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Neurocysticercosis in the United States

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Neurocysticercosis (NCC) is typically considered a disease of the developing world. Nonetheless, NCC is also diagnosed in the developed world. The rise in the number of cases of NCC in developed countries, especially in the United States of America, has largely been driven by the influx of immigrants from endemic to non-endemic regions and the widespread access to neuroimaging. Cases of local transmission have also been documented particularly in the setting of a tapeworm carrier present in the household, which highlights the relevance of NCC as a public health problem in the USA. Although accurate incidence data in the USA are not available, estimates range from 0.2 to 0.6 cases per 100 000 general population and 1.5–5.8 cases per 100 000 Hispanics. We estimate that between 1320 and 5050 new cases of NCC occur every year in the USA. The number of NCC cases reported in the literature in the USA increased from 1494 prior to 2004 to 4632 after that date. Parenchymal cases remain the most commonly reported form of the disease; however, a slight increase in the percentage of extraparenchymal cases has been described in the most recent series. NCC is associated with significant morbidity resulting from hydrocephalus, cerebral edema, and seizures. Although uncommon, NCC is also a cause of premature death in the USA with a calculated annual age-adjusted mortality rate of at least 0.06 per million population.

Keywords: Cysticercosis, Neurocysticercosis, Non-endemic, Hispanics

Introduction

Neurocysticercosis (NCC) refers to a parasitic infection caused by the larvae of the pork tapeworm *Taenia solium*, a common helminth infection of the human central nervous system and major cause of acquired epilepsy worldwide.[1,2] NCC is acquired by the accidental ingestion of *T. solium* eggs, which have been shed in the stools of a person carrying the tapeworm in her gut (tapeworm carrier).

NCC is typically considered a disease of the developing world. Nonetheless, NCC is also diagnosed in the developed world. There are more cases of imported NCC diagnosed in the USA every year than in all other developed countries combined.[3]

The rise in the number of cases of NCC in developed countries, especially in the USA, has largely been driven by the influx of immigrants from endemic to non-endemic regions and the widespread access to neuroimaging. Confirmed cases of local transmission have also been documented[4] particularly among US born patients. There are several possible explanations for this. Cases in immigrants are usually acquired prior to immigration and, with the short lifespan of the tapeworm, it may no longer be present. US-born cases may also enter medical care earlier in the course of disease. Persons infected with the adult *T. solium* tapeworm are typically asymptomatic and may not be aware of the potential risk to themselves and others. This makes cysticercosis particularly amenable to public health measures and directed control efforts.[4]

In recent years, cysticercosis has been considered a neglected infection of poverty in the USA because it disproportionately affects impoverished and underrepresented minority populations.[5] In this article, we provide an update of clinical studies on NCC occurring in non-endemic areas by focusing on the USA.

Material and Methods

We searched the English literature in January 2012 with PubMed using the search terms [epidemiology AND neurocysticercosis] and [non-endemic AND neurocysticercosis]. We also searched references from previous literature. Abstracts were reviewed, and papers that presented original information were reviewed in detail.

History of Reporting on NCC in the USA

Before 1970s, the number of cases of NCC was limited, perhaps due to limitations of diagnostic tests. In 1954, Campagna and Swartzwelder[6] found a total of 42 cases reported since 1857. Three years later, White and colleagues[7] described three additional cases.[7] The spectrum of disease described in these articles was skewed towards cases that were obvious

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(ocular cysticercosis) or more severe (intraventricular disease).

In the late 1970s, computed tomography scanning became widely available in the USA. The result was that parasites in the central nervous system could be identified without invasive testing. At about the same time the number of immigrants from endemic areas began to increase. Widespread availability of non-invasive neuroimaging tests along with increased immigration resulted in a dramatic increase in recognition of NCC.[3] This was clearly illustrated by Richards and collaborators[8] in their review of 497 patients treated for cysticercosis at four hospitals in Los Angeles County during 1973–1983. They observed a dramatic rise in the number of cases after 1977, which coincided with the introduction of the computed tomographic scan.

