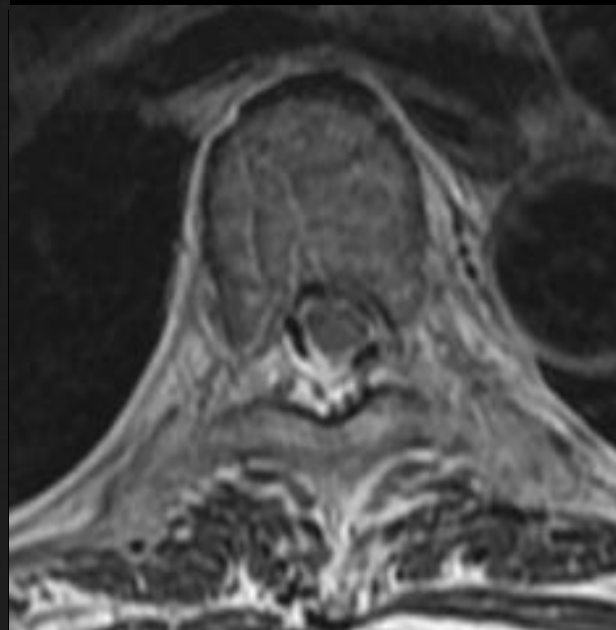
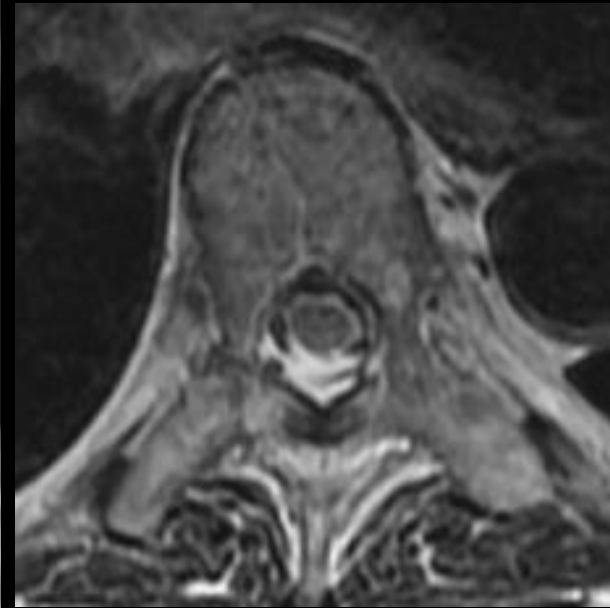
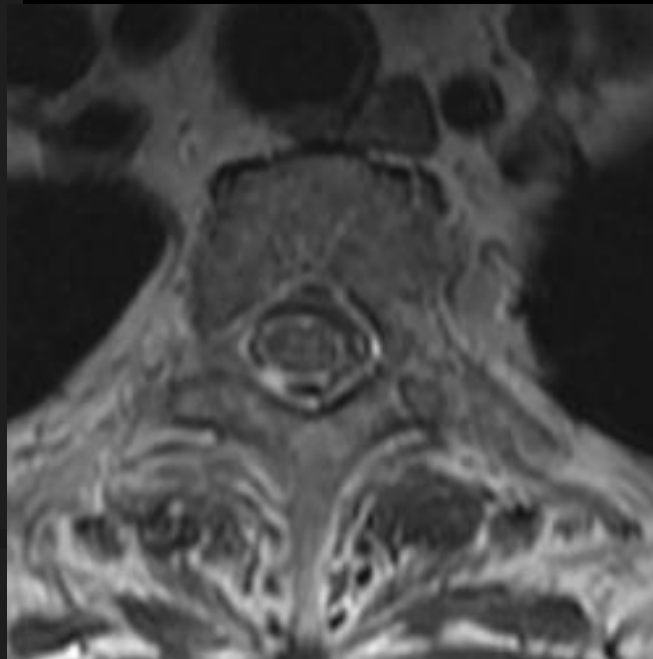
- ◎ 頸椎造影MRI(7/9)
- ◎ 頭部造影MRI(7/10)
- ◎ 胸椎單純MRI(7/24)







