Article

A SURVEY STUDY ON NEUROCYSTICERCOSIS EPIDEMIOLOGY IN A RWANDAN HOSPITAL

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ABSTRACT

Background: Cysticercosis is a parasitic infection that results from ingestion of eggs from the adult tapeworm, Taenia solium (T.solium).When Cysticercosis involves the central nervous system, it is called neurocysticercosis; it is the most prevalent infection of the brain and one of the leading causes of adult-onset seizures woldwide. The disease has a world-wide distribution and is endemic in Mexico, Central and South America, and parts of Africa, Asia, and India with an estimated 20 million persons infected with cysticerci yearly worldwide. The study aimed at determining the epidemiological and clinical profile of neurocysticercosis at BUTH.
Methods: It is a retrospective descriptive study carried out on patients admitted/treated for neurocysticercosis in Internal Medicine/Neurology Department of BUTH for a period of eighteen months, from February 01, 2008 to July 31, 2009. Registers and files for patients were consulted to collect data and MS Word 2007, Epi data 3.1, SPSS 14.0 are the software used.
Results: Out of 2387 patients admitted in Internal Medicine during our study period 34 were diagnosed and treated for neurocysticercosis i.e. a hospital prevalence rate estimated at 1.4% in the department of Internal Medicine/Neurology, and our study noted an increase in number of cases diagnosed since 2008; patients from Huye and Nyaruguru districts are the most affected. Epilepsy was present in 24 patients (70.5%), headache in 18 patients (52.9%). CT-scan was an important tool to confirm the diagnosis. Albendazole plus corticosteroids (dexamethasone or prednisolone) and antiepileptics if seizures are the common means used to treat neurocysticercosis at BUTH; neurosurgery was required in three patients.
Conclusion: Neurocysticercosis is a common diagnosis in the department of Internal Medicine/Neurology at BUTH. Epilepsy and headache are the commonest presenting complaints and the diagnosis is made by the means of brain CT-scan; the treatment is based on albendazole and corticosteroids. It is a potentially preventable disease and preventive strategies such as more intense meat inspection and preparation, improvement of hygiene standards and vaccination against T.solium should be undertaken. A study on the community prevalence is necessary

Key words: Neurocysticercosis - Fecal-oral contamination - Epilepsy - Headache

RESUME

Introduction: La cysticercose est une infection parasitaire résultant d'une ingestion des oeufs d'un ver de porc adulte, Taenia solium. On appelle neurocysticercose la localisation de cette infection au niveau du système nerveux centrale; c'est l'infection la plus fréquente du cerveau et l'une des premières causes de l'épilepsie à l'âge adulte dans le monde entier. La maladie est répartie dans le monde entier et est endémique au Mexique, en Amérique latine, en Afirique , en Asie et sur le sous-continent indien avec environ 20 millions de personnes atteintes de cysticercose chaque année dans le monde. Notre étude avait comme objectif, déterminer le profil épidémiologique et clinique de la neurocysticercose au CHUB.
Méthodologie: C'est une étude descriptive retrospective menée sur les patients admis ou traités pour la neurocysticercose au département de Médecine Interne/Neurologie du CHUB pour une période de 18 mois, depuis le 01/02/2008 au 31/07/2009. Les registres et dossiers des patients ont été consultés pour la collecte des données et les logiciels MS Word 2007, Epi data 3.1, SPSS 14.0 pour le traitement des textes et analyse des données.
Résultats: Sur un total de 2387 patients admis en Médicine Interne au cours de la période d'étude, 34 ont été diagnostiqués et traités pour la neurocysticercose soit un taux de prévalence de l'hopital estimé à 1.4% dans le département de Médecine Interne/Neurologie et nous avons remarqué une augmentation du nombre de cas diagnostiqués depuis l'année 2008; les patients originaires des districts Huye et Nyaruguru sont les plus touchés. L'épilepsie était présente chez les 24 patients (70.5%), céphalées chez 18 patients (52.9%). Le scanner a été l'outil important pour le diagnostic positif. L'albendazole plus les corticoïdes (dexamethasone ou prednisolone) et les antiepileptiques en cas de crises convulsives sont la base de traitement de la neurocysticercose au CHUB; la neurochirurgie était indiquée chez trois patients.
Conclusion: La neurocysticercose est un diagnostic commun dans le département de Neurologie au CHUB. Epilepsie et céphalées sont les motifs de consultation les plus fréquents et le diagnostic est fait à l'aide du scanner cérébral.La base du traitement est fait par l'albendazole et les corticoïdes . C'est une maladie potentiellement évitable et les mésures préventives telles que l'inspection et la préparation plus rigoureuses de viande, l'amélioration des conditions d'hygiène et la vaccination contre le T.solium devraient être entreprises. Une étude de prévalence sur toute la population du pays est nécessaire.