In 2004, Wallin and Kurtzke[9] reviewed all large case-series ($n>20$) of patients with NCC in the USA between 1980 and early 2004 and found a total of 1494 cases.[9] They included 13 large case-series in the study period. The number of NCC cases reported in each series ranged between 23 and 497 patients. Diagnostic criteria for NCC were not uniform across studies, and most were published prior to the release of formal diagnostic criteria.[10] A combination of compatible neuroimaging and epidemiologic history; compatible neuroimaging with positive CSF or serum *T. solium* antibody titers; or surgical pathologic specimen confirming the infection was utilized for NCC diagnosis. Serological tests may miss cases of single parenchymal or calcified lesions, which are the most common presentations of NCC.

NCC cases included in this review were largely concentrated in the southwest United States. Indeed, more than 75% of NCC cases presented in this review came from series from California. Cases from other regions of the country namely Texas, Oregon, Colorado and Illinois were also identified, which underscores the widespread presence of the infection throughout the country.

Since 2004, there have been, to our knowledge, a total of seven large case series of NCC totaling 4632 additional cases (Table 1).

Calculating the Real Burden of NCC in the USA

Few states require reporting of cysticercosis: Arizona, California, New Jersey, New Mexico, Oregon and Texas. Thus, population-based epidemiologic data in the USA are limited. In 1989, California became the first state to require reporting; 112 cysticercosis cases were reported during the first year, for a crude annual incidence of 0.02 cases per 100 000 non-Hispanic Whites and 1.5 cases per 100 000 Hispanics.[11] Sorvillo and collaborators reported a total of 138 cases in Los Angeles County between 1988 and 1990 for an average crude annual incidence rate of 0.6 per 100 000 general population and 1.6 per 100 000 Hispanics.[12] In a seroprevalence study of rural Ventura County, California, which is a Hispanic predominant community, it was found that 1.8% of that population had antibodies against cysticercosis antigens.[13] A retrospective case-series from Oregon based on hospital discharge diagnoses during 1995–2000 estimated an annual incidence of 0.2 cases per 100 000 general population and 3.1 cases per 100 000 Hispanics.[14] In 2002, Oregon adopted administrative rules for *T. solium* reporting. Between 2006 and 2009, O'Neal conducted a population-based active surveillance in Oregon and found an annual incidence of 0.5 cases per 100 000 general population and 5.8 cases per 100 000 Hispanics.[15] Shandera and collaborators,[16] extrapolating from their data in Houston, estimated that the incidence of NCC in the USA among Hispanics was at least 8 to 10 per 100 000 per year with 1000 new cases of NCC diagnosed each year.[16]

Table 1 Overview of large neurocysticercosis case series within the United States published after 2004

Author	Location (collection period)	No. of cases/ M : F ratio/age (years)	Hispanic ethnicity	Type of disease
Del La Garza *et al.*[31]	Houston, Texas* (1994–1997)	114 patients/NA/NA	95%	NA
Daniels and Moore[28]	Wichita, Kansas*(1986–2001)	42 patients/NA/NA	95%	NA
Figueroa *et al.*[27]	New Mexico* (1998–2004)	37 patients/NA/36	100%	30% EP
Croker *et al.*[20]	Los Angeles, California† (1991–2008)	3937 patients/1.1/38	92%	NA
Serpa *et al.*[21]	Houston, Texas* (1997–2005)	111 patients/2/29	93%	32% EP 54% P‡
O'Neal *et al.*[15]	Oregon† (2006–2009)	87 patients/1.4/NA	96%	4% EP 85% P 11% M
Croker *et al.*[36]	California† (2009)	304 patients/1.4/44	85%	NA

Note: NA: information not available, P: Parenchymal neurocysticercosis; EP: Extraparenchymal neurocysticercosis; M: mixed, parenchymal and extraparenchymal.
*Case-series.
†Population-based study.
‡Some patients had both parenchymal and extraparenchymal neurocysticercosis.