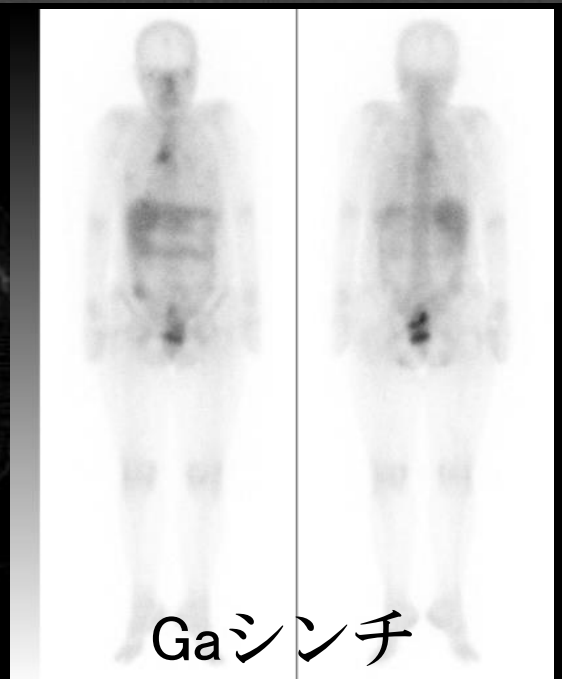




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# 診断は？

次から解説スライド



Gaシンチ

# 縦隔腫瘍の組織診断

- ◎ 開胸縦隔腫瘍生検(易出血性であり，摘出は断念) → 腫瘍検体は**扁平上皮癌のリンパ節転移**
- ◎ CD5(-) → 血液系腫瘍ではない
- ◎ TTF-1(+) → **肺癌 > 胸腺癌**
- ◎ ただし，CT上は肺野に原発巣と思える腫瘍は映っていない
- ◎ 肺癌として治療を開始(カルボプラチン＋ナブパクリタキセル)

肺扁平上皮癌  
抗Ma-2腦炎  
(抗Ma腦炎)

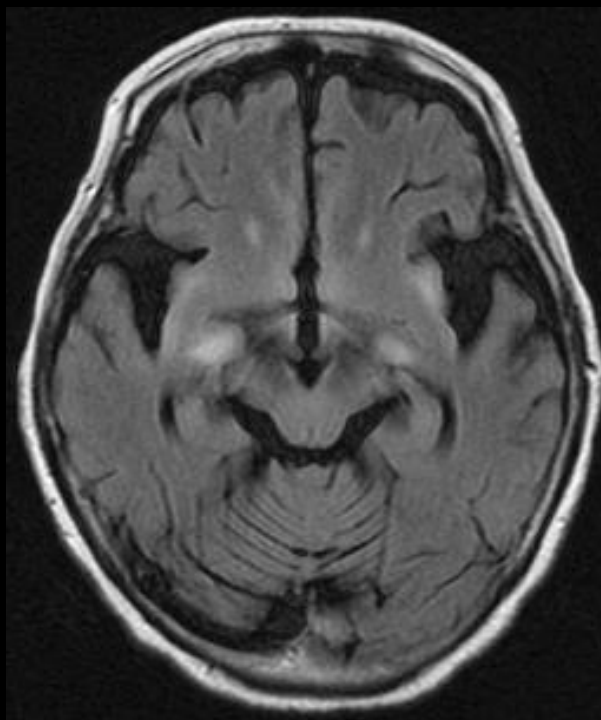
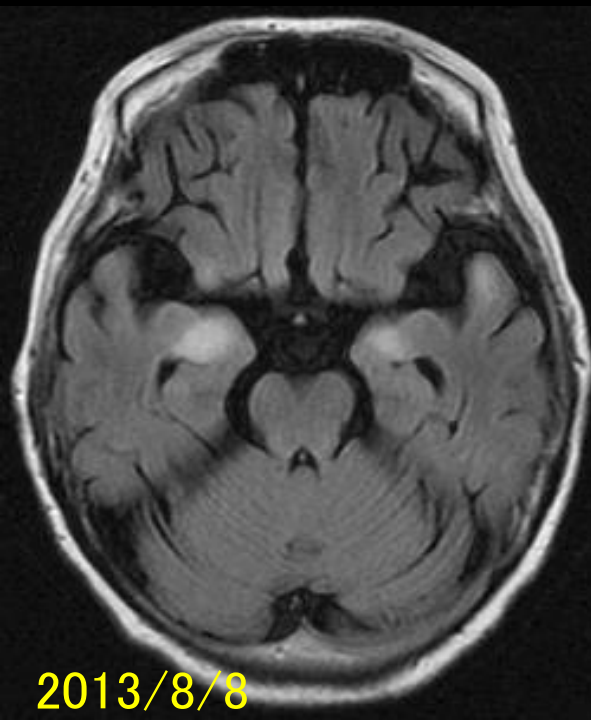
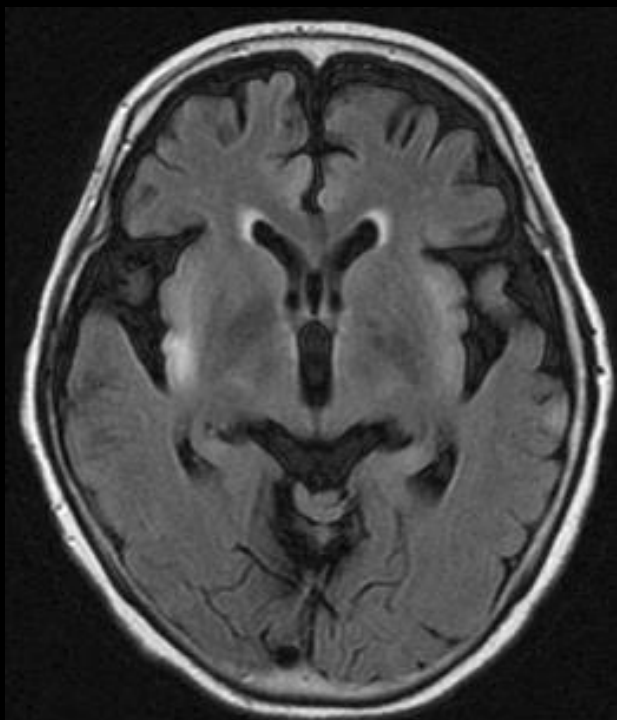
SCC of the lung  
anti Ma-2 encephalitis  
(anti Ma encephalitis)

