IVIG in ADEM treatment

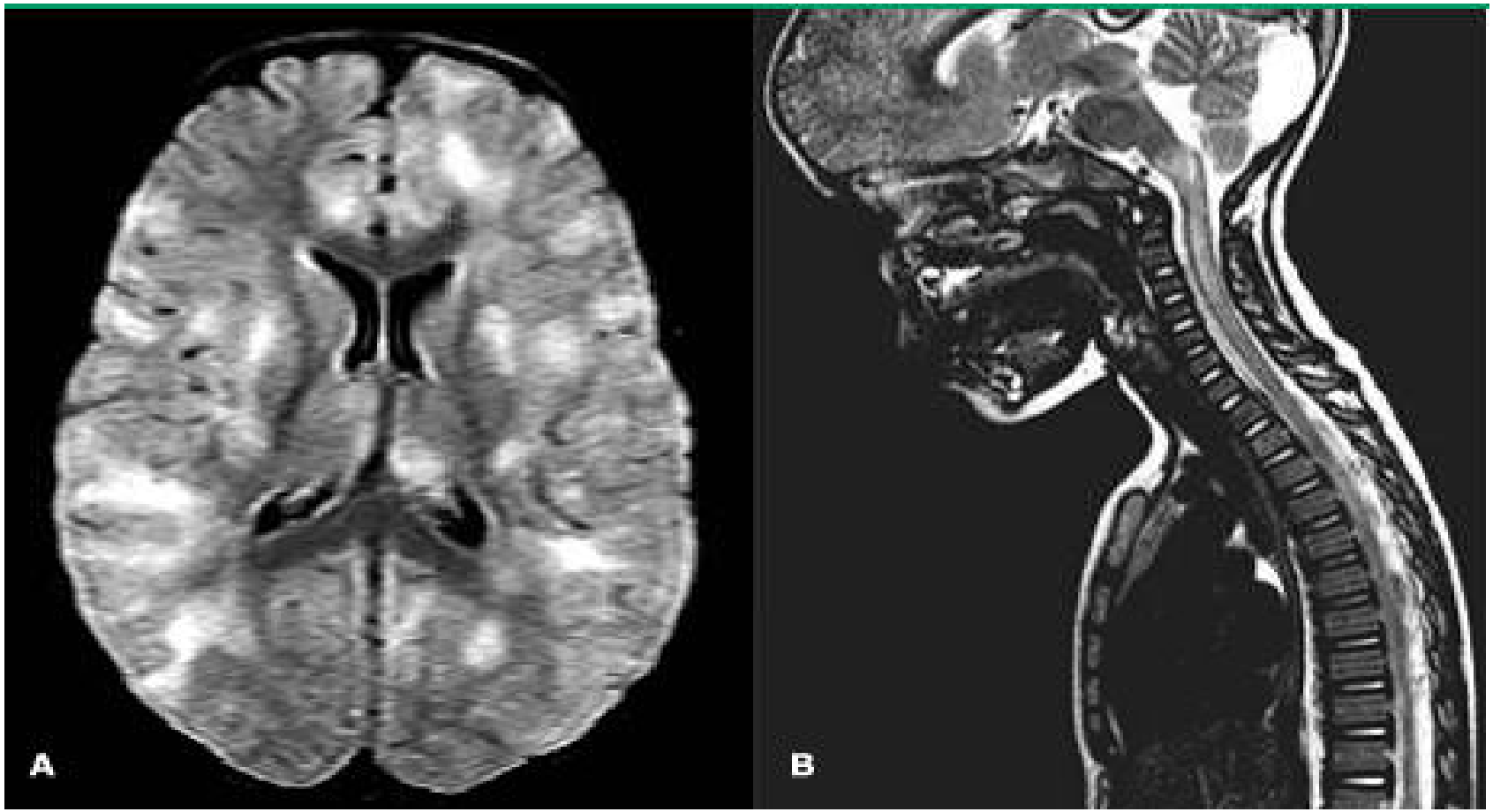
Presented by Dr. Pham Hai Uyen
Pediatric Neurology Department
Children Hospital 2

Introduction

- 1931 McAlpine, Lancet, 3 cases: acute disseminated encephalomyelitis (ADEM):
  - postvaccinial
  - post-measles
  - idiopathic

Introduction

- Up to now, ADEM:
  - acute inflammatory demyelinating disorder of CNS
  - postinfectious or postvaccinal
  - monophasic, recurrent or multiphasic
- Annual incidence : 0.4–0.8/100,000
- Affects children and young adults.
- Age mean: 3 – 8 yrs-old
- Male= female



A) An Axial MRI of the brain (FLAIR image) in a child with acute disseminated encephalopmyelitis (ADEM) demonstrates multifocal areas of hyperintensity in both cerebral hemispheres involving cortical gray matter, centrum semiovale, and deep gray nuclei.