According to the 2010 Census, 308.7 million people resided in the USA on April 1, 2010, of which 50.5 million (16%) were of Hispanic origin. The Hispanic population increased from 35.3 million in 2000 when this group made up 13% of the total population. This 15.2 million increase between 2000 and 2010 accounts for over half of the 27.3 million increase in the total population of the USA. In other words, between 2000 and 2010, the Hispanic population grew by 43%, which was four times the growth in the total population at 10%.[17] The poverty rate also increased for Hispanics to 26.6% in 2010 from 25.3 in 2009, and the number of Hispanics in poverty increased to 13.2 million from 12.4 million.[18] If we assume annual incidence rates of cysticercosis of up to 10 cases per 100 000 Hispanics, and a population at risk of 50.5 million, then there may be as many as 5050 new cases of NCC every year in the USA. A more conservative approach assuming 13.2 million of Hispanics living in poverty as the population at risk would estimate 1320 new cases per year. Active surveillance of cases and contacts will be needed in order to obtain accurate incidence and prevalence rates of NCC in the USA. As it has been previously shown in developing countries, we suggest active surveillance of NCC cases in the USA by using a combination of neuroimaging, positive serology and history of seizures.[19]

Epidemiology of NCC in the USA

Wallin and colleagues[9] noted a male predominance among large case-series reported in the USA until 2004. The average age ranged between 24 and 35 years and the vast majority of cases occurred in foreign-born Hispanics. Mexicans represent more than 70% of cases. Similarly, Croker *et al.*[20] in his large series of over 3900 NCC cases hospitalized in Los Angeles County between 1991 and 2008 found that most cases occurred primarily among Latinos (92%) aged between 20 and 39 years (48%) with little difference by gender (male 53.0%, female 47.0%). Demographic findings of NCC do not seem to have changed much between those observed in studies published in the literature prior and after 2004 (Table 1). Therefore NCC in the USA continues to affect mainly young Hispanic adult immigrants and this has remained unchanged for over two decades.[21]

The relevance of NCC as a public health problem in the USA has been highlighted by well-documented cases of domestic transmission of NCC. For instance, in a cysticercosis surveillance system conducted in Los Angeles County from 1988 through 1990, 10 (7%) of 138 incident cases were locally acquired.[12] At least one tapeworm carrier was found among contacts of 7% of NCC patients. Carriers were more likely to be found among contacts of patients born in the USA (22.2%) than among those of foreign-born (4.8%) patients. One of the most striking reports on local transmission of NCC was described by Schantz and collaborators[22] in their report of an outbreak of the infection in four unrelated families of an Orthodox Jewish community in New York City in 1990–1991. In all the exposed households, there was a history of employment of live-in housekeepers who had recently emigrated from Latin American countries. Examination of six housekeepers currently or previously employed in the four case households revealed an active taeniasis in one and a positive serological test result in another. O'Neal studied the seroprevalence of cysticercosis in four refugee populations from Asia and Africa resettling to the United States and found rates ranging between 18.3 and 25.8%.[23] Sorvillo and collaborators[4] reviewed all documented cases of cysticercosis acquired in the USA between 1954 and 2005. They found a total of 78 cases reported in 12 states. A confirmed or presumptive source of infection was identified among household members or close personal contacts of 16 (21%) case-patients. The authors argued for implementation of public health control efforts of NCC due to several reasons including fecal–oral transmission, availability of a sensitive and specific serologic diagnostic test for infection by adult *T. solium* tapeworms,[24] the demonstrated ability to find a probable source of infection (tapeworm carrier) among close contacts,[25] and the protracted and potentially fatal clinic course of the infection.

In a study using a statewide hospital discharge data in Los Angeles County, Crocker reported 3937 hospitalizations from 1991 through 2008. The total of all NCC hospitalizations charges was $136.2 million, averaging $7.9 million per year.[26] This clearly illustrates the significant economic burden of NCC in Los Angeles County.

