Management of Neurocysticercosis (NCC) in resource limited endemic areas

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Prevalence of NCC – setting the scene

- **Latin America:** Meta-analysis of epilepsy and NCC revealed a median NCC proportion among people with epilepsy of 32.3% (*Bruno et al. 2013*).

- **Asia:** Study from a south Indian community recruiting people with active epilepsy found 34% had NCC based on CT and serology (*Rajshekhar et al. 2006*).

- **Africa:** Study from northern Tanzania recruiting people with epilepsy from an epilepsy clinic found 18% had NCC based on CT and serology (*Winkler et al. 2009*).
- **Africa:** Study from an eastern Zambian community recruiting people with epilepsy found over 50% had NCC based on CT and serology (*Mwape et al. 2015*).
- **Africa:** Studies from Tanzania, Uganda and Malawi in over 1000 people with epilepsy receiving a CT scan indicate NCC prevalence estimates from 2-3% in urban areas and over 10% in rural areas (*Winkler et al. unpublished data*).

- **Worldwide:** 30% of people with epilepsy in endemic areas have got NCC (*Ndimubanzi et al. 2010*).
Distribution of *Taenia solium* infection worldwide, 2015

Part 1: Pathological aspects and classification of NCC as well as clinical characteristics
Pathology I

- Focal lesions (with and without inflammation)
- Encephalitis (rarely, Meningitis < 10% of all cases)
- Vasculitis
- Infarcts
- Hydrocephalus
- Myelopathy

Pathology II

- Focal lesions (with and without inflammation)
- Encephalitis (rarely; Meningitis < 10% of all cases)
- Vasculitis
- Infarcts
- Hydrocephalus
- Myelopathy

Classification

- Active (cysts)
- Transitional (granuloma and ring enhancing lesions)
- Inactive (calcifications)
- Parenchymal NCC
- Extraparenchymal NCC (ventricle, subarachnoid space)

Clinical characteristics

- Symptomatic seizures
- Epilepsy
- Headache
- Increased i.c. pressure
- Focal neurological signs
- Psychiatric problems
- Learning difficulties
- Very sick patient with encephalitis!

Part 2: Diagnosis of NCC with emphasis on epilepsy
Epileptic seizures/epilepsy most likely due to NCC

CT scan

CT suggestive of NCC

Antigen ELISA

Positive

Confirmed as NCC

Negative CT scan refer back to the system

Immunoblot

Positive

Negative

Negative
CT scan in sub-Saharan Africa - why so important?

- Within a few weeks or months the situation in the brain can change for better or for worse.
- If the number of cysts has increased, antihelminthic treatment may harm the patient seriously.
- If the number of cysts has decreased, antihelminthic treatment may be unnecessary altogether.
- Triaging of patients suitable for neurosurgery or those that would require special treatment regimes (subarachnoid/ventricular forms).
Locally adapted classification for epilepsy

- Causes are different (e.g. infection, perinatal brain damage)
- Limited diagnostic possibilities (no electroencephalogram (EEG), MRI)
- Few specialized clinics
- Few trained personnel
- Limited medication
Algorithm for epilepsy in resource limited settings

Neurological signs obvious?

Yes

Diffuse cerebral impairment (non-progressive)

Further clinical work-up only in selected cases

Close follow-up necessary

Drug of choice: 1.CBZ 2.PHT

No

Focal neurological signs (progressive)

Onset outside 6-25 years

Further clinical work-up EEG/CT necessary

Close follow-up necessary

Drug of choice: 1.CBZ 2.PHT or PB

Onset between 6-25 years

Further clinical work-up only in selected cases

Close follow-up NOT necessary

Drug of choice: children: PHT adults: PB

Explanations: CBZ=Carbamazepine; PHT=Phenytoin; PB=Phenobarbitone
Advantages of the adapted epilepsy classification

- Easy to use also for untrained personnel
- No need for EEG and imaging
- Transferrable to the ILAE classification
- Quick therapeutic triage
- Choice of right antiepileptic medication
- Approximate prognostic estimation
Part 3: Treatment of NCC in resource limited endemic countries
Factors that determine therapeutic approach in general:

- Localisation of cysts (intra- extraparenchymal)
- Stage of cysts (active, transitional, inactive)
- Number and size of cysts (single lesion – many lesions)
- Inflammatory response (contained – widespread)
- Severity of clinical symptoms
- Potential risk of future complications
Sentences to remember

