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Neurocysticercosis, a Retrospective Review of a Neglected Tropical Disease in two Academic Centers in South Florida

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Introduction

Taeniasis and cysticercosis are neglected zoonotic diseases caused by the parasite Taenia solium. While taeniasis is generally asymptomatic, cysticercosis in the central nervous system of humans carries a significant impact, accounting for 30 to 70% of cases of epilepsy in some communities [1, 2]. In contrast to taeniasis, which arises after the ingestion of cysticerci in raw or undercooked pork, cysticercosis is transmitted by the ingestion of T solium eggs shed in the stool of a human tapeworm carrier. Following the ingestion of eggs, embryos hatch in the small intestine, invade the bowel wall and disseminate hematogenously to the central nervous system, known as neurocysticercosis (NCC) but can also involve eye, muscle, liver and/or other tissues [1, 2].

Epidemiological evidence suggests that the most common source of these infective eggs is an asymptomatic household carrier and thus this disease is largely transmitted from person to person, with infected pigs as intermediate hosts [3-5]. NCC is endemic to regions of Central and South America, the Caribbean, sub-Saharan Africa and Asia [6]. However, cysticercosis is also diagnosed in non endemic areas particularly where there is a significant influx of immigrants. As an example, there are reports of NCC outbreaks in individuals without a history of travel or pork consumption in an orthodox Jewish group of children in New York City and another one in Kuwaiti nationals [7, 8]. In the United States (US), the highest disease burden has been reported from Southwestern states, mostly California, Texas, New Mexico, with some from Oregon, New York and Kansas [9,10]. However, only a few states (California, Texas, New Mexico, New Jersey, and Oregon) require reporting of cysticercosis and thus, population-based epidemiologic data in the US are limited [11]. Although accurate incidence data in the U.S. is not available, estimates range from 0.2-0.6 cases per 100 000 in the general population and 1.5-5.8 cases per 100 000 in Hispanics. Wallin et al reported that Mexicans represented about 70% of the NCC cases from Latino origin.12 The study also found that NCC poses

considerable health and economic problems in the US, especially among the Hispanic population with charges of more than US$ 908 million, of which 40% was billed to publicly funded insurance programs. Hospitalization stays were prolonged and expensive, reflecting the complicated nature of acute disease management. A review of a national database estimated that there were more than 18,000 hospitalizations for NCC in the U.S. between 2003 and 2012, particularly among young male Hispanic adults [2, 12-14]. Limited data has been reported from other areas of the U.S. It would be expected to see NCC in the Southeast area, specifically the state of Florida, given its active immigration activity from the Americas [15, 16]. As per the American Immigration Council Florida fact sheet, in 2018, 4.5 million immigrants comprised 21% of the Florida population. The top countries of origin were Cuba (23%), Colombia (6%), Mexico (6%) and Jamaica (5%) [17]. Additionally, 41% of immigrants from the Caribbean live in Florida, making Miami-Dade County home to the highest concentration of Caribbean immigrants among all U.S. counties.18 Furthermore, 2.7 million US born people in Florida (13% of the state population) had at least one immigrant parent. With this high immigration population in Florida and limited data, further investigation into NCC cases is warranted. Our group provides insight into cases of NCC in South Florida in two large academic centers in Miami Dade County, Florida from 2009-2022.

Methods

Description of Study Sites

This study is a retrospective chart review conducted in two large tertiary care academic hospitals. They are located within the metro area of Miami Dade County and are referral centers to South Florida. The University of Miami Hospital (UMH) is a 560 bed private academic hospital. Jackson Memorial Hospital (JMH) is the county hospital and one of the largest hospitals in the United States with 1547 beds. Both hospitals provide care to underserved and non-insured patients in South Florida.

Data Collection and Analysis

Electronic health records at the UMH and JMH were searched for patients with an inpatient, outpatient or emergency department visit diagnosis of neurocysticercosis, cysticercosis and others (ICD10 codes: B69.9' ,'B69.0' ,'B69.1' ,'B69.89' ,'Z77.9' ,'B69.81' ,'R76.8' ,'123.1' ,'123.1' ,'123.1' ,'123.1' ,'V15.89' ,'123.1' ,'795.79') from January 2009-December 2022. We consolidated data into one list to avoid duplicate records from patients that were admitted in both hospitals or patients admitted multiple times for the same diagnosis.