Anti Ma-1, anti Ma-2 antibody(+)

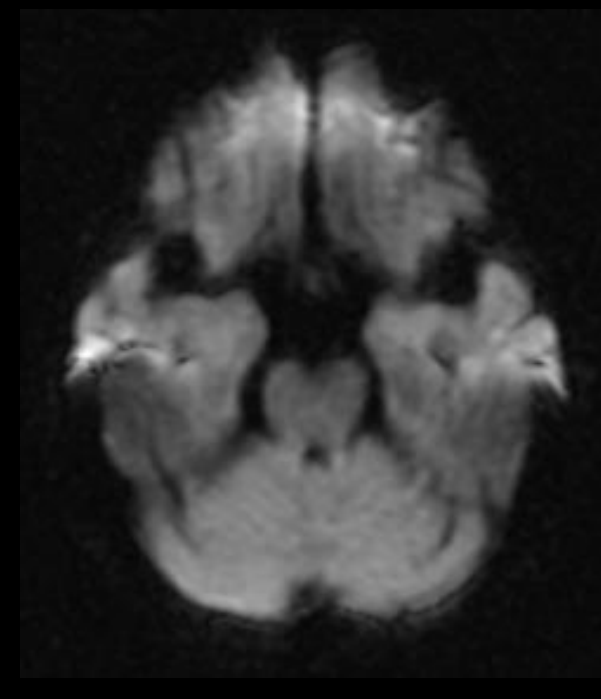
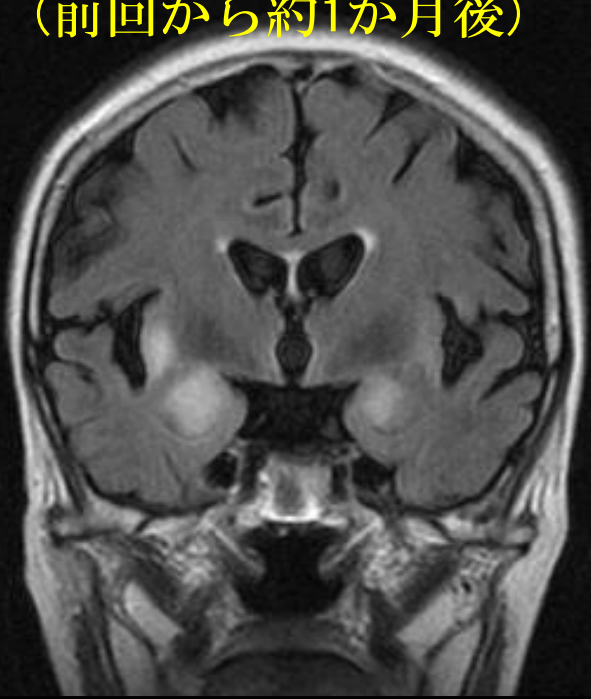
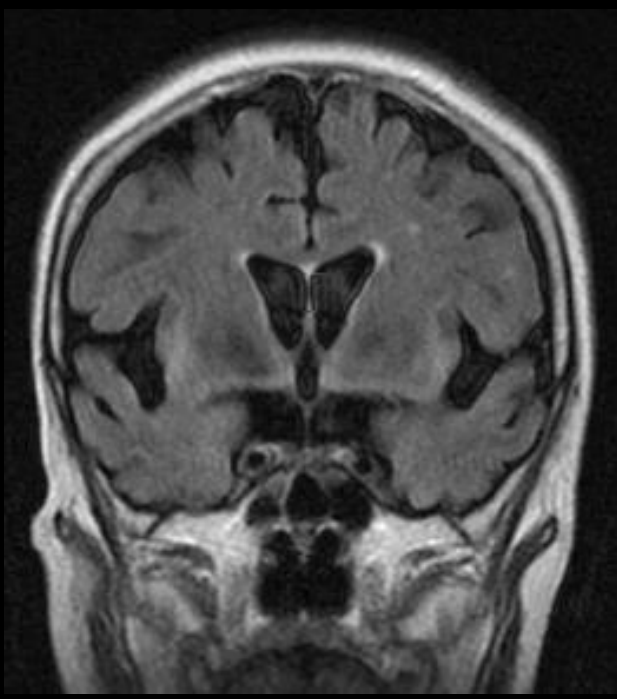
# 抗Ma-2脳炎の治療