Mots clés: Neurocysticercose - contamination oro-fécale - Epilepsie - Céphalées

INTRODUCTION

Cysticercosis is a parasitic infection that results from ingestion of eggs from the adult tapeworm, Taenia solium (T.solium). When cysticercosis involves the central nervous system it is called neurocysticercosis (Figure 1). The pork tapeworm T.solium can cause two distinct forms of infection in humans: adult tapeworms in the intestine or larval forms in the tissues (cysticercosis). Humans are the only definitive hosts for T.solium; pigs are the usual intermediate hosts, although other animals may harbor the larval forms [1]. The clinical features of cysticercosis depend on the location of the cysts and overall cyst burden. Cysts can lodge in the brain and spinal column, eyes, skeletal muscle, and subcutaneous tissues. Brain and eye cysts cause most of the morbidity, with the brain being the most common location for cysts (60 to 90 percent of all cases) and the eye being the least common (1 to 3 percent) [12]. The initial host reaction is often avoided through the encystment of the larvae, a process that includes enlisting defense mechanisms against destruction by the host. This phase may last for years

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and is often clinically silent except when the location or size of cyst causes signs or symptoms. Most cysts are unable to maintain these protective barriers indefinitely, and degenerating cysts release larval antigens that produce a vigorous host response and cause the clinically apparent syndrome through inflammatory mediators and surrounding edema. Infection with T. solium adult worms is generally asymptomatic, but gastrointestinal symptoms may occur. Infection is generally recognized after fecal passage of proglottids [1,12].

Neurocysticercosis (NCC) is the most prevalent parasitic infection of the brain and one of the leading causes of adult-onset seizures . The disease has a world-wide distribution and is endemic in Mexico, Central and South America, and parts of Africa, Asia, and India. It also occurs in industrialised nations, largely as a result of the immigration of infected persons from the endemic areas [4,10,11]. An estimated 20 million persons are infected with cysticerci yearly, leading to about 400,000 persons with neurologic symptoms and 50,000 deaths (WHO). Antibody prevalence rates up to 10% are recognized in some endemic areas, and the infection is one of the most important causes of seizures in the developing world and in immigrants to the United States from endemic countries [13]. Epilepsy and headache are the commonest reasons for consulting the neurological out patient department. One very important differential diagnosis in these patients is neurocysticercosis; other manifestations of NCC are focal neurologic deficits, nausea, vomiting, changes in vision, dizziness, ataxia or confusion. Specific and objective criteria have been proposed, based on histopathological, neuroimaging (CT-scan, MRI) serologic, clinical and epidemiological aspects for the diagnosis [3]. Treatment of NCC is controversial on whether there are clinical benefits associated with the use of anti-parasitic drugs. The current recommended regimen is albendazole 15 mg/kg/day orally for 7-28 days; an alternative anti-parasitic drug, praziquantel, can be used orally with the standard 15 to 30-day regimen of 50–100 mg/kg/day or a single-day regimen [1, 5, 12]. Steroids(dexamethasone 0.1 mg/kg/day or prednisolone) to treat cerebral oedema are administered before or on initiation of antihelminthic medications to blunt the inflammatory reaction that may result in increased seizures. Mannitol also is an option to reduce cerebral edema as an adjunct to steroids. Surgical procedures, e.g. placement of a ventriculoperitoneal shunt or endoscopic third ventriculostomy (ETV) for obstructive hydrocephalus, are sometimes required. Antiepileptic medications in standard dosages, most commonly phenytoin and carbamazepine, are key for symptom control.

