

Epidemiology of sequelae following infectious encephalitis

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Talking about encephalitis sequelae

- Encephalitis is an inflammation of the brain
- Can be associated with necrosis, bleeding, destruction of parenchyma
- Similar to traumatic brain injury (TBI)
- Possible persisting functional symptoms or sequelae after the recovery of the infectious episode
- Individual and collective burden
 - Need for medical intervention and public health policies

Domains possibly affected by post-encephalitis sequelae

- Cognitive functions
- Behavior and mood (psychiatry)
- Neurological/physical functions
- Resulting in :
 - Limited participation in routine activities
 - Dependence for everyday basic activities
 - Disorders/withdrawal from social interaction
 - Inability to return to work
 - Decreased quality of life
- All domains can be affected at various level in a single patient
- Tropism of infectious agents → « specific » profile of sequelae

Available data about post-encephalitis sequelae

- Few case-series, many single-case reports
- Major limitations
 - Neuro-invasive syndrome vs encephalitis
 - Evaluation limited to those evaluable
 - Not all domains evaluated in all case-series
 - Various delays between onset and assessment
- Crude figures to be taken very cautiously
- Global picture is relevant

Herpes simplex encephalitis sequelae

- Neuropsychiatric sequelae 45-50 % (*Mc Grath 1997, Mailles 2012*)
 - Behavioral changes: Aggressiveness, Disinhibition, inappropriate behavior, ADHD in Children : 66%, tic disorders 50% (*Michaeli 2014*)
 - Depression, Anxiety 17% (*Mc Grath 1997*)
- Neurological/physical sequelae: unfrequent compared to other agents, and compared to cognitive and behavioral sequelae following HSE
- Seizures 3% to 20% (*Hjalmarsson 1997*)

Flaviviruses

- TBE, WNE, JE: different populations affected
- Most studies enroll encephalitis, encephalomyelitis, meningitis, even non neuroinvasive infections
- Similar tropism for thalamus, basal ganglia, brainstem
→ similar sequelae

But specificities exist

Tick-borne Encephalitis

- Cognitive impairment
 - Memory impairment : 20 to 35 % (*Lämmlli 2000, Gustav-Rothenberg 2008, Mickiene 2002*)
 - Global IQ significantly lower than the average in children (*Fowler 2013*)
- Need for psychiatric therapy in up to 44% patients after discharge (*Czupryna 2011*)
 - Depression and anxiety 29% (*Lämmlli 2000, Czupryna 2011, Karelis 2012*)
 - Sleep disorders up to 42%
 - Mood disorders in 47 % (*Karelis 2012*)



TBE : neurological sequelae

- Neurological deficit 24%-27%
 - Shoulder girdle paralysis 14%
 - Visual accommodation deficit 19%
 - Facial palsy 5%
 - Hearing loss 11%
 - Hemiparesis 3%
- Muscle weakness 16 to 20%
- Parkinsonism, tremors 5% to 10%
- Balance disorders/dizziness 21 to 40%
- Movement coordination disorders 39%

(Kaiser 1999, Lammler 2000, Mickiene 2002, Laursen 2003, Czupryna 2011, Karelis 2012)

West Nile virus Encephalitis

- Cognitive functions impaired in at least one cognitive domain after 1 year in 56% of patients (*Sejvar 2008*)
 - Memory in 40 to 60% in WNND after 18 months (*Klee 2004, Carson 2006, Anastasiadou 2013*)
 - Still impaired in 9% after 8 years (*Murray 2014*)
 - Attention/concentration : 38% at 18 months (*Klee 2004, Sadek 2010*)
 - Executive functions in 36% (*Carson 2006, Sadek 2010*)
 - Cognitive slowness observed in 56% (*Sadek 2010*)



West Nile virus encephalitis

- Psychiatric sequelae (*Klee 2004, Murray 2007*)
 - Depression, anxiety : 21 to 31% after 1 year, major depression for half of them
 - Sleep disorders : 47% after 18 months
 - Personality change 45% : irritability, social withdrawal, increased sensitivity
- Neurological sequelae
 - Ataxia : 43% at 18 months (*Klee 2004*)
 - Tremors, « parkinsonism » 23% (*Sadek 2010*)
 - Motor deficit: 48% (*Sadek 2010, Anastasiadou 2013, all WNND including myelitis and AFP*)
 - Hearing loss 13% in Greek patients (*Anastasiadou 2013*)

Japanese encephalitis



- Cognitive sequelae
 - Memory impaired in 30% of children 6 months after onset (*Ooi 2008*)
 - Intelligence : 28% subnormal, 18% with global IQ < 70 (*Ding 2007*)
 - Significant improvement in most patients by 5 years (*Sarkari 2012*)
- Behavioral disorder
 - 70% at discharge (*Sarkari 2012*)
 - 38 to 50% after a couple of months (*Maha 2009, Ooi 2008*)
 - (Psychosis)
 - Depression in a third of patients