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- ◎ 7/16～ IVIg 5日間
- ◎ 8/2 ～ ステロイドパルス 3日間
- ◎ PSL内服 40mg/day(後療法)
  
- ◎ 9/13の頭部MRIで正常化
- ◎ 10/30の頸椎MRIで改善も，異常は残存
- ◎ 下肢症状は改善し歩行可能となったが，上肢症状や聴力症状は残存



2013/8/8  
(前回から約1か月後)



# Autoimmune mediated encephalitis(AME)

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- Paraneoplastic AME
- Nonparaneoplastic AME
- Cell surface antigen associated AME
  - ・ 治療に反応しやすい
  - ・ Anti-NMDAR, anti-GABABR, anti-AMPA, anti-VGKC
- Intracellular antigen associated AME
  - ・ 治療に反応しにくい
  - ・ Anti-Hu, anti-Yo, anti-Ri, anti-CV2, anti-Ma2

**Table 1— Summary of common paraneoplastic autoimmune-mediated CNS disorders.**

Antibody	Neoplasms	Clinical Syndrome	MR Imaging Patterns
AMPA	Breast cancer, SCLC	Limbic encephalopathy, agitation	Limbic encephalitis
CV2 (CRMP-5)	SCLC, thymoma	Chorea, pancerebellar syndrome, limbic encephalopathy	Striatal encephalitis, cerebellar degeneration, limbic encephalitis
GABA <sub>B</sub> R	SCLC	Seizure disorder, limbic encephalopathy	Limbic encephalitis, normal
Hu (ANNA-1)	SCLC	Sensory neuropathy, limbic encephalopathy, cerebellar ataxia, brain stem dysfunction	Limbic encephalitis, cerebellar degeneration, brain stem encephalitis
Ma2	Testicular germ cell tumor	Limbic encephalopathy, narcolepsy, hyperthermia, endocrine dysfunction, vertical gaze paresis	Limbic encephalitis, brain stem encephalitis, diencephalic encephalitis
NMDAR	Ovarian teratoma	Psychosis, memory deficits, seizures, dysautonomia, hypoventilation	Limbic encephalitis, normal
Ri	Neuroblastoma, breast cancer, ovarian cancer	Opsoclonus-myoclonus, pancerebellar syndrome, brain stem dysfunction	Cerebellar degeneration, brain stem encephalitis
Yo	Ovarian cancer, breast cancer	Pancerebellar syndrome	Cerebellar degeneration, normal

**Table 2— Summary of common nonparaneoplastic autoimmune-mediated CNS disorders.**

Disorder	Antibody	Clinical Syndrome	MR Imaging Patterns
Anti-GAD	GAD	Stiff-person syndrome, pancerebellar syndrome, limbic encephalopathy	Limbic encephalitis, cerebellar degeneration, brain stem encephalitis
Anti-VGKC-associated	LGII	Limbic encephalopathy, neuromyotonia, SIADH	Limbic encephalitis, striatal encephalitis
Gluten sensitivity (celiac disease)	Endomysial, TTG	Pancerebellar syndrome, epilepsy, headaches, transient neurologic deficits, dementia	Cerebellar degeneration, occipital calcifications, leukoencephalopathy
HE	TPO, TG	Dementia, psychosis, seizures, focal neurologic deficits, tremor, myoclonus, gait ataxia	Normal, leukoencephalopathy, limbic encephalitis, small vessel infarcts