Adequate treatment of tapeworm carriers is crucial to interrupt the transmission of cysticercosis. Intestinal Taenia solium can be cured with a single dose of niclosamide (2 grams) or praziquantel (5 mg/kg). Niclosamide is the drug of choice because it is not absorbed in the intestine, thus avoiding the risk of developing neurologic symptoms if the patient also has NCC [5].

METHODOLOGY

1. Type and period of the Study

It is a retrospective descriptive study carried out on a period of eighteen months, from February 01, 2008 to July 31, 2009.

2 .Study population and area

All the patients admitted/treated for neurocysticercosis in internal Medicine/Neurology Department of Butare University Teaching Hospital (BUTH/CHUB) from February 01, 2008 to July 31, 2009. Also were included in the study, some patients in other departments followed by the Neurologist for neurocysticercosis. A total number of 34 patients were found to have the diagnosis during our study period. BUTH is a referral hospital located in Butare town, Huye district of Southern province, at~ 130 km from the capital city-Kigali.

3 .Data collection and analysis

Data from files and registers of patients were collected on a printed pre-established form; from collected data a new form for data entry was elaborated using Epi Data 3.1 and SPSS 14.0 was used for data analysis. The text is written using MS Word 2007.

4. Inclusion and exclusion criteria

Only patients with confirmed Neurocysticercosis (by at least one major criterion) were selected; suspicion of the diagnosis was not a criterion for selection

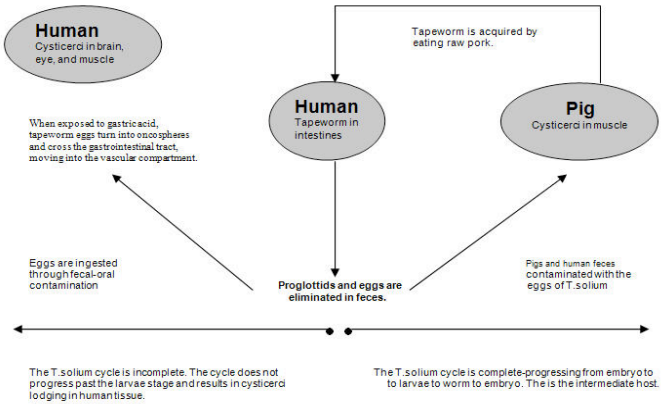

Figure 1 : Life cycle of Taenia solium [2]

RESULTS

1. SOCIO-DEMOGRAPHIC ASPECTS OF THE STUDY POPULATION

Our study population consists of 34 patients (67.6% or 23 are male); of 32 with known age (from 7 to 67 years old) 50% are between 21 and 40 years old 0f 27 patients with identified origin 22 or 81.5% are from the Southern province, Huye and Nyaruguru districts representing 33.3% and 25.9% respectively (Figure 2). Also 4 out of the remaining 5 patients from other provinces lived or have antecedents of living in Huye at the time of diagnosis. 22 patients or 64.7% were diagnosed from January 01 to July 31, 2009. And out of 2381 patients admitted in Internal