Japanese Encephalitis

- Neurological sequelae
 - Motor deficits
 - AFP, Cortical-spinal deficits
 - At discharge 21% to 38% (*Kakoti 2013, Sarkari 2012*)
 - Movements disorders (*Kalita 2009, Sarkari 2012*)
 - Hyperkinetic movements 21%
 - Parkinsonism, dystonia 56%
 - Seizures 6%-8% (*Ding 2009, Ooi 2008*)
 - Speech disorders (*Sarkari 2012*)
 - Mixed cognitive and neurological deficits in 78% at discharge
 - Persisting dysarthria and monotonous speech

Case 1 : Strasbourg hospital, France

- Male patient, 44 y.o., German-French border
- Diagnosed with TBE encephalitis
- Hospitalized for 14 days
- On discharge
 - Arm and shoulder girdle paralysis,
 - Aggressiveness, insomnia,
 - Prescription for physical rehabilitation and psychiatric follow-up



Case 1 : 1 month after discharge

- Rehabilitation still ongoing
- Favorable evolution of the shoulder paralysis
- Amyotrophy of shoulder girdle, major muscle weakness
- Still attention deficit, loss of inhibition

- Anosognosia: Patient reports a complete resolution of aggressiveness butrelatives strongly disagree

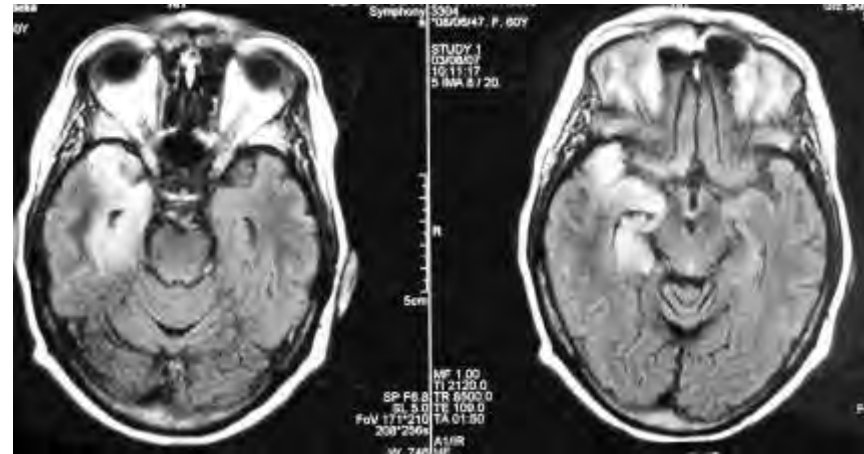
Case 1 : 6 months after discharge

- Resumed part-time work
- Improvement of muscular strength (4/5), complete resolution of shoulder paralysis
- Complete resolution of insomnia and mood disorders
- Persistence of attention deficit

- Conclusion
 - improvement thanks to physical rehabilitation and psychiatric follow-up,
 - no major sequelae,
 - favorable outcome, not full recovery

Case 2, St Denis hospital, France

- Portuguese female patient, 60 yo,
 - Living in France since the age of 24, fluent in French
 - Diagnosed with HSV encephalitis
 - Acyclovir for 14 days
 - Discharged at D18 with prescription for follow-up
-and then disappears



Case 2: 1 year later

- Back in neurology : important memory loss and major spatial disorientation, visual agnosia
- Prescription : comprehensive neuropsychological/psychiatric assessment + MRI+ EEG
→ refused by the patient ...

BUT

- Patient accepts a follow-up in a rehabilitation facility by a neuropsychologist and a psychiatric accepted by the patient

And she disappears again...

Case 2: 2 years after onset

- Hospitalized in ER for headaches
 - addiction to pain killers
 - abandoned neuropsychological and psychiatric follow-up
 - various subjective complaints : diffuse pain, social withdrawal, not being considered by her medical entourage
- Refuses neuropsychological/psychiatric examination
- Refuses to involve any caregiver or family members

And she disappears again...

Case 2: 3 years after onset

- Back in neurology and finally accepts the neuropsychological evaluation !
- Results :
 - Major time and space disorientations : unable to go out alone
 - Global anterograde and retrograde amnesia
 - Speech difficulties : lack of words, cannot properly articulate, difficulties with French speaking
 - Unable to analyse a global situation, focuses only on details
 - Now dependant on her 85-y-o father !
- But..

Patient still is able to implement some by-pass to her deficits

- Patients uses her Smartphone for time orientation and to program reminders
- Carries an amount of paper-notes to write/remember everything
 - rehabilitation and help from a social worker still can be useful for this patient
- Conclusion:
 - Some patients can still improve and be offered efficient interventions even several years after the encephalitis
 - Never give up !

Conclusions

- Infectious encephalitis is not limited to infection
- High benefit in organizing early the assessment and follow up of patients
- Need for multidisciplinary team for such patient
- Caregivers should be involved in the long-term process : they are impacted by the patient's sequelae
- Sequelae assessment and rehabilitation guidelines in preparation by the International Encephalitis Consortium

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