



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a CT scan indicate NCC prevalence estimates from 2-3% in urban areas and over 10% in rural areas (*Winkler et al.* unpublished data).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



Source: WHO (2016) *Taenia solium* taeniasis/cysticercosis diagnostic tools, report of stakeholder meeting, December 2015 http://www.finddx.org/wp-content/uploads/2016/06/Taenia-solium-Taeniasis-cysticercosis-diagnostic-tools.pdf





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



Source pictures: Top left and right: Hughes and Biggs. *Internal Medicine Journal* 2002; 32: 541-553. Bottom left: Takayanagui and Odashima. *Parasitology International* 2006; 55: S111-S115. Bottom right: Chang and Han. *Journal of Magnetic Resonance Imaging* 1998; 8: 297-307.





Pathology II

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



Source pictures: Top and bottom left: Kimura-Hayama et al. *RadioGraphics* 2010; 30: 1705-1719. Top right: picture Winkler, unpublished. Bottom right: Takayanagui and Odashima. *Parasitology International* 2006; 55: S111-S115.





Classification

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









Source pictures: Top left: Nash and Garcia. *Nature Reviews Neurology* 2012; 7(10): 584-59. Top right and bottom left: picture Winkler unpublished. Bottom right: Kimura-Hayama et al. *RadioGraphics* 2010; 30: 1705-1719.





Clinical characteristics

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







Source pictures: Top left and right: Hughes and Biggs. *Internal Medicine Journal* 2002; 32: 541-553. Bottom left: Takayanagui and Odashima. *Parasitology International* 2006; 55: S111-S115. Bottom right: Chang and Han. *Journal of Magnetic Resonance Imaging* 1998; 8: 297-307.





Part 2: Diagnosis of NCC with emphasis on epilepsy











Diagnostic algorithm for NCC







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



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











Therapy when?

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



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





DESCRIPTION: Each tablet contain 600 mg of praziquantel, 2-(cyclohexylcarbonyl)-1,2,3,6,7, 11b-hexahvdro-4H-ovrazino

tore Below 86°F (30°C)

Expires:





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







Treatment algorithm according to availability of CT scans







Part 4: Future aspects of management of NCC in resource limited endemic countries











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New Development Agenda



«Ensure healthy lives and promote well-being for all at all ages»





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3 GOOD HEALTH AND WELL-BEING Ensure healthy lives and promote well-being for all at all ages

Goal 3. Ensure healthy lives and promote wellbeing for all at all ages

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

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





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Winkler AS, Richter R. Landscape analysis: management of neurocysticercosis with emphasis on low- and middle-income countries. *World Health Organization* 2015.

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