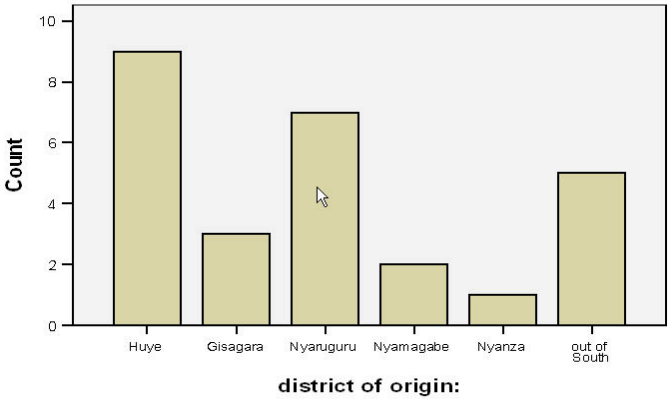

Figure 2 : Distribution according to district of origin

Medicine from February 01, 2008 to July 31, 2009 (plus 3 followed as outpatients, 1 admitted in Pediatrics, 1 in ICU and 1 in Surgery), the hospital prevalence of NCC is estimated at 1.4% in Internal Medicine/Neurology department.

2. CLINICAL MANIFESTATIONS AND DIAGNOSIS

Seizures or epilepsy were present in a total of 24 patients or 70.5%, headache in 18 patients or 52.9%. Other signs and symptoms of raised ICP and focal neurological deficits were found in 10 and 9 patients (or 29.4% and 26.4%) respectively. 11 patients (37.9%) had their symptoms for more than five years and 2 of them reported to having seen the first manifestations for more than 15 years.

In 28 out of 31 patients a brain CT-scan was done to confirm the diagnosis and all stages were found, living cysts being the most common findings. Hydrocephalus was seen in 3 patients or 9.7% EEG was done for 14 patients and ten of them had a pathological setting out /outline; no epileptic focus found. In about 50% of our patients, no lab results (stool,FBC,CSF,HIV) were found or tests were not done: all stool analyses were negative for T.solium. One patient presented eosinophilia and elevated CSF proteins were found in 3 patients.

Muscles/subcutaneous tissue were the only location of cysticercosis found outside the CNS (23.5 %)

3. TREATMENT, EVOLUTION, AND FOLLOW-UP

Table 1: Brain CT-scan Diagnosis

		Frequency	Percent	Valid Percent	Cumulative Percent
CT-scan findings	Not done	3	8.8	9.7	9.7
	Living cyst	4	11.8	12.9	22.6
	Multiple living cysts	15	44.1	48.4	71.0
	Calcifications	3	8.8	9.7	80.6
	Giant cysts	1	2.9	3.2	83.9
	living cyst(s) and calcifications	2	5.9	6.5	90.3
	Hydrocephalus with living cyst(s) or calcifications	3	8.8	9.7	100.0
	Total	31	91.2	100.0	
Missing	System	3	8.8		
Total		**34**	**100.0**		

Table 2: Revised diagnostic criteria for neurocysticercosis [3]

Categories of criteria	Criteria
Absolute	1. Histologic demonstration of the parasite from biopsy of a brain or spinal cord lesion 2. Cystic lesions showing the scolex on CT or MRI 3. Direct visualization of subretinal parasites by funduscopic examination
Major	1. Lesions highly suggestive of neurocysticercosis on neuroimaging studies 2. Positive serum EITB for the detection of anticysticercal antibodies 3. Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel 4. Spontaneous resolution of small single enhancing lesions
Minor	1. Lesions compatible with neurocysticercosis on neuroimaging studies 2. Clinical manifestations suggestive of neurocysticercosis 3. Positive CSF ELISA for detection of anticysticercal antibodies or cysticercal antigens 4. Cysticercosis outside the CNS
Epidemiologic	1. Evidence of a household contact with *Taenia solium* infection 2. Individuals coming from or living in an area where cysticercosis is endemic 3. History of frequent travel to disease endemic areas

