CEREBRAL MALARIA AND EPILEPSY

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Global prevalence figures of epilepsy

Epilepsy in tropical countries

Does this high burden of infectious diseases in Africa could explain the burden of epilepsy there?
The role of certain parasitoses have been described:

- **Onchocerciasis**
  
  *(Druet-Cabanac et al., 1999, Farnarier et al., 2000; Boussinesq et al., 2002)*

- **Neurocysticercosis**
  
  *(Dumas et al., 1990; Preux et al., 1996; Nsengiyumva et al., 2003)*

→ **Why focus on cerebral malaria?**
Seizures

Cerebral malaria

(the presence of PF in the blood and a combination of fever and coma)

Severe clinical forms

Why focus on cerebral malaria?

The depth of coma is an important prognostic factor:

Children with CM frequently develop abnormal postures

Mortality of 10 to 40% (with children)

Neurological deficits after *P. falciparum* malaria

(7 to 16% of the survivors)

Epilepsy?
Epilepsy frequently evoked as a neurological sequel of CM

(Dumas et al., 1986; Senanayake et al., 1991; ILAE, 1994; de Bittencourt et al., 1996; Preux et al., 2002)

Few studies have been done to quantify this possible relation

Recent studies:

- Carter et al., Epilepsia 2004; 45: 978-81.
- Ngoungou et al., Epilepsia 2006; 47: 2147-53.
Epidemiological studies in sub-Saharan Africa

- Ngoungou et al., 2006
- Carter et al., 2004
Our studies

(Ngoungou et al., 2006a; 2006b)
Matched case-control study in Gabon

- **Population:**
  - patients aged between 6 months to 25 years
  - admitted between January 1990 and May 2004

- **Type of study:**
  - matched case-control study
  - each control was matched to a case according to:
    - age, year of hospitalization
Results

 ➢ Relationship between cerebral malaria-epilepsy

Matched case-control study in Gabon

Cerebral malaria:

Matched Odds ratio: 3.4; 95% CI = [1.6 – 7.4]
(univariate analysis)
Exposed-non exposed study in Mali

- **Initial study**
  - A cohort survey of patients with malaria (6 months to 14 years old) in Mali by Malaria Research and Training Center, since 1999

- **Our study: exposed-non exposed**

Exposed group [CM]
(criteria WHO)

Non exposed group [NCM]
(criteria WHO)

1999

Epilepsy?

2003
Results

Exposed-non exposed study in Mali

Bamako- Bandiagara cohort studies (n = 688)

Uneligible (n = 288)

Eligible (n = 400)

Lost to study (n = 41)
Deceased (n = 35)
Refusal to participate (n = 1)

Included in the study (n = 323)

Exposed group [CM] (n = 101)

Epilepsy suspected cases [CM]
 n = 34 (33.7 %)

Epilepsy confirmed cases [CM]
 n = 6 (5.0 %)

Epilepsy associated with CM
 n = 5 (4.9 %)

Epilepsy -bacterial meningitis
 (n = 1)

Nonexposed group [NCM] (n = 222)

Epilepsy suspected cases [NCM]
 n = 20 (9.0 %)

Epilepsy associated with NCM
 n = 1 (0.5 %)

Diagnosis and confirmation

Screening: identification of epilepsy suspected cases

Epilepsy suspected cases [CM]
 n = 34 (33.7 %)

Epilepsy confirmed cases [NCM]
 n = 1 (0.5 %)

Epilepsy associated with NCM
 n = 1 (0.5 %)
Results

- Incidence rate was:
  - 17.0 per 1000 person-year in the CM group
  - 1.8 per 1000 person-year in the NCM group

- Relative risk (RR) was 9.4 (95% CI: 1.3–80.3) p = 0.02

   After adjustment on age and duration of follow-up

   adjusted RR : 14.3 (95% CI: 1.6 – 132.0) p=0.01

Ngoungou et al., Epilepsia 2006; 47: 873-9
Physiopathological mechanisms

- Sequestration
- Metabolites modifications

→ Cerebral lesions

Could act as epileptogenic foci in survivors
Cerebral malaria is a cause of epilepsy in tropical regions (for a review see: Ngoungou et al., Epilepsia 2008;49:19–24)

Epidemiological evidence
- 3 recent studies have showed a link between cerebral malaria and epilepsy (reproducibility of results)
- Risk factors statistically significant
- Temporal sequence (exposed/non exposed study)
- Biological plausibility (sequestration...)

But the role of convulsions must be thoroughly studied
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