# Ma タンパク

- mRNAの生合成を担い，神経細胞や抗Ma-2脳炎の原因となる腫瘍細胞で発現される
- Ma familyにはMa-1, 2, 3があり，このうちMa-2が最も主要な抗原
- 1999年，Voltzらにより精巣腫瘍の腫瘍随伴性辺縁系・脳幹脳炎の血清マーカーとして抗Ma-2抗体が報告された

# 抗Ma-2脳炎

- ◎ 自己免疫媒介性脳炎の一つ
- ◎ 抗Ma脳炎と抗Ta脳炎にわかれる

	抗Ma脳炎	抗Ta脳炎
抗Ma-1抗体	○	×
抗Ma-2抗体	○	○
年齢，性別	中年，男女	若年，男性
原因腫瘍	多彩 NSCLC，乳癌…	精巣GCTがほとんど
治療反応性	不良	概して良好
予後	不良	概して良好

# 抗Ma-2脳炎-症状-

- Limbic encephalitis(LE), diencephalic encephalitis(DE), brainstem encephalitis(BE)の3領域の症状が主体

(右図)

38人の抗Ma-2脳炎患者中、上記3領域のいずれの症状も呈さなかったのは4例のみ

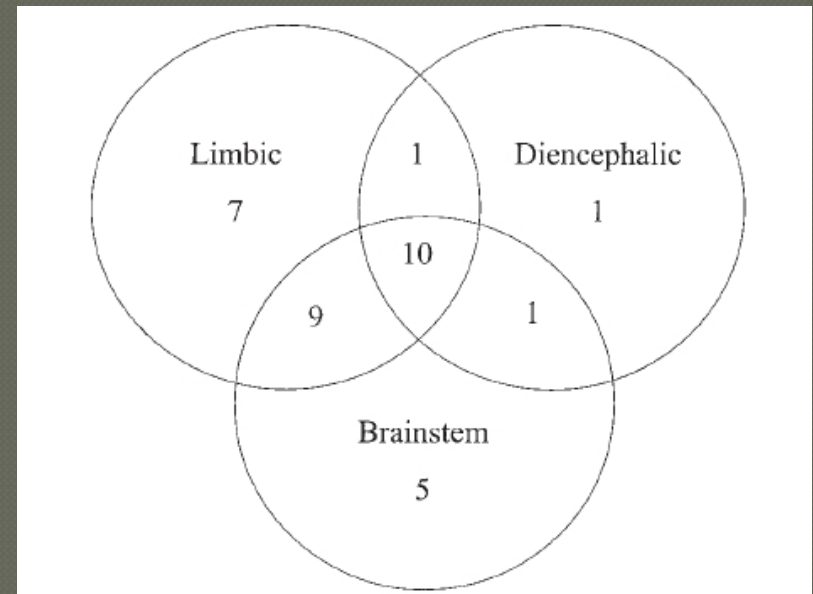
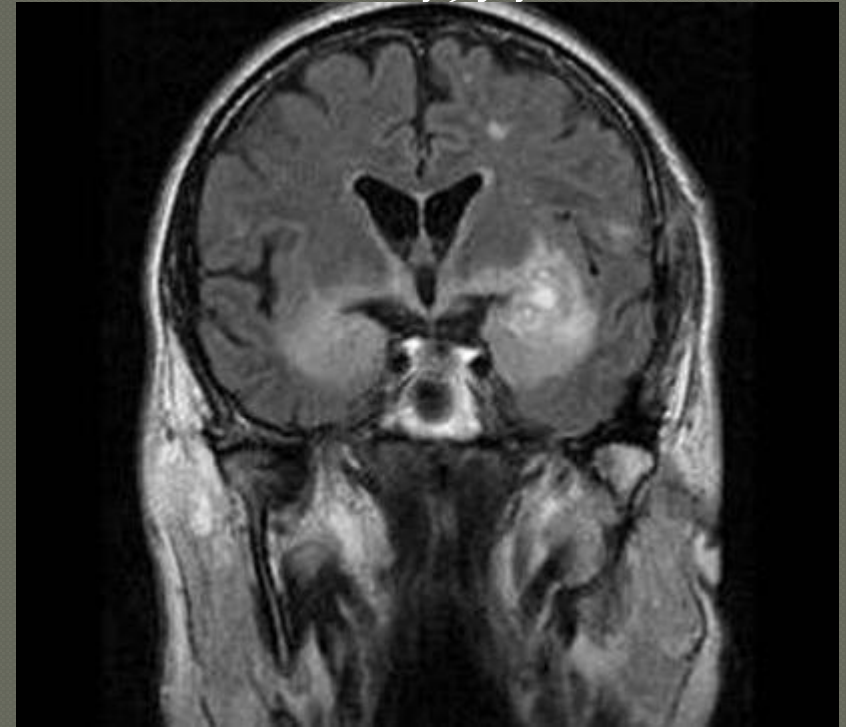
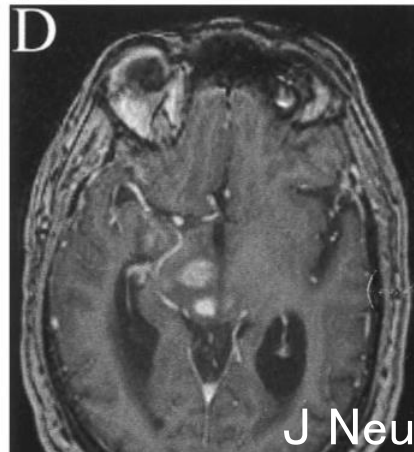
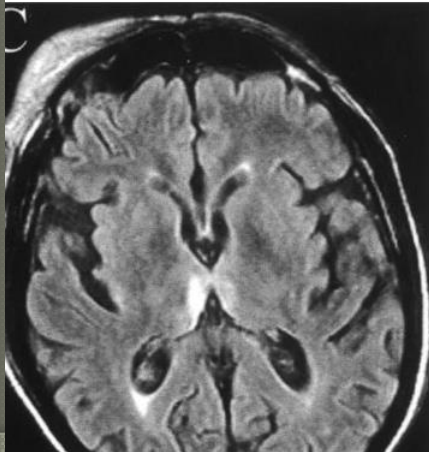
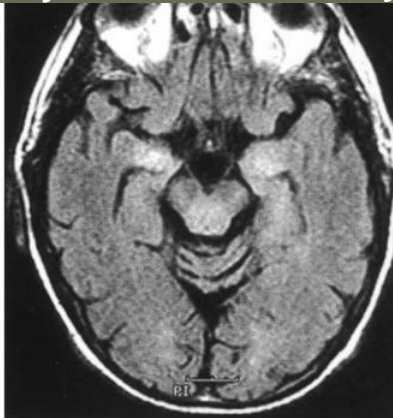
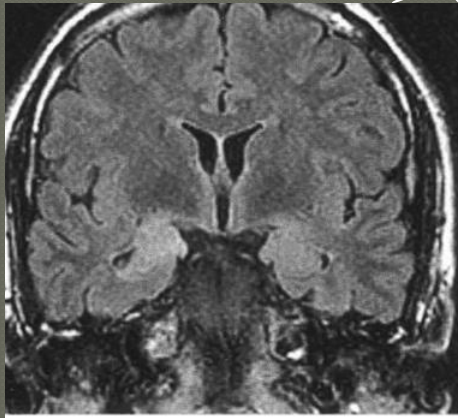


Fig. 1 Distribution of predominant syndromes in 34 patients with anti-Ma2 encephalitis. Twenty-one patients developed symptoms