31 out of 32 patients have been treated with albendazole and dexamethasone or albendazole and prednisolone(not dexamethasone and prednisolone at the same time); one remaining patient was followed in another hospital. 23 patients with seizures have received antiepileptics, phenobarbital being the most common used (in 21 patients), others are phenytoin and carbamazepine; diazepam has been used to stop seizures(10 patients) and paracetamol used in patients with headache(16 cases). In addition to corticosteroids patients with very high ICP have been treated with mannitol (3 cases). A surgical operation (ventriculo-peritonial shunting) was performed for one patient with hydrocephalus and it was planned for 2 others who died shortly before operation. 20 patients (58.8%) had improved at their disharged from hospital, 5 (i.e.14.7%) died and 4 have been treated as outpatients; one patient who has still presented with the same clinical manifestations was thought not to adhere correctly to treatment. 3 patients were followed-up in OPD till six months after discharge : headache was better for 2 and disappeared for 1 while epilepsy was disappeared for 2 and better for 1 of them. There are data of follow-up after 1 month for 10 patients and headache and epilepsy had disappeared for 5 out of 7 and 7 out of 8 respectively

DISCUSSION

In our research period, 34 cases of neurocysticercosis were diagnosed out of a total number of 2381 patients admitted in the department of Internal Medicine/Neurology and 6 others not admitted with a hospital prevalence estimated

at 1.4% in the department. 22 patients(64.7%) were diagnosed from January to July 2009 ie the mean of 3 patients per month or prevalence rate of 1.9% in a total number of 1113 patients; this indicates the increase in number of cases of neurocysticercosis diagnosed in 2009

Table 3: Revised degrees of certainty for the diagnosis of neurocysticercosis

Diagnostic certainty	Criteria
Definitive	1. Presence of one absolute criterion 2. Presence of two major plus one minor and one epidemiologic criterion
Probable	1. Presence of one major plus two criteria 2. Presence of one major plus one minor and one epidemiologic criterion 3. Presence of three minor plus one epidemiogic criterion

compared to 12 cases in 2008 ie the average of 1 patient per month while there was not any case in 2007(our study first included the year 2007 but we did not find any case and decided to drop the period that has no patient).

In a preliminary study of UWIZEYEMARIYA C.(2008) for a period of 1 year (from July 01,2007 to June 30, 2008) in the same department on clinical and therapeutic aspects of neurocysticercosis, 7 cases of the disease were found. This increasing number of cases diagnosed may be explained in part as a positive result of community based health insurance systems that have increased the rate of health facilities utilization but it is especially by far the result of the permanent Neurologist in BUTH since late 2007 and the establishment of the department of Neurology; increasing awareness of all the doctors in the department of Internal Medicine/Neurology plays also an important role. This is supported by the fact that 11 patients (37.9%) had had symptoms for more than 5 years and 15 (44.1%) for more than 2 years at the time of diagnosis and that was not the first time of consultation for number of them.

In their antecedents the majority our patients were not asked in a routine way about a close contact with pigs or with possible potential T.solium carriers; pork meat consumption was the most frequenly asked question (up to 39.3%). This is probably because most of medical staff believe that pork meat consumption directly results in cysticercosis. Neurocysticercosis is associated with living conditions where hygiene standards are low; the mode of transmission is a fecal-oral contamination and the disease is acquired after consuming food (eg. raw vegetables) or water contaminated with T.solium eggs from stool of infected pigs or humans[see T.solium life cycle above]. Thus risk factors include close contact with pigs and/or carriers, poor hygiene, living in endemic areas or living together with immigrants from endemic zones or in community where pork meat is frequently consumed. The disease is equally likely for both vegetarians and non-vegetarians.

Since the normal life cycle of T.solium is known , strategies to eradicate the disease may include decreasing pork tapeworm carriers (e.g. eradication programs in schools and more intense meat inspection and preparation), eliminating exposure of pigs to human feces, improving hygiene standards (sanitation, proper water supply and sewage system,personal hygiene) and developing a vaccine against T. solium

