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ORIGINAL ARTICLE

Spinal *Taenia solium* cysticercosis in Mexican and Indian patients: a comparison of 30-year experience in two neurological referral centers and review of literature

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Abstract
Objective To present a retrospective study from patients with spinal cysticercosis (SC), diagnosed within the last 30 years in Mexican and Indian neurological referral centers.
Methods This is a retrospective and comparative study of the clinical and radiological profile between Mexican and Indian patients with spinal neurocysticercosis during a 30-year period and a review of the literature during the same period.
Results Twenty-seven SC patients were included: 19 from Mexico and 8 from India. SC presented predominantly with motor symptoms (21/27 patients): paraparesis and paraplegia were the most common signs; one-third of patients presented sphincter dysfunction. Imaging studies showed that parasites in vesicular stage were more frequent in patients from Mexico, while degenerative stages predominated in India. Association of subarachnoid cysticerci and hydrocephalus was observed only in Mexican patients.
Conclusions Despite the limitations of this study, the collected information supports the existence of differences in the clinical and radiological traits of SC patients between Asian and Latin-American hospitals. The possible biological factors that may underlie these differences are discussed.

Keywords Neurocysticercosis · Spinal cysticercosis · *Taenia solium* · CSF · Arachnoiditis · Hydrocephalus

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Introduction

Neurocysticercosis (NC), caused by the metacestode stage of *Taenia solium,* is one of the most frequent parasitic diseases affecting the central nervous system (CNS) and a public health concern in most developing countries of Asia, Latin America, Central and South Africa [1, 2]. An estimate of 50 million people are affected by cysticercosis worldwide, and nearly 50,000 annual deaths have been reported in endemic areas [3].

NC may involve all CNS locations, but parenchymal and subarachnoid spaces are the most frequently affected sites. On the other hand, the spinal cord is an uncommon location for cysticerci. Indeed, spinal cysticercosis (SC) accounts for 1.2–5.8 % of NC cases, according to different reports [4–7]. In SC, cysts can be lodged either outside (extramedullary) or within the spinal cord (intramedullary). In turn, extramedullary lesions can be either extradural (epidural) or intradural [6–8].

Published data show clear differences in the radiological and clinical pictures of NC cases from different continents

[9]. Among these differences, are found the apparent higher frequency of solitary parenchymal NC by damaged cysticerci in Indian patients, as well as the less frequent cyst location in the ventricles or the subarachnoid space of the base [10]. In contrast, the latter forms of the disease are frequently found in Mexican hospitals [1, 11]. In India, brain parenchyma is the most common infection site, followed by meninges, ventricles, eye, and spinal cord [2].

Taking these observations into account, a comparative study of the clinical and radiological traits between Mexican and Indian SC patients as reported within a 30-year period in two neurological centers, as well as literature cases during the period of study, is herein reported.

Methods

A retrospective study of SC patients was performed, covering from January 1980 to December 2010, at two neurological referral centers: the Instituto Nacional de Neurología y Neurocirugía (INNN) in Mexico City, and the National Institute of Mental Health and Neurosciences in Bangalore, India.

Presumptive SC diagnostics was based on clinical and neuroimaging findings. Epidemiological data (residence in a disease-endemic area and positive enzyme-linked immunosorbent assay for cysticercal antigens in CSF) gave further support to cysticercosis diagnosis. All cases were confirmed by pathological examination of surgical specimens or by radiological response to albendazole (ABZ) (Fig. 1).

Statistical analysis

Qualitative variables were expressed in percentages and compared using χ^2 distribution. Statistically significant differences were considered at $P < 0.05$. Quantitative variables were expressed as median with standard deviation. The two-tailed Student́s t or Mann–Whitney test, based on their behavior in the Kolmogorov–Smirnov test, was used for