Demographics, reasons for visit, clinical symptoms, diagnostics, NCC treatment, outcomes and follow up were extracted, tabulated for both hospitals and analyzed as percentages. Recurrence was defined by history of previously treated disease with new symptoms or imaging findings. Imaging (CT and/or MRI) were reviewed to determine classification of disease (parenchymal, ventricular, subarachnoid, cerebellar, spinal, ocular, multiple sites of infection or unknown). Countries of birth were separated into four regions (United States, Caribbean, Central America and South America) and unknown. We did not report on race or language spoken as we felt the country of origin was most descriptive and relevant. Treatment included antiparasitics (albendazole, praziquantel or both), antiinflammatories (corticosteroids) and follow up was calculated as any clinic visit with Primary Care Provider, Neurology, Neurosurgery or Infectious Disease within 1 year. The study was reviewed and approved by the University of Miami/Jackson Health Systems Review Board and a waiver of consent was granted. Data were analyzed using Microsoft Excel 365® (Microsoft, Redmond, WA).

Results

Our query yielded 127 unique cases that were treated at our hospitals (86 JMH, 41 UMH) and an additional 69 patients with a

history of NCC but were not treated for active infection and admitted for a different reason not included in the below analysis.

Forty-two (33.1%) patients were originally from the Caribbean, of which 36 (85.7%) were from Haiti and 3 cases in the United States but with unknown travel history (Figure 1).The most common symptom, as noted in history of presenting illness was headache (63%), followed by seizures (45.7%), nausea/vomiting (21.3%), altered mentation (13.4%), and vision changes (13.4%). Fever was rare at 3.9%. Most had no personal or family history of cysticercus infection (63.0% and 81.9%, respectively), nor seizure (74.0%), nor family history of it (percentage?). HIV co-infection was recorded in 4/72 of patients. A normal physical examination was recorded in 82.7% of the cohort. CT and MRI of the brain were commonly ordered (82.7% and 92.9%) but most did not have MRI spine, cysticercus antibodies, or stool ova and parasites (Table 3 and 4). Of the imaging findings, 70.1% had parenchymal lesions with similar rates of calcified (39.4%) and noncalcified lesions (43.3%). Multiple sites of infection (n=16) usually included parenchymal and another site, most commonly ventricular (n=8) but also subarachnoid (n=3), cerebellar (n=2) and 1 case each of cerebellar/spinal, subarachnoid/spinal and cerebellar/arachnoid. There was a similar number of single lesions (43.3%) compared to 2-10 lesions (37%) but only 15% having greater than 10 lesions (table 4). The majority of patients were prescribed antiparasitics (80.3%) and steroids (73.2%) and 35.4% underwent surgery. There was significant variation in treatment duration (between <10 days to >14). Follow up was done in 62.2% of patients with resolution of imaging findings on 22%. Recurrence and reinfection were low at 12.6% and 5.5%, respectively (Table 5). Only 1 (0.8%) death attributed to NCC was reported through the time of chart review.

When comparing treatment and follow up according to location of the lesions, only 21.3% of parenchymal lesions required surgery, compared to 78.9% of ventricular and 64.3% of lesions in multiple sites. Recurrence was also higher in the group with multiple sites of infection at 28.6% and 14.3% (table 6). Those with ventricular and multiple sites of lesions received longer duration of antiparasitics (table 7).