Diagnosis challenge

Epilepsy and headache are the most common clinical manifestations found (70.5% and 52.9% repectively); other manifestations include focal neurologic deficts (26.4%) such as hemiparesis or hemiplegia, signs of raised ICP like visual disturbances , dizziness, vomiting, deterioration of mental state,etc. Skin nodules may be the first sign to reveal cysticercosis and ultrasound is helpful for the diagnosis. The diagnosis was confirmed for 28 patients(82.3%) by a brain CT-scan accessed especially thanks to the community based health insurance (table 1). Laboratory investigations like stool, CSF or blood analyses are less helpful in the diagnosis of neurocysticercosis and findings don't differ from the literature where epilepsy is reported in 50-90% of all cases, intracranial hypertension in 20-30% [2,4]. An electroencephalogram (EEG) was also performed and in some cases an epileptic focus can be found which can contribute to the diagnosis. As mentioned earlier there have been specific diagnostic criteria proposed and revised to facilitate objective diagnosis of NCC (tables 2, 3).

Treatment and evolution

Two courses (or more if necessary) of Albendazole plus dexamethasone or prednisolone for 21 days each and 4 weeks break in between are prescribed to treat neurocysticercosis. Antiepileptics (phenobarbital in most cases) are given in patients with seizures. This regimen seems to be efficient as data show improvement at hospital discharge but a long-term follow-up, ideally with a CT-scan control, is needed to evaluate the efficacy of anticysticercal as literatue is controversial on this issue.This CT-scan control has to be carefully indicated as it could easily overburden the existing insurance in the context of a low income country. Five patients died and in 3 cases the death is associated with intracranial hypertension and hydocephalus (sugery was planned), one died of status epilepticus while the death of the last patient was not associated with neurocysticercosis.The literature also says that morbidy and mortality are much higher when the parasites locate in the subarachoid space and ventricles causing CSF pathways blockage [4]. Early diagnosis and immediate neurosurgical treatment could improve the prognosis.

The findings in BUTH raised our curiosity to know more about the scale of the problem in the county and we consulted the department of satatistics of Kigali University Teaching Hospital (KUTH/CHUK) about the diagnoses made in the hospital for the years 2006, 2007 and 2008. In their records, no single case of neurocysticercosis reported for these 3 years. There were 20 cases of epilepsy reported in 2008 and 19 in 2007. Does this mean that neurocysticercosis is only confined to the areas covered by BUTH? This might not be true. KUTH is referral hospital that covers about 2 thirds of the country, and being in the capital city we expect patients from all over the country to consult there. It is most probably because the hospital does not have a department for Neurology as it was the case for BUTH almost 4 years ago on one hand, or this may be related to a defective data record system in the unit of Satatistics of

CHUK on the other hand. A thorough study shall put light on that.

CONCLUSION

Neurocysticercosi exists in Rwanda especially in the southern province where it is a common diagnosis in the department of Neurology at BUTH. 34 cases were diagnosed in a period of 18 months of our study and its prevalence is estimated at 1.4 % of all patients in Internal Medicine department of this referral hospital. Our study shows increasing numbers in cases diagnosed every year for the last three years with the establishment of a department of Neurology.The onset of symptoms varied from hours to many years; for 11 patients or 37.9% symptoms had started more than 5 years before and 2 of them more than 15 years before. Epilepsy and/or headache are the commonest clinical manifestations found; others include signs of intracranial hypertension and focal neurological deficits. Brain CT-scan was required to confirm the diagnosis in about all cases. Muscle/ cutaneous cysticercosis is sometimes associated with or preceeds the CNS location in a third of the patients.
Albendazole associated with dexamethasone or prednisolone are used to treat neurocysticercosis and phenobarbital is the antiepileptic frequently precribed; sugery is often required in case of hydrocephalus (shunt placement). Most of the patients improved after treatment. Deaths occured in patients in whom neurosurgery was indicated. Adopting a more active approach towards prevention and control of the disease through more intense meat inspection and preparation, eliminating exposure of pigs to human feces, personal and community hygiene, together with campaigns aiming at educating the population about neurocysticercosis and eventually eradication programs may be effective measures to reduce or eradicate the disease. A countrywide study on prevalence of neurocysticercosis, its place among other causes of epilepsy and and a long term follow-up is needed.

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