Immunomodulatory Therapies in Pediatric MS

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Introduction

- acquired chronic immune-mediated inflammatory condition of CNS.
- MS in children: 10%

  +relapsing–remitting MS:97-99%

  +secondary progressive MS: rare

  +primary progressive MS: rare

Definition

- neurologic symptoms disseminated in time and space.
- Multiple episodes of demyelination of CNS (brain, optic nerves, spinal cord) separated with time intervals of at least 30 days.

Clinical

- Vary
- Encephalopathy may a first episode of MS
- Optic neuritis, isolated brain stem syndrome, symptoms of encephalopathy (headache, vomiting, seizure, altered consciousness): commonly in children

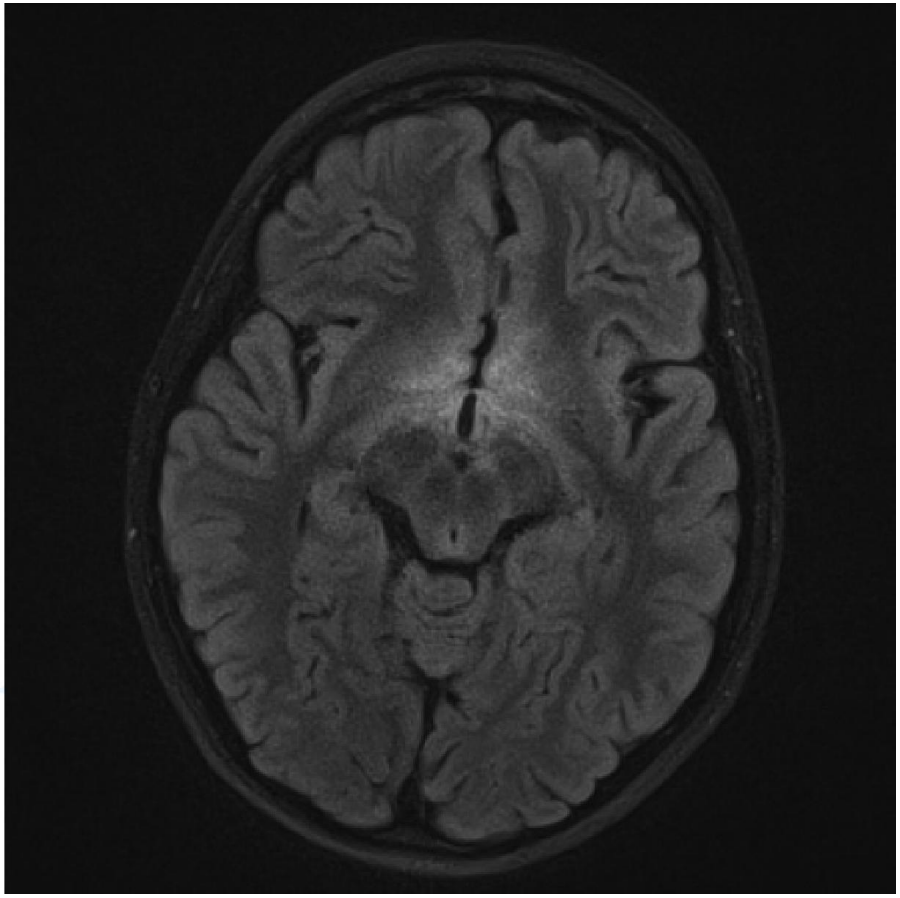
Laboratory

- CSF:+ 0-50 cells/mm3 (lymphocytic predominance)

  + IgG↑ (68% >11y, 35% <11y)

