Acute polyradiculoneuropathy and Dengue Fever infection

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1- Introduction

Neurological complications of dengue virus infection

- Proportion of Dengue virus infection with neurological manifestations:
  - 0.5% to 5.4% in four studies from southeast Asia
  - 21% of cases in a prospective study from Brazil.

- Neurological complications of Dengue fever can be categorised into:
  - Encephalopathy
  - Encephalitis
  - Immune-mediated syndromes
  - Dengue muscle dysfunction
  - Neuro-ophthalmic disorders

- Peripheral nervous system manifestations:
  5% of neurological manifestations of Dengue fever
1- Introduction

Guillain–Barré Syndrome

Nobuhiro Yuki, M.D., Ph.D., and Hans-Peter Hartung, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

• **GBS is characterized by** acute areflexic paralysis with albuminocytologic dissociation (present in only 50% of patients during the first week of illness)

• **Preceded by** infectious symptoms 3 days to 6 weeks in 2/3 of cases with a peak incidence between 1 and 2 weeks

• **Evolution in 3 phases**: progress (1-3 weeks) plateau (weeks or months) and recovery (weeks or months)

• **Autoimmune origin** of this syndrome is well established.

• **2 subtypes of GBS**:
  - Acute inflammatory demyelinating polyneuropathy
  - Acute motor axonal neuropathy
1- Introduction

Figure 1  Relation between infections, antiganglioside antibodies, and clinical course of GBS

Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome
The Lancet Neurology Volume 7, Issue 10 2008 939 - 950
More than 20 cases of GBS following dengue virus infection were reviewed.

Neurological symptoms occurred at least one week after Dengue fever onset.

Two cases of concomitant SGB and Dengue fever
But in one case RT-PCR in both blood and CSF samples were negative.
In the other case RT-PCR was not performed.
Both were treated by intravenous immunoglobulins and one recovered in one week.

One case of concomitant Miller Fisher Syndrome (GBS variant) and dengue virus infection
Latency between neurological manifestations and dengue fever symptoms: 2 days
Viral RNA in blood and CSF samples: both positive
Complete recovery: one week without treatment
During the last dengue epidemic, we report 3 cases of concomitant Dengue virus infection and acute inflammatory demyelinating polyneuropathy.
Acute polyradiculoneuropathy and Dengue Fever

2- Case reports

- Characteristics of the 3 patients:
  - Gender: 2 males, 1 woman
  - Origins: melanesian, indonesian and caucasian
  - Mean age: 60 years old (55-68)
  - Medical history: one present old history of Basedow’s disease, no treatment

- Dengue fever symptoms:
  - Acute fever, headaches, muscle and joint pain
  - No dengue haemorrhagic fever

- Neurological symptoms:
  - Tetraparesia with gait disorder and areflexia: 100% of cases
  - Multiple cranial nerve palsies: 66% of cases
    (Ptosis, bilateral facial palsy, swallowing troubles)

Mean latency between Dengue fever and neurological symptoms: 2 days (1-3)
2- Case reports

• Paraclinical Data :

  - Electroneuromyography :
Demyelinating disorders according to Cornblath criteria in all cases
Motor conduction velocity slowed : 33%
Distal motor latencies prolonged : 66%
F waves latencies prolonged : 100%
Conduction blocks : 100%

- Cerebrospinal fluid (CSF) analysis :
Normal, no pleiocytosis and protein level normal in all cases
Intrathecal immunoglobulin synthesis analysed in the only case : negative

- Biology :
RT-PCR for dengue virus positive in both blood and CSF in all cases
IgM realised 2 cases : 100 % positive
IgG realised in all cases : 100 % negative
2- Case reports

• **Diagnosis of Dengue Fever** was performed before AIDP in only 1 case

• **Treatment**
  - Standard care for Guillain Barre Syndrome
  - **Polyvalent intravenous immunoglobulins** for all cases (2g kg)

• **Evolution**
  - Maximum motor deficit reached in a **one or two days**
  - No other complication of dengue virus infection
  - **Global recovery** after 1 week for all cases
For us these cases are not Guillain-Barré Syndrome

- Concomitant infection
- Viral RNA positive in CSF
- No albuminocytologic dissociation in CSF
- Maximum neurological symptoms reached in a few days
- Plateau phase lasting a few days before complete recovery
3- Discussion

- **Physiopathological hypothesis**

  - Secondary infection, antibody-dependant enhancement?
    
    -> But serology IgG Dengue negative for all 3 patients

  - Early Guillain Barré Syndrome?
    
    -> But GBS generally occurs from 3 days to 6 weeks after infection

  - Demyelinisation or oedematous lesion directly due to Dengue virus?
    
    -> The neurotropism of Dengue virus is well established for the central nervous system

    -> The neurotropism of Dengue virus for peripheral nervous system has not been studied
3- Discussion

• Utility of intravenous immunoglobulins?

- 6 cases of Acute Inflammatory Demyelinating Polyneuropathy occurring at early stage or seroconversion of acute VIH infection

  -> 50% of them were treated with intravenous immunoglobulin therapy before starting highly active anti-retroviral therapy and completely recovered.

- 1 case of concomitant GBS and dengue virus infection

  -> Recovery in one week after intravenous immunoglobulins

- But the Miller Fischer syndrome reported by our colleagues was extremely similar

  -> Recovery was spontaneous within 1 week.
Acute inflammatory demyelinating polyneuropathy can be observed at the first days of dengue fever infection.

The mechanism is not understood, demyelinisation directly due to Dengue virus is not impossible.

The use of intravenous immunoglobulins seems to be safe and efficient.
• Colleagues who actively contributed to this work: S. BILLOT, D. GUYON and N. MOLKO (Neurology CHT)
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