- Do not treat asymptomatic cysts!
- Do not treat inactive lesions with antihelminthic drugs!
- Do not treat transitional lesion with antihelminthic drugs!
- Never use antihelminthic drugs in widespread inflammation!
- Never use antihelminthic drugs if cysts are scattered throughout the brain (encephalitis!)!
- Subarachnoid and ventricular forms need special treatment considerations!
Medication used for treatment of NCC

- Analgesics
- Steroids
- Antiepileptic drugs
- Antihelminthic medication
Steroids

- Prednisolone: 1mg/kg/day p.o. or Dexamethasone 10-20 mg/d
- Length of treatment variable, according to symptoms
- Without antihelminthics in cases with cerebral oedema, signs of increased intracranial pressure, vasculitis, compression of the brainstem, spine or optic nerve
- In most parenchymal NCC together with antihelminthics; in subarachnoid forms high doses of both drugs and long treatment
- Increased metabolism by antiepileptic medication
Antiepileptic medication

- Phenytoin, Phenobarbitone, Carbamazepine (usually well controlled with monotherapy on standard dosage)
- Therapy may be lifelong if calcifications are present.
- In active NCC after successful treatment for two years (no calcifications!) trial of tapering (Bustos et al. 2016)
- Additional antihelminthic medication reduces severity but not frequency of epileptic seizures (Garcia et al. 2004).
Antihelminthics (active NCC)

- Albendazole: 15 mg/kg per day x 8-15 days
- Praziquantel: 50 mg/kg per day x 8-15 days; short course: 100 mg/kg for one day!
- Albendazole and Praziquantel for 10 days in the above indicated dosage clears 95% of cysts as opposed to 30% when Albendazole is given alone (Garcia et al. 2016)
- Albendazole is more effective than Praziquantel (better penetration into CNS)
- Increased metabolism by steroids and antiepileptic drugs (Praziquantel > Albendazole)
- Only in active NCC; be aware of sudden increased intracranial pressure with „sudden death“; combination with steroids and control-CTs are essential!
- Contraindicated in encephalitis, increased intracranial pressure and ophthalmological cysticercosis
Surgery in resource limited areas

- Ventricular form (endoscopically)
- Hydrocephalus shunting (mainly ventricular and subarachnoid form – prognosis poor)
- Accessible cysts with mass effect (e.g. Sylvian fissure)
- Potential danger of hydrocephalus post-OP
- High perioperative risks
- Potential danger of dissemination of cyst material
Summary of NCC treatment

**Parenchymal neurocysticercosis**
- Active: Antihelminthics, Steroids, AED
- Transitional: Steroids, AED
- Inactive: (Steroids) AED

**Extraparenchymal neurocysticercosis**
- Subarachnoid: Antihelminthics, Steroids (AED)
- Ventricular: Neurosurgery

- Steroids
- AED

**Summary of NCC treatment**
- Active: Antihelminthics, Steroids, AED
- Transitional: Steroids, AED
- Inactive: (Steroids) AED
- Subarachnoid: Antihelminthics, Steroids (AED)
- Ventricular: Neurosurgery
- Steroids
- AED
Treatment algorithm according to availability of CT scans

1. Epileptic seizures/epilepsy most likely due to NCC
   - CT scan (not older than a couple of months)
     - CT scan possible – active NCC confirmed
       - Antihelminthics and steroids
         - Follow up with CT?
         - Follow up with serology?
           - Treatment for how long?
             - What to do with defaulters?
             - What to do with treatment failure?
     - CT scan not possible
       - Treatment with steroids (without antihelminthics) based on serology under very close observation by a specialist??
       - Symptomatic treatment, i.e. AED only, and follow wait and see policy

Part 4: Future aspects of management of NCC in resource limited endemic countries
«Ensure healthy lives and promote well-being for all at all ages»
Goal 3. Ensure healthy lives and promote well-being for all at all ages

3.3 By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases.

3.4 By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote Mental Health and well-being.
One Health

- Environmental health
- Veterinary medicine
- Public health
- Human medicine
- Molecular and microbiology
- Health economics

Comparative medicine / Translational medicine

- Metabolic disorders in humans and animals
- Joint and skeletal diseases in humans and animals
- Cancer and cardiovascular disease in humans and animals
- Human - animal bond
- Environmental hazards exposure to humans and animals

Zoonotic infections

- Bacterial infections
- Viral infections
- Vector-borne infections
- Parasite infections
- Antimicrobial resistance
- Global health
- Food safety

Intervention

- Vaccines and therapeutics
- Vector control
- Sanitation
- Surveillance