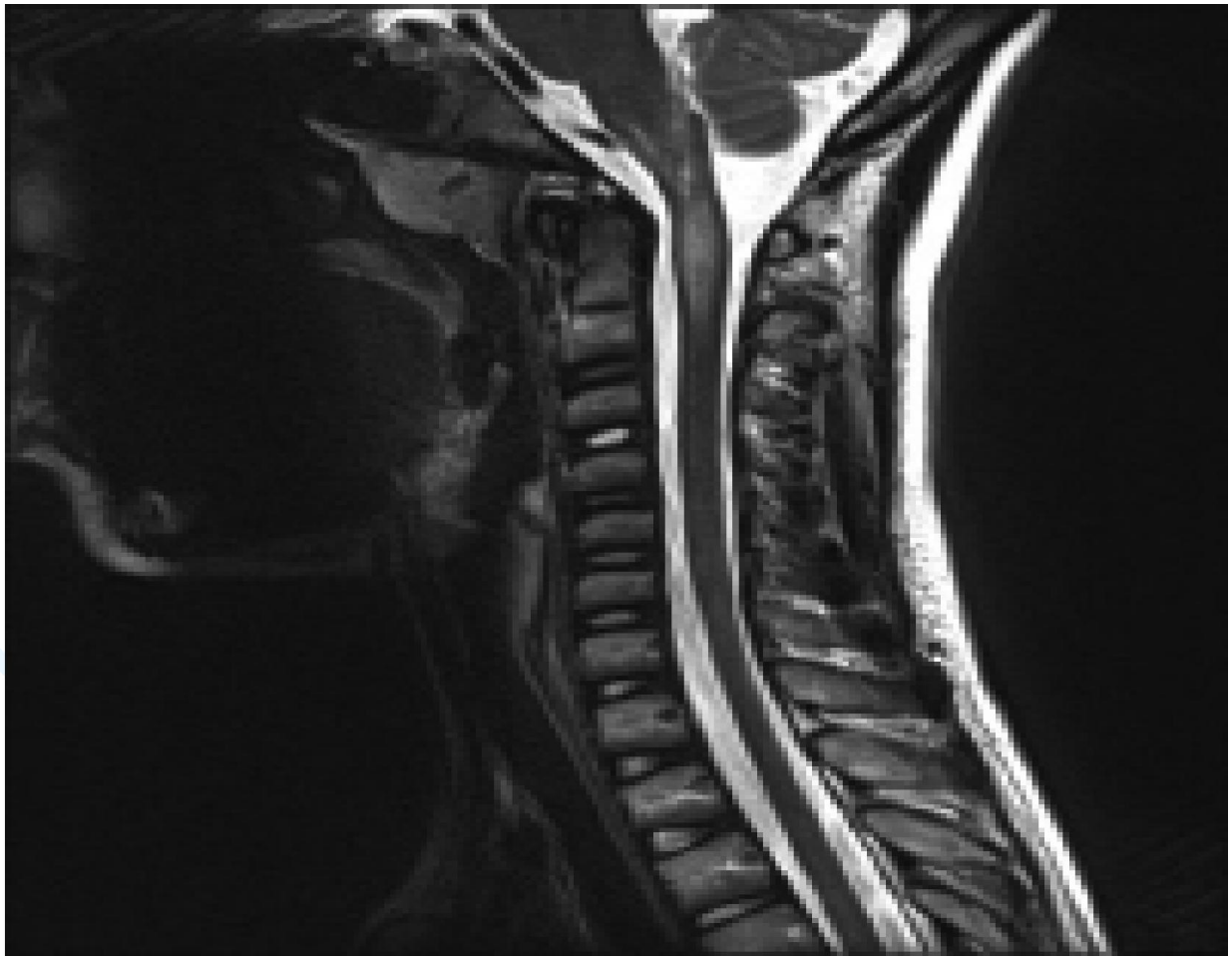
Imaging

- Periventricular increased T2 signal



Imaging

Increased T2 signal