Pediatric-Onset MS

- 2–10% of all patients with MS have clinical onset before 18 years of age[1]
- Median age at presentation of pediatric-onset MS: 13.7 years[3]
  - Onset before puberty relatively uncommon[4]
- >95% of cases follow a relapsing-remitting course[2]
- Brain volume loss occurs early, may accelerate over the first 2 years, and is linked to disease activity[5]

Pediatric-onset compared with adult-onset MS[5]

- Higher relapses rates
- Relapses may be more severe, but recovery more likely to be complete or near-complete
- Higher volume of brain lesions in first few years[6]
- Slower rate of disability accrual, especially in the initial years
  - However, disability is accrued at a younger age

1. Waldman A et al. *Lancet Neurol.* 2014;13:936-948; 2. Krupp LB et al. *Mult Scler.* 2013;19:1261-1267; 3. Hacohen Y et al. *Mult Scler.* 2020;26:1372-1380;
4. Hacohen Y et al. *Mult Scler.* 2021;27:1970-1976; 5. Waldman A et al. *Neurology.* 2016;87(Suppl 2):S74-S81; 6. Ghassemi R et al. *PLoS One.* 2014;9:e85741.

Pediatric-Onset MS: Diagnostic Considerations

Application of latest (2017) McDonald diagnostic criteria:

- Large prospective pediatric cohort study showed high reliability when applied at disease onset[1]
- Data from at least 2 cohort studies suggest similar sensitivity and specificity in older (>11 years) and younger (≤11 years) patients, although criteria may be less sensitive in younger patients[1,2]

Other acute demyelinating syndromes to exclude[3]

ADEM[4,5]

- Typically, monophasic but can multiphasic
- Associated with anti-myelin oligodendrocyte glycoprotein (MOG) antibodies

NMOSD[3]

- Typically associated with antibodies against aquaporin-4 (AQP4)

MOG antibody-associated disease[5]

- Present in 30% of children with acquired demyelinating syndromes
- More frequent in children with ADEM or younger than 11 years
- Rarely present in children meeting MS diagnostic criteria

ADEM, acute disseminated encephalomyelitis; NMOSD, neuromyelitis optica spectrum disorder; MOG, myelin oligodendrocyte glycoprotein.

1. Fadda G et al. *Lancet Child Adolesc Health*. 2018;2:191-204; 2. Hacohen Y et al. *Mult Scler.* 2020;26:1372-1380; 3. Hacohen Y et al. *Neurology*. 2017;89:269-278; 4. Pohl D et al. *Neurology.* 2016;87(suppl 2):S38-S45; 5. Waters P et al. *JAMA Neurol.* 2020;77:82-93.

Pediatric MS: Treatment Trends and Considerations

2012

International Pediatric MS Study Group guidelines recommended early initiation of DMT with older injectable therapies (ie, IFNβ or GA)[1]

Treatment failure rate: 25% to 64%[2]

2020

US Network of Pediatric MS Centers study[3]

741 patients <18 years

197 on newer therapies (fingolimod, dimethyl fumarate, teriflunomide, natalizumab, rituximab, ocrelizumab)

544 on older injectable DMTs (IFNβ, GA)

Newer therapies associated with lower relapse rates and less MRI activity (infusions > orals)

NNT: 3.7 person-years to prevent 1 relapse

Off-label use of DMTs approved for use in adults

2018

Fingolimod was first drug approved for pediatric use

2021

Evidence-based expert recommendation:
"…we would recommend treating pediatric MS as a highly active disease, favoring the early use of highly effective DMTs rather than injectable DMTs."

IFN, interferon; GA, glatiramer acetate; NNT, number needed to treat.

1. Krupp LB et al. *Mult Scler.* 2013;19:1261-1267; 2. Ghezzi A et al. *Neurology.* 2016;87: S97-S102;
3. Krysko KM et al. *Ann Neurol*. 2020;88:42-55; 4. Hacohen Y et al. *Mult Scler.* 2021;27:1970-1976.