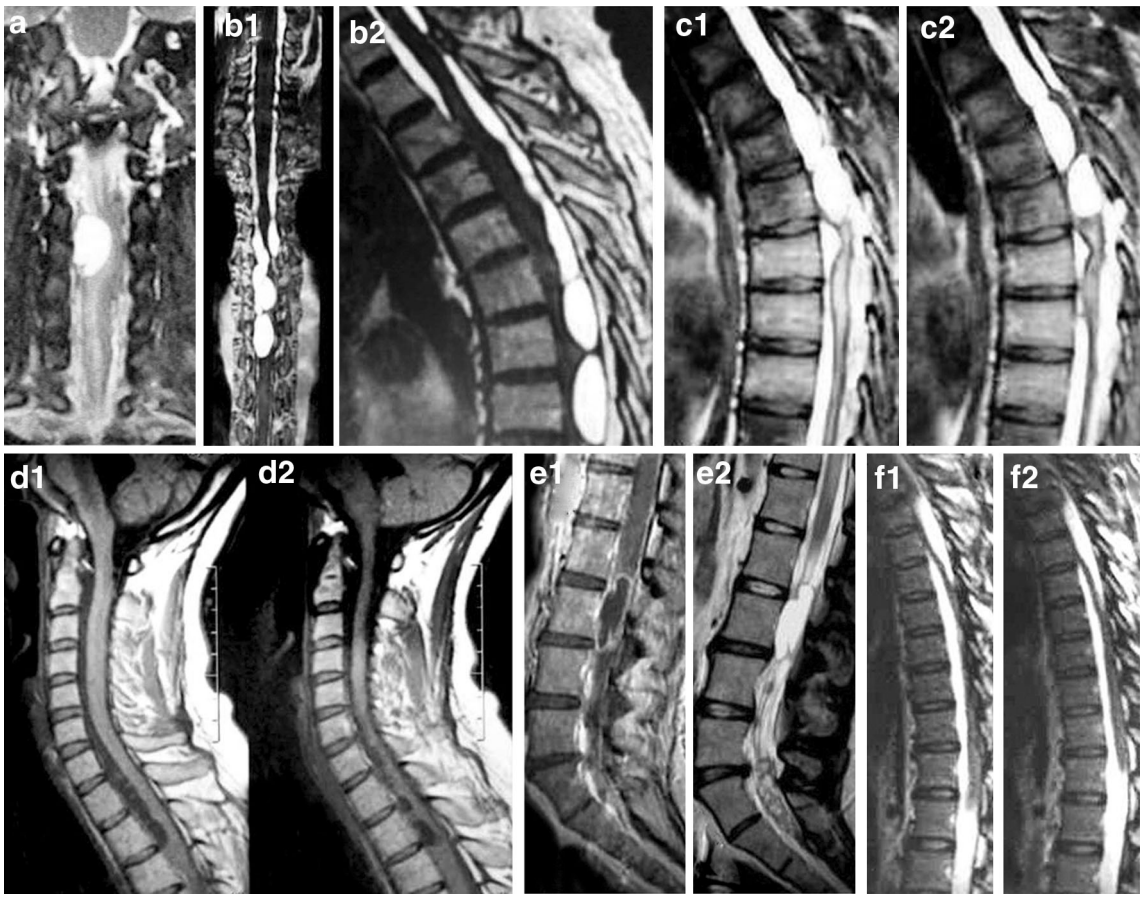

Fig. 1 Mexican cases. **a** T2-weighted coronal axis MR shows a single cervical cysticercus (Case 1). **b1**, **b2** T2-weighted MR coronal and sagittal axes show multiple thoracic cysticerci (Case 2). **c1**, **c2** T2-weighted MR sagittal axes show multiple vesicular cysticerci at the thoracic level (Case 4). **d1**, **d2** T1-weighted MR sagittal axes show multiple cervical cysticerci in the anterior portion of the cervical spinal cord (Case 5). **e1, e2** Gadolinium-enhanced T1- and T2-weighted MR sagittal axes show lumbar cysticerci (Case 16). **f1, f2** T2-weighted sagittal MR shows multiple thoracic cysticerci (Case 19)

comparison between Mexican and Indian cases as well as the sub-analysis of literature cases (Latin-American Vs Indian patients). All data were recorded in Excel software (Microsoft Co., Redmond, WA) and analyzed using the SPSS version 21 Software (IBM Inc., Armonk, NY).