at the cervicomedullary



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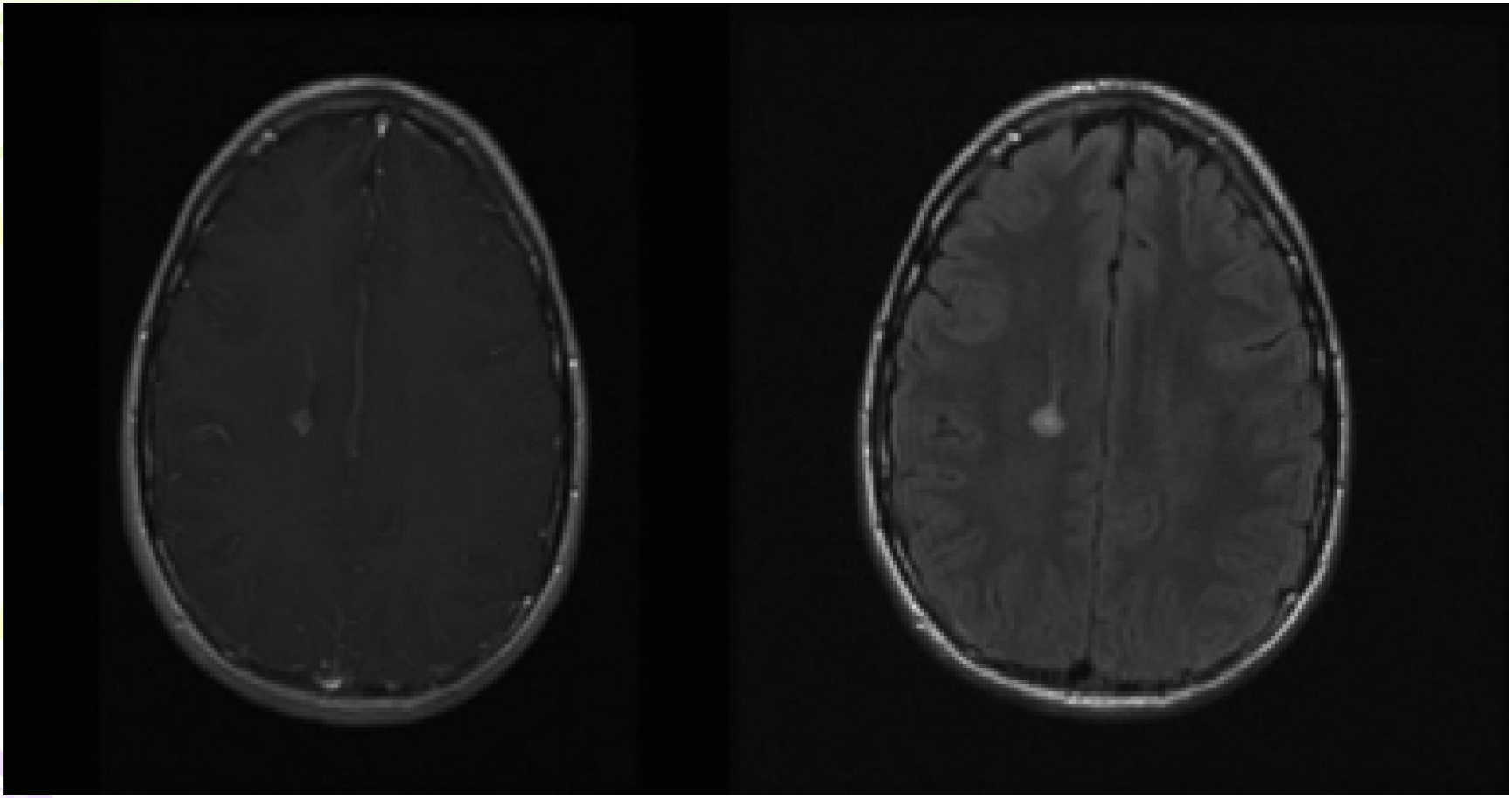