# 抗Ma-2脳炎-画像-

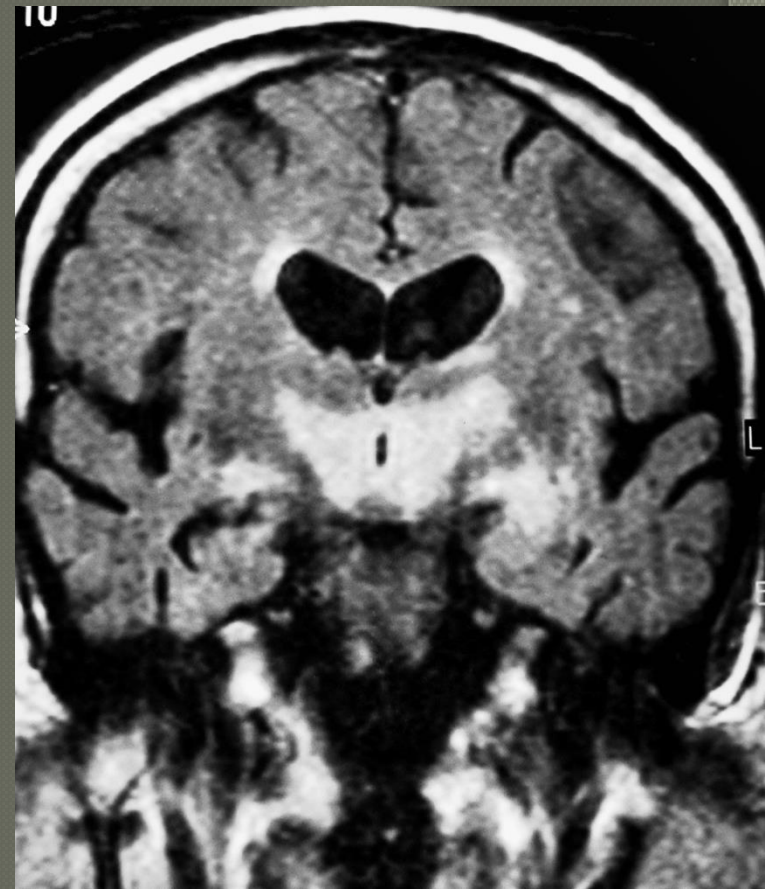
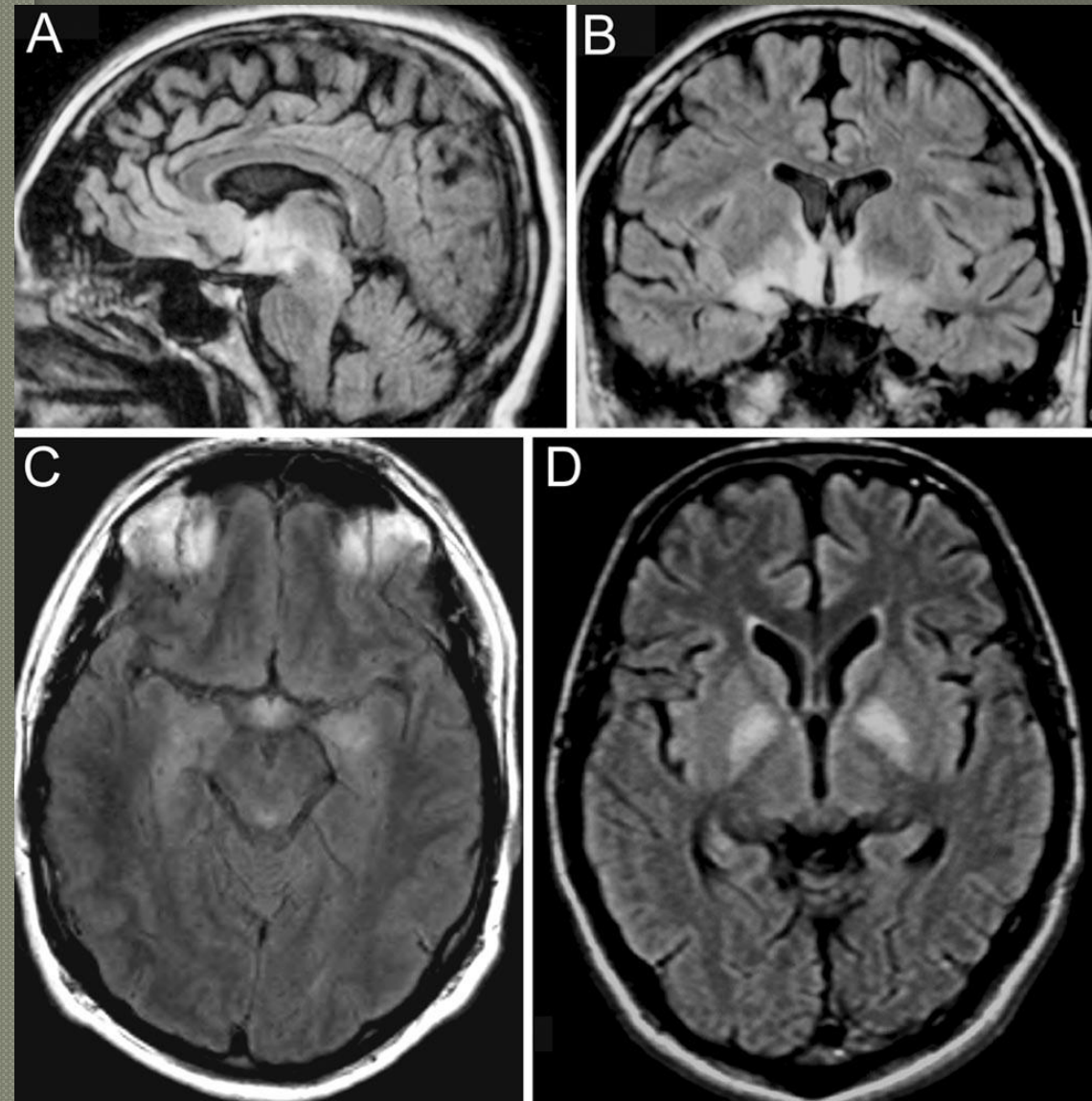
- 症状同様にLE, DE, BEの組み合わせ
- MRIでの異常は38人中28人(74%)で陽性