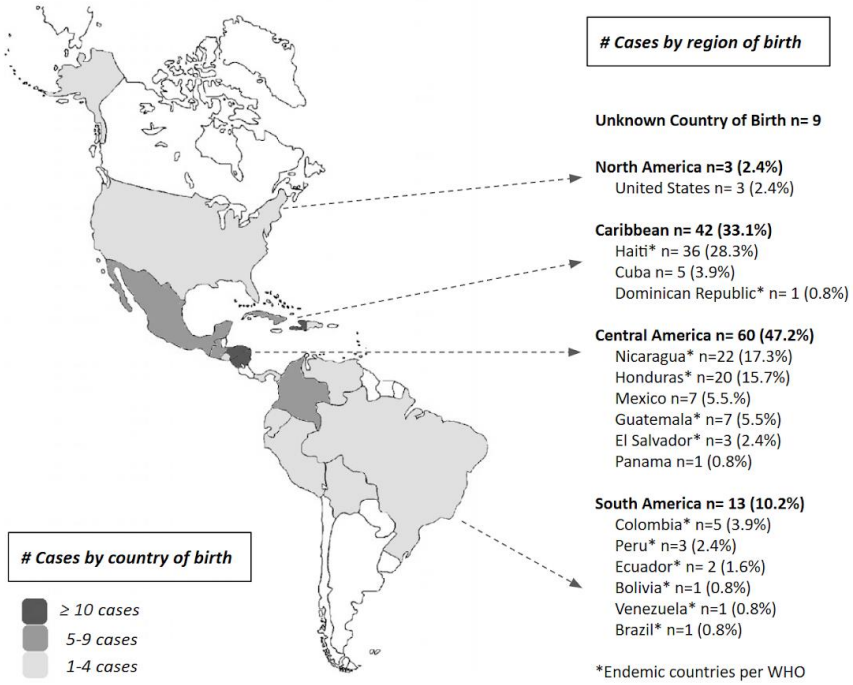

Figure 1: Cases of NCC by region and country of birth

Table 1. Diagnostic studies performed in our cohort patients with NCC (Suggest Merging Table 3, Table 4). Table 2. Outcomes of patients with NCC (Suggest Merging Table 5,6,7)

Discussion

An increased incidence of NCC has been recognized in high income, non endemic countries with a higher hospitalization rate than any other neglected tropical disease [6, 12, 14, 19-21]. Cases have been reported in the United States, Europe, Australia, Canada, Israel, Japan and Middle Eastern countries and changes in migration and travel patterns prompts further discussion into the epidemiology and characterization of this disease [22-24]. In the U.S., Florida has one of the highest immigration populations with a large percentage coming from endemic countries in Latin America and the Caribbean, but there is minimal data on NCC in this region [25]. In our study, we outlined the demographics of NCC in South Florida, which have largely involved California and Texas (Table 8). We found 127 treated cases identified between years 2009 through 2022, where 86 cases are from JMH and 41 cases from the UMH. The majority of the patient population when combining both hospitals came from Central America (47.2%) followed by the Caribbean (33.1%) and South America (10.2%). Of these, 33.1% of patients were from the Caribbean, 85.7% were from Haiti. Patients from 16 different countries were identified (Figure 1), of which the WHO has classified 12 with endemic cysticercus, 2 with few pigs as risk factors and 2 non-endemic countries (USA and Cuba) [6, 21]. Florida has the highest number of Haitian immigrants in the U.S. and NCC disease prevalence in Haiti is similar to other Latin American and African countries, which explains why they have such a significant disease burden [26, 27]. Comparing to the population described in California by Croker et al the majority of their cases were from Mexico and Central America, with no description of patients from the Caribbean [9]. Two studies, combining for 225 total patients, from Houston, Texas described their epidemiology of NCC which showed ¾ of patients were from Mexico, followed by 11-16% from Central America and 4-6% from the United States [11, 28, 29]. This may reflect the immigration patterns of these individual cities or the overall immigration pattern of the U.S..

Summary of reviewed studies of NCC epidemiology in the USA (Table 8)

Location	# of cases	Years evaluated	Year published	Authors
United States	1494	1980-2004	2004	Wallin MT, Kurtzke JF[12]
Texas	114	1994-1997	2005	del la Garza Y, Graviss EA, Daver NG, Gambarin KJ, Shandera WX, Schantz PM, White AC Jr.[28]
Kansas	42	1986-2001	2006	Daniels T, Moore T[31]
California	3937	1991-2008	2010	Croker C, Reporter R, Mascola L[10]
Texas	111	1997-2005	2011	Serpa JA, Graviss EA, Kass JS, White AC Jr[29]
New Mexico	37	1998-2004	2011	Figueroa JJ, Davis LE, Magalhaes A[30]
California	304	2009	2012	Croker C, Redelings M, Reporter R, Sorvillo F, Mascola L, Wilkins P[9]
United States	18584	2003-2012	2015	O'Neal SE, Flecker RH[19]
Oregon	125	2010-2013	2016	Flecker RH, O'Neal SE, Townes JM[35]
New York	52	2005-2016	2020	Spallone A, Woroch L, Sweeney K, Seidman R, Marcos LA[36]
Texas	78	2011-2020	2022	Kaplan J, Centeno FH, Hayon J, Bottazzi ME, Hotez PJ, Weatherhead JE, Clark E, Woc-Colburn L[37]

The most common symptoms on presentation were headaches (63%) followed by seizures with 45.7%, nausea and vomiting with 21.3%. This contrasts with previous studies which reported the most common symptoms related to NCC in the U.S. include seizures (38-82%), hydrocephalus related symptoms (16-31%) and headaches (3-34%).9,8,12,29-31 Data collected at 11 emergency departments at geographically diverse urban hospitals showed that 2.1% of cases had seizures attributable to NCC. Among Hispanics presenting with seizure, the prevalence increased to 9-13.5%.32 NCC can have a variable clinical presentation with a normal physical exam.

Radiographic imaging was done for the majority of patients - CT head at 82.7% followed by MRI brain at 92.9%. Parenchymal lesions were the highest identified in our patient population compared to extraparenchymal lesions. An earlier article analyzing 1494 NCC cases between 1980-2004 in the U.S. showed higher rates of parenchymal disease (91%) but our study showed 70.1% of parenchymal disease with a higher incidence of extraparenchymal disease, which is similar to recent studies (28-32%) [12, 20, 29-31]. This is notable as there is significant morbidity resulting from hydrocephalus, cerebral edema and seizures associated with extraparenchymal cysts. Of note, our cohort had six cases of subarachnoid disease. Per IDSA guidelines, additional MRI spine is recommended when this is present, but in our study, only two of the six had this done [33]. We found two total cases involving the spine, one which also had lesions in the subarachnoid and one with cerebellar lesion.

Following the WHO and IDSA NCC guidelines, treatment is guided by location of the lesion. In our results, 80.9% of parenchymal lesions were treated with anthelmintic therapy (albendazole, praziquantel or both), with only 24.7% treated between 10-14 days as recommended. It is important to mention that 50.6% of these lesions were described as calcified, with only symptomatic management recommended. The majority (70.8%) of parenchymal lesions received steroids and while dose and duration are not as well defined, steroids are recommended prior to antiparasitic therapy [33]. For the reported ventricular lesions, 78.9% received surgery, with concomitant medical treatment in 68.6%. By comparing treatment and follow up according to location of lesion (parenchymal, ventricular, multiple sites and other that included: one cerebellar site, one subarachnoid and three unknowns) we saw that there were more surgeries in the ventricular and multiple site groups, as well as steroid treatment. In addition, there was more recurrence, longer duration of treatment and noncalcified lesions, which is in accordance with the pathophysiology of these sites.

We registered follow-up on 62.2% of our cases, with imaging resolution in 22%. However, most MRI follow up was not per the IDSA guideline of every 6 months until resolution of the cystic component, but rather for post surgical management or for changes in clinical status. In the case of our specific population, it is important to highlight that challenges in follow-up could be related to a high incidence of an uninsured population, as JMH is the main county hospital of the area. We also noted that the follow-up rate was lower in the parenchymal group; this may reflect their decreased severity of illness, decreased surgical needs or better defined duration treatment. In the reports from California and Texas, there was 2% and 0% death respectively, compared to 0.8% cases for ours [9, 29]. In our study, one patient died from cerebral hemorrhage from ruptured parenchymal cysts at age 65. Death certificate data from the US in 1990-2002 reported 221 cysticercosis deaths with an average age of 40.5 years. They noted 21 states that reported at least 1 death, with California being the highest with 126 deaths, and Texas, New York and Florida being the next highest with 21, 16 and 14 deaths, respectively. The authors noted that this may be an underestimate of true rates given potential lack of recognition of disease and limited data on death certificates but neurocysticercosis is uncommon but causes premature death in the United States, which is also reflected in our study [34].

Conclusions

In conclusion, NCC remains a neglected zoonotic disease with increased incidence and prevalence in the U.S., giving the significant increase in immigration for the past several decades. We describe a high prevalence of NCC cases in a unique population that was not previously reported in the literature. This highlights the importance of considering NCC as a possible diagnosis

for a broader population in the US, especially patients from the Caribbean and in particular Haiti. As more literature reports NCC with its high disease burden in the U.S. with high morbidity in particular to underserved patient population, this renders the importance of potentially including this disease as a reportable infection nationwide, not just to California, New Mexico, Oregon, Texas and Arizona. By making NCC a reportable disease, it will allow more information and data for better understanding of the disease, and its impact in the U.S.

We support the current recommendation for diagnostic testing, including obtaining MRI spine for subarachnoid disease and ocular examination when a patient is diagnosed with NCC for a complete and thorough assessment for proper treatment and treatment duration. This would require a multidisciplinary team to address the socio economic challenges of this population to be able to provide appropriate follow up and treatment. Overall, bringing awareness about NCC is essential to help with the diagnosis and treatment of patients in the U.S.

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