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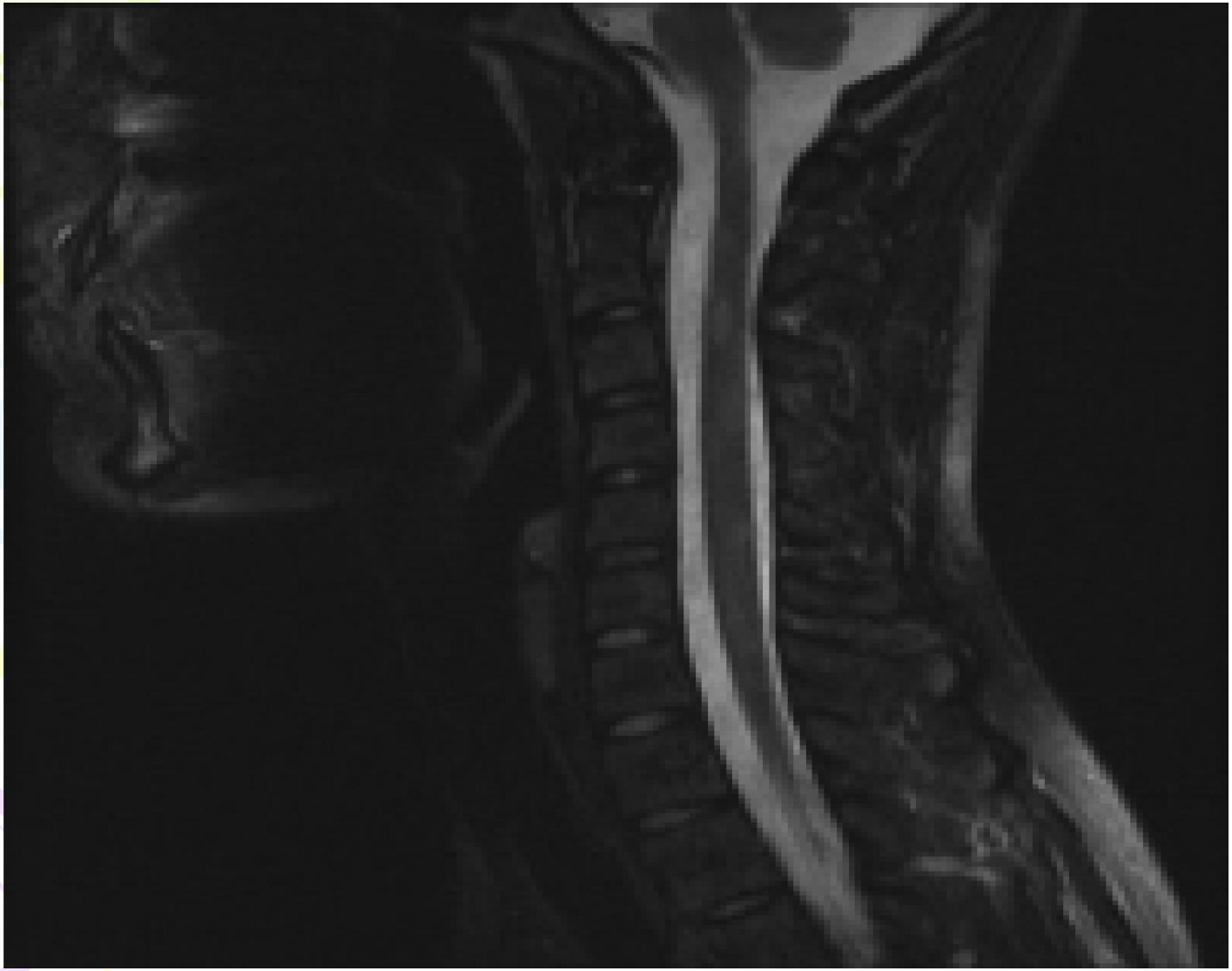
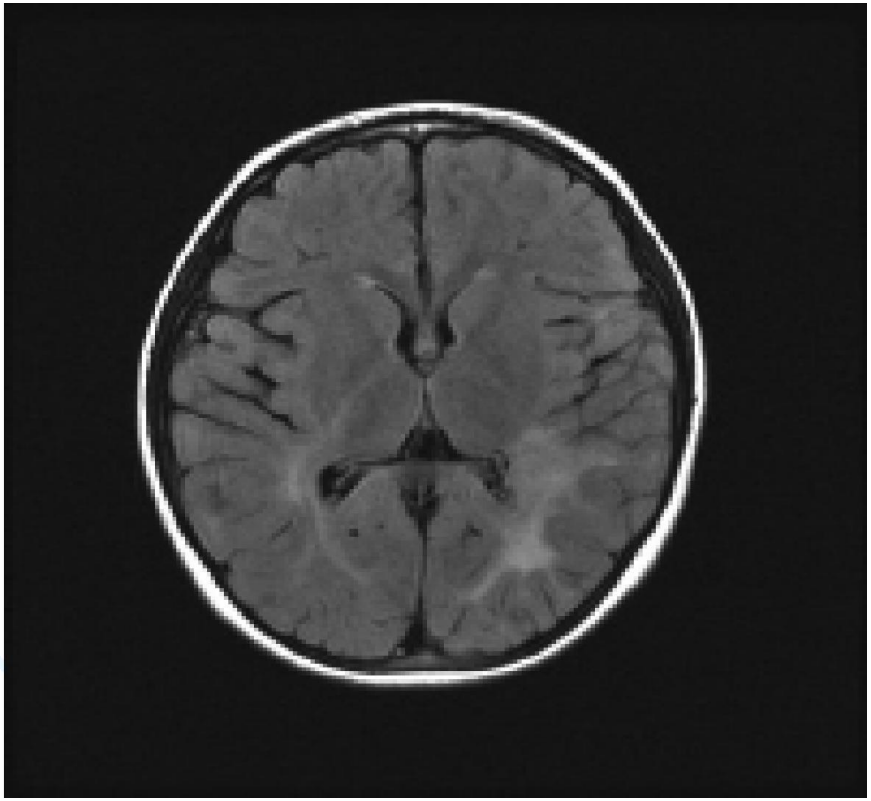