Clinical Presentation and Forms of NCC

In large case-series of NCC published prior to 2004, the most common onset symptoms included seizures (66%), hydrocephalus (16%) and headaches (15%). The majority of cases presented with parenchymal NCC (91%), with the remainder having ventricular cysts (6%), subarachnoid cysts, and spinal cysts (0.2%).[9] Among those with parenchymal disease, most had a single enhancing lesion. More recently, in the series from New Mexico, 30% of cases were extraparenchymal.[27] In our series from Houston, Texas (1997–2005),[21] 54% of patients had parenchymal disease, 20% intraventricular, 12% subarachnoid, and 12% calcifications only. This observed increase in the proportion of extraparenchymal cases might represent a reporting bias. The most common onset symptoms of parenchymal, intraventricular and

subarachnoid NCC included seizures (82%), hydrocephalus (86%) and headaches (85%), respectively. Most common presenting symptoms among patients with calcifications were seizures and headaches in 77 and 38%, respectively. In the case-series from Kansas, 71% of NCC cases presented with seizures.[28] In Oregon, 87% of cases had parenchymal lesions. The most common symptoms included seizures (38%) and headaches (34%).[15] More recently, a longitudinal study done in a low-income country found an association between NCC and mild cognitive deficits.[29] The frequency of this finding in high-income countries remains to be determined.

Data collected at 11 university-affiliated, geographically diverse, urban emergency departments of patients presenting with a seizure who underwent neuroimaging showed that 2.1% of cases had seizures attributable to NCC. Among Hispanics presenting with seizure, the prevalence of the infection ranged from 9 to 13.5%.[30] Similar numbers were noted in a review of records from a neurology clinic for indigent patients in Houston.[31]

Treatment and Outcome of NCC

Prior to the introduction of antiparasitic drugs in the late 1970s, the only treatment for NCC was surgical. Praziquantel was the first available antiparasitic but its use has now been eclipsed by albendazole.[9,21] In our most recent case-series in Houston (1997–2005),[21] antiparasitic drugs were used in 40% of patients compared with 65% of patients in our previous study (1985–1991).[16] In 2006, a meta-analysis of parenchymal NCC published by Del Brutto and coworkers[2,32] suggested that cysticidal drug therapy results in better resolution of viable and degenerating parenchymal cysticerci, lower risk for recurrence of seizures in patients with degenerating cysticerci, and a reduction in the rate of generalized seizures in patients with viable cysticerci. Neuro-endoscopic procedures for the removal of intraventricular cysticercal lesions have also been described in tertiary centers in the USA.[33] There is a growing consensus that symptomatic therapy including antiepileptic drugs, corticosteroids and selected surgical procedures aimed at controlling seizures, inflammatory responses and intracranial hypertension, respectively, should become the initial priority in the management of NCC.[34] NCC is associated with significant morbidity resulting from hydrocephalus, cerebral edema, and, less frequently, seizures.[21] A review of death certificates in the USA from 1990 to 2002 found a total of 221 NCC-associated deaths. Over the 13-year study period, the annual age-adjusted mortality rate was 0.06 per million population.[35] Deaths frequently occurred outside of the hospital or in emergency rooms, suggesting that poor access to care may have been a contributing factor. By contrast, most hospital-based series note deaths in $<1\%$ of cases; none in one recent large series.[21] Mortality rates were higher for Hispanics and men. The mean age at death was 40.5 years. Thus although uncommon, NCC is a cause of premature death in the USA.

In summary, although our understanding of the epidemiology, treatment and control of NCC in the USA has significantly increased in the last two decades, much work remains to be done. Active surveillance of cases and household contacts, better serologic methods that allow us to predict clinical response to therapy, multicenter randomized clinical trials to evaluate new therapeutic strategies and novel preventative strategies are urgently needed.

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