B) A saggital MRI of the spine (T2 image) in the same child demonstrates high signal intrinsic to the spinal cord, consistent with longitudinally extensive transverse myelitis.

Diagnostic Criteria – An important paper was recently published by the International Pediatric Multiple Sclerosis Study Group, which proposed diagnostic criteria for ADEM in children.[1] The criteria are important for the purpose of arriving at better decisions about treatments and are meant to facilitate research on ADEM. The major criteria include:

1. A first clinical attack of central nervous system demyelinating disease with acute or subacute onset, polysymptomatic neurologic features, and encephalopathy

2. Brain MRI showing focal or multifocal lesions, predominantly involving the white matter, without evidence of previous white matter changes

3. Encephalopathy as a presenting symptom, with the onset of encephalopathy corresponding with the occurrence of the disease state (encephalopathy is defined to include behavioral changes, such as lethargy or irritability, or severe changes in the level of consciousness such as coma)

These features help distinguish ADEM from other clinically isolated syndromes, which have a greater risk for recurrence and subsequent diagnosis of MS.

Treatment

(1) supportive

(2) Immunomodulation: specific - high-dose intravenous methyl prednisolone, intravenous immunoglobulin (IVIg), and plasma paresis

(3) physical and rehabilitation therapy

Standard treatment: Intravenous methyl prednisolone

is the first-line drug:

- 10–30 mg/kg/day, up to a maximum of 1 g/day): for 3–5 days
- 50%–80%
- Oral corticosteroid : 4-6 weeks to reduce the risk of relapses

Class II, Level C

Problem

1. Do not respond to high-dose corticosteroids,
2. Contraindications to steroids and
3. Relapsing ADEM.

What should we do?

IVIG was recommenced

1. As a reasonable option as second-line therapy for monophasic ADEM in patients who do not respond to high-dose corticosteroids,
2. In patients with monophasic ADEM who have contraindications to steroids and
3. May be considered as an option to eliminate steroid dependency or for those patients who fail to respond, or have contraindications, to steroids in relapsing ADEM.

Intravenous Immunoglobulins in Neurological Diseases: Established and Novel Clinical Applications

Konstantina G. Yiannopoulou
Neurological DepartmentLaiko General Hospital of Athens
Greece

standard treatment is high-dose steroids. The use of IVIg (0.4 g/kg/day for 5 days or 1 g/kg/2 days) has been reported in case reports and small series suggesting that IVIg may have favourable effects when used as an initial therapy in both adults and children (class IV evidence). IVIg may have beneficial effects also as second line therapy (class IV evidence) [149–152] especially in patients who could not receive or failed to respond to steroids (class IV evidence) or in patients with peripheral nervous system involvement and steroid failure (class IV evidence). Alternatively combination therapy by steroids and IVIG (class IV evidence) or steroids, IVIg and PE were suggested to have favourable effects especially if given early in the course of disease (class IV evidence) (EFNS task force 2008).

The England guidelines

Neurology. 2000 Mar 28;54(6):1370-2.

Treatment of acute disseminated encephalomyelitis with intravenous immunoglobulin.

Sahlas DJ[1], Miller SP, Guerin M, Veilleux M, Francis G.

ADEM is a “grey” indication (grey indications are those diseases for which the evidence is weak, in many cases because the disease is rare) and may be considered for acute disseminated encephalomyelitis where high-dose corticosteroids or plasma exchange have failed **(grade C recommendation, level III evidence)**.

The Canadian guidelines

Medical Condition	Recommendations	Dose/Frequency of Administration
Acute disseminated encephalomyelitis[3,5] (ADEM)	IVIG is an option for monophasic ADEM when first-line therapy with high-dose corticosteroids fails or when there are contraindications to steroid use, and for treatment of relapsing ADEM to eliminate steroid dependency or for those patients who fail to respond, or have contraindications, to steroids.	Adults: Total dose of 2 g/kg divided over 2 to 5 days. Pediatric: Total dose of 2 g/kg divided over 2 days.

Ontario IVIG Utilization Management Guidelines Version 3.0 May 30, 2016

However,

IMMUNE GLOBULIN (IVIG and SCIG)

47 Diseases

Protocol: PHA017
Effective Date: December 1, 2015

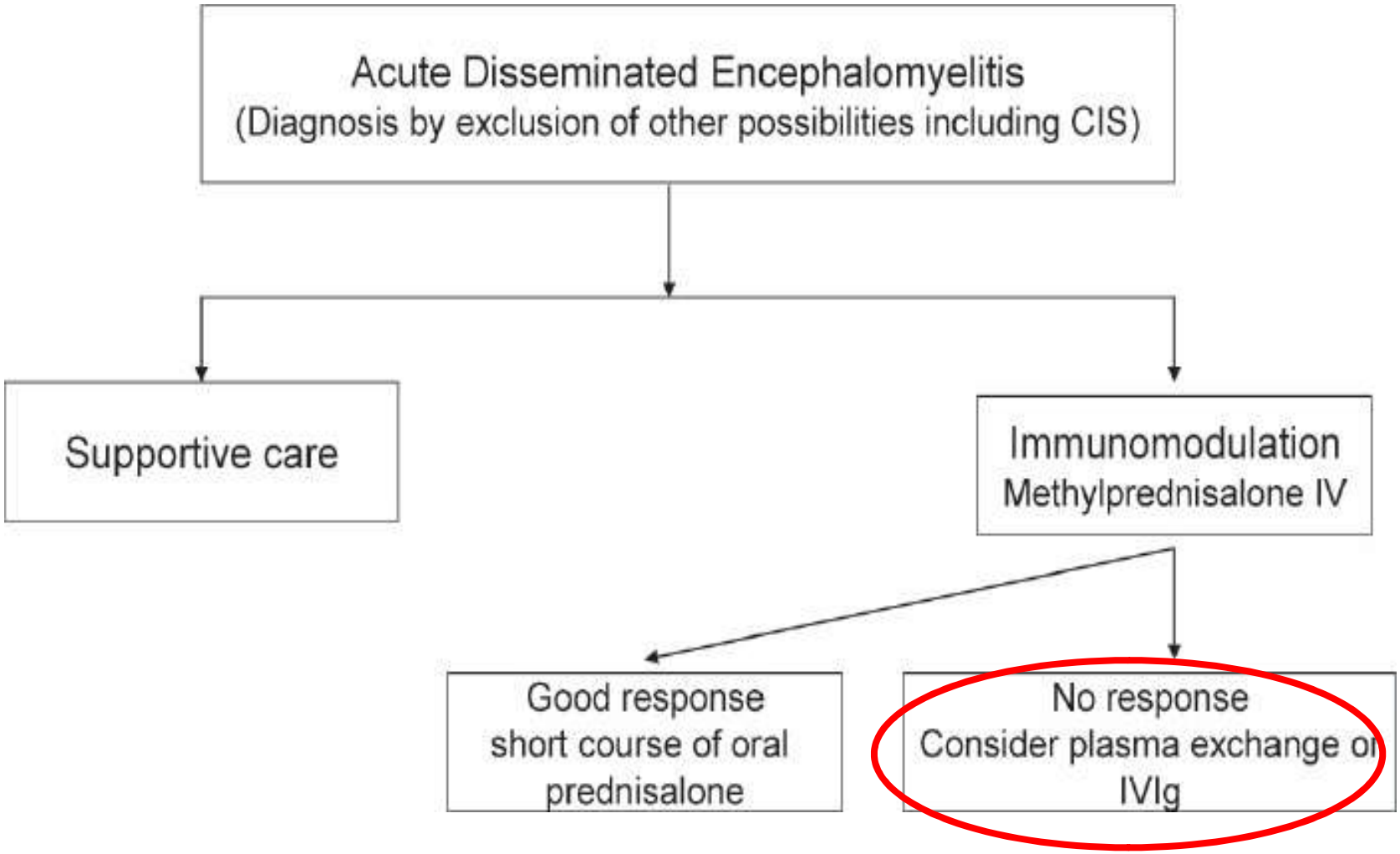
Immune globulin is **not medically necessary** for:

1. Acquired hemophilia
2. Acute disseminated encephalomyelitis (ADEM)
3. Adrenoleukodystrophy
4. Alzheimer's disease
5. Amyotrophic lateral sclerosis (ALS)
6. Antiphospholipid antibody syndrome (APS) in pregnancy
7. Asthma, non-steroid dependent
8. Atopic dermatitis
9. Autism spectrum disorders
10. Autoimmune hemolytic anemia

Conclusion

- IVIG in ADEM treatment:
  - class III – IV, Level C
  - is not the first-line drug
  - was recommenced in some specical condition of ADEM

Take home message



Chân thành cám ơn!