Imaging

- This image would not be sufficient to distinguish an episode of ADEM from pediatric MS in a pre-pubertal child



The 2010 McDonald Criteria for Diagnosis

Clinical presentation	Additional data needed
≥2 attacks; objective clinical evidence of>2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack	
≥2 atracks; objective clinical evidence of one lesion	≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS or Await a further clinical attack implicating a different CNS site

The 2010 McDonald Criteria for Diagnosis

Clinical presentation	Additional data needed
1 attack; objective clinical evidence of ≥ 2 lesions	Simultaneous presence of asymptomatic gadolinium-enhancing and non enhancing lesions at any time: or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack

The 2010 McDonald Criteria for Diagnosis

Clinical presentation	Additional data needed
1 attack; objective clinical evidence of 1 lesion (clinically isolated syndrome)	For DIS: ≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS; or Await a second clinical attack implicating a different CNS site: and For DIT: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI irrespective of its timing with reference to a baseline scan; or Await a second clinical attack

The 2010 McDonald Criteria for Diagnosis

Clinical presentation	Additional data needed
Insidious neurological progression suggestive of MS	One year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteriad: 1. Evidence for DIS in the brain based on ≥1 T2 lesions in the MS characteristic (periventricular, juxtacortical, or infratentorial) region 2. Evidence for DIS in the spinal cord based on≥ 2 T2 lesions in the cord 3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index)

Refractory MS

- the occurrence of three or more relapses in a 12-month period, significant increase in MRI lesions, or progression of disability in spite of immunomodulatory therapy.

Therapies In Acute Attack

1. Glucocorticoids: 20-30 mg/kg x 5days

   1mg/kg/day

2. IVIG: 0,4g/kg/day x 5days
   + refractory to glucocorticoids
   + suspected infection
   + contraindication for steroid
3. Plasmapheresis: severe fluminant replase, refractory to glucocorticoids or IVIG

Therapies For Long Term

- Immunomodulating agents:
  + glatiramer acetate [GA]
  + IFN beta-1a (IM)
  + IFN beta-1a (SC)
  + IFN beta-1b (SC)
- Immunosuppressive medications:
  + mitoxantrone
  + cyclophosphamide
  + rituximab
  + daclizumab
- Oral agents: fingolimod, teriflunomide.

Glatiramer acetate

- 3 small studies in pediatrics:

  decreased the mean annualized relapse rate
- Side-effects: injection-site reactions

  chest pain (rare).

IFN beta

- be safe and well tolerated
- discontinuation rates: 30-50%
- side effects:
  + flulike symptoms: 35-65%
  + leukopenia: 8-27%
  + thrombocytopenia:16%
  + anemia:12%
  + elevated transaminases:10-62%
  + Injection-site reactions

Therapies

- Fingolimod, Teriflunomide, Natalizumab, Mitoxantrone: no reports in children.
- Rituximab: highly effective treatment in a female adolescent.
- Cyclophosphamide (Neurology.2009)

  + well tolerated.

  + side effects:vomiting, transient alopecia, osteoporosis, amenorrhea, bladder carcinoma.

Conclusion

- Treatment pediatric MS is based on randomized controlled data in adults.
- No randomized controlled trials in children.
- It’s very difficulty to prevent relapses of MS in our hospital because of no drugs (IFN-beta, glatiramer acetate).
- We have only cyclophosphamide.(?)