Brain (2004), 127, 1831-1844

J Neurol Neurosurg Psychiatry 2008;79:767-773

# 抗Ma-2腦炎-画像-



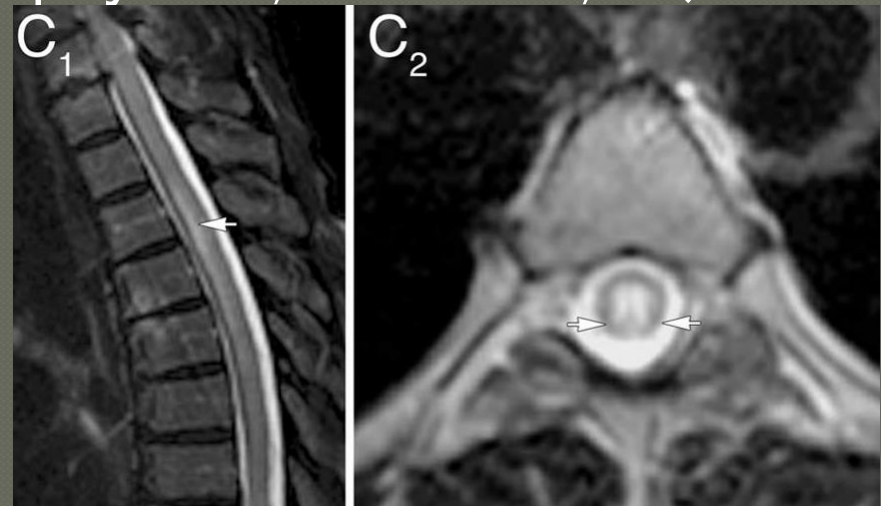
# Isolated autoimmune mediated myelopathy

## ◎ 31人(女20人)のstudy

- ・ 原因腫瘍さまざま(肺癌 9, 乳癌 7, 腫瘍なし 4)
- ・ 自己抗体さまざま(amphiphysin 9, CRMP5 9, ...)

## ◎ MRIの検討

- ・ T2WIでの異常 20/31
- ・ 3椎体以上 14/20



- ・ “対称性” かつ “白質 or 灰白質に限定” 15/20
- ・ 増強効果 13/20 → うち8例で対称性

# 抗Ta脳炎-原因腫瘍-

- 精巣GCT(germ cell tumor)がほとんど
- 抗Ma-2脳炎46人中50歳未満は全て男性(25人)で19人に精巣GCTがあった
- 残り6人全員に精巣摘除術が施行され、IGCNU(intratubular germ cell neoplasm unclassified type)があった(術前には腫瘍の証拠なし)
- 6例中5例で最初の病理報告はno tumorであった

# 抗Ma脳炎-原因腫瘍-

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- ◎ 多彩
- ◎ NSCLC, 乳癌, 消化管癌, 非ホジキンリンパ腫, GCT, 唾液腺癌, 腎rhabdoid tumor, 卵巣癌, melanoma...

# まとめ

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- まれな症状(末梢神経障害, 聴力障害), まれな画像所見(脊髄炎)を呈した抗Ma2脳炎(抗Ma脳炎)の症例を経験した

# Take Home Point

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- ◎ 抗Ma2脳炎と診断したら**高率に腫瘍を合併**するので、徹底的な全身腫瘍検索が必須
- ◎ 特に**若年男性では精巣腫瘍**の存在が予見され、積極的に腫瘍を疑えなくても症状次第で精巣摘除に踏み切る必要がある