Results

Mexican patients

A total of 51,503 new patients were admitted for hospitalization at the INNN during the period of study. Among them, 662 patients (1.28 %) were diagnosed with NC and 19 (2.8 %) of these were diagnosed with SC. Eleven (58 %) were female and 8 (42 %) were male [M:F = 1.4:1, mean age was 47.9 ± 14 years (range 21–68)]. Sixteen (84 %) patients showed arachnoiditis and/or hydrocephalus. Neurocysticercosis in the subarachnoid space of the base (NC SAB) had been previously diagnosed in 6 (31.5 %) of these patients. Clinical manifestations were limited to the lower limbs (paresthesias, paraparesis, or paraplegia) in 14 patients (74 %), and affected all four extremities (quadriparesis/quadriplegia) in 5 (26 %). The parasite stage was vesicular in 12 (63 %), degenerative (vesicular–colloidal, colloidal, or calcified) in 6 (33 %), and only one patient showed arachnoiditis. As Table 1 shows, a single cysticercus was found in 7 patients (37 %) and multiple cysts in 12 (63 %). Cysticercal lesions were found at cervico-medullar or cervical level in five cases, at thoracic level in seven cases, and at lumbar level in three cases. All other patients were affected in more than one level. CSF analysis was available for 14 patients: mean CSF glucose level was 49.7 ± 9 mg/dL, protein level was 118.8 ± 30 mg/dL, and cell count was 61.3 ± 106/mm^3. Four patients were given drug treatment only; the rest of patients underwent surgical procedures, and from these one received pharmacological treatment (corticosteroids, ABZ, or a combination of both). Clinical improvement was observed in 12 patients (67 %), with complete recovery in two; no improvement was observed in 7 (37 %), and one patient in this group died some months after discharge (Table 1).

Indian patients

A total of 486,265 new patients were admitted for hospitalization at the National Institute of Mental Health and Neurosciences during the period of study. Among them, 1458 patients (0.3 %) were diagnosed with NC and 8 (0.54 %) of these were diagnosed with SC.

Five patients were male and three were female [M:F = 1.6:1, mean age was 28.6 ± 14 years (range 16–50)]. All patients showed motor signs, and all patients showed solitary lesions. Cysticercal lesions were located at thoracic level in five patients, at lumbar level in two patients, and at cervico-medullar level in one patient. Most parasites were lodged intramedullary, and only two were extramedullary, intradural. No data on CSF characteristics were available from the records.

All patients underwent surgical cyst excision, and two of them also received ABZ treatment. The parasite was identified in vesicular stage with an intact scolex in two patients, while cysts showed signs of degeneration (vesicular–colloidal or colloidal) in the others. No fatal outcome was reported. No information regarding the clinical follow-up was available, because all patients were referred to their local hospital after treatment. Clinical and radiological information of these patients is summarized in Table 2. The main differences in patient characteristics between both neurological centers are summarized in Table 3.

Clear differences between Mexican and Indian SC cases were found in this study. Indeed, multiple ($P = 0.003$) and extramedullary ($P = 0.006$) cysticerci were more frequently found in Mexican patients than in Indian patients.

Review of the literature cases

A Medline search with the key words "spinal cysticercosis" during the period of study retrieved a total of 75 articles (133 patients) [4–8, 12–78]. Fifty-one were female (38 %) and 56 male (42 %); no information about gender was available in the remaining 27 patients. Mean age at presentation was 37.85 ± 1.4 years (range 5–80); the time to evolution of clinical symptoms was 10.42 ± 17.5 months. Most patients were from American origin [68 of 133 (51 %) (63 Latin-American and 5 North-American)], followed by Asian [44 (33 %)], European [14 (10.5 %)], African [5 (3.75 %)], and from Oceania [1 (0.75 %)]; there was no information for the remaining two cases. The countries with highest prevalence of reported cases were Brazil and India.

With regard to the topographical level, cysticerci were located at the cervicomedullary junction or in the cervical level in 27 cases (20 %), thoracic in 40 (30 %), lumbar in 25 (19 %), and in more than one level in 15 (12 %). No information was available in the remaining cases.

Parasites were lodged intramedullary in 51 cases (38.3 %), extramedullary-intradural in 47 (35.3 %), extramedullary-epidural in 16 (12 %), and no information was available in 19 patients. CSF cytochemical characteristics were glucose 47.5 ± 65 mg/dL, protein concentration 211.5 ± 37.4 mg/dL, and cell count 39.05 ± 11.8/mm^3.

The stage of the parasitic lesion was vesicular in 67 cases (50.3 %) and degenerative (either colloidal or calcified) in 35 (26.3 %). There was no information for the rest

Table 1 Mexican spinal cysticercosis patients from the Instituto de Nacional de Neurología y Neurocirugía (1980–2010)

Age/sex	Parasite stage	Clinical symptoms	Radiological localization	Hydrocephalus/ arachnoiditis	CSF characteristics			Treatment		Clinical outcome
					Glucose (mg/dL)	Protein (mg/dL)	Cells (mm^3)	Pharmacological	Surgical	
64/M	Damaged (S)	Quadriplegia	CMJ, EM, ID	No/no	ND	ND	ND	None	CM	NI
57/M	Vesicular (S)	Asymmetric brachial, paraparesis	CMJ, EM, ID	Yes/yes	ND	ND	ND	ABZ	C	NI
60/F	Vesicular (M)	Paraparesis, urinary incontinence	T1–T7 EM, ID	No/yes	55	90	0	ABZ	L	NI
68/M	Vesicular-damaged (M)	Paraparesis, urinary and rectal incontinence	T12–L3, EM, ID l	Yes/yes	51	365	12	PDN	L	PI
55/F	Damaged (M)	Quadriparesis and urinary incontinence	C3–C4, EM, ID	Yes/yes	58	90	9	PDN	None	PI
26/F	Vesicular (M)	Paraplegia, urinary and rectal incontinence	C7–T2, EM, ID	Yes/yes	47	299	400	ABZ, DXM	L	TI
57/F	Vesicular (M)	Lower extremities paresthesia	T5–T7, EM, ID	No/yes	65	12	13	ABZ, DXM	L	NI
21/M	Vesicular (M)	Lower extremities paresthesia	T5–T7, EM, ID	Yes/yes	11	179	21	ABZ, DXM	L	PI
50/M	Vesicular (S)	Paraplegia, urinary and rectal incontinence	L4–L5, EM, ID	Yes/yes	5	115	32	ABZ, DXM	L	Death
48/M	Vesicular-damaged (M)	Slight paraparesis	L3–L4, EM, ID	Yes/yes	51	78	27	ABZ, DXM	VPD	PI
29/F	Vesicular-damaged (M)	Paraplegia, urinary, rectal incontinence	T4–T8, EM, ID	No/yes	91	22	3	DXM	L	TI
52/M	Vesicular (M)	Lower extremities paresthesia, urinary incontinence	L3–L5, EM, ID	Yes/yes	ND	ND	ND	DXM	L	PI
45/F	Vesicular-damaged (M)	Quadriplegia, urinary, rectal incontinence	C1–C5, C5–T8, EM, ID	No/yes	ND	ND	ND	ABZ, DXM	L	PI
64/F	Damaged (S)	Lower extremities paresthesia	T1–T2, EM, ID	Yes/yes	ND	ND	ND	None	L	PI
32/M	Vesicular (S)	Seizures, upper extremities paresthesia	C2–C3, EM, ID	Yes/yes	59	38	4	ABZ, DXM	None	PI
38/F	Vesicular-damaged (M)	Paraparesis	L2–L4, EM, ID	Yes/yes	3	166	67	ABZ, DXM	None	NI
49/F	Vesicular-damaged (M)	Slight quadriparesis	CMC–C2, EM, ID	Yes/yes	108	45	128	ABZ, DXM	CL	NI
33/F	Vesicular (M)	Upper extremities paresthesia	C3–C4, L2–L4, EM, ID	Yes/yes	10	46	122	DXM	L	PI
62/F	Vesicular (S)	Paraparesis	T5–T8, EM, ID	No/no	82	32	20	DXM, ABZ	None	PI

Parasite stage: *S* solitary, *M* multiple

Radiological localization: *CMJ* Cervicomedullary junction, *EM* extramedullary, *ID* intradural, *CMC* Cerebellomedullary cistern

Treatment: pharmacological: *ABZ* albendazole, *DXM* dexamethasone, *PDN* prednisone, *ND* non-data available; surgical: *CM* craniectomy and myelotomy, *C* craniectomy, *L* laminectomy, *VPD* ventriculoperitoneal derivation

Clinical outcome: *NI* no improvement, *PI* partial improvement, *TI* total improvement

Table 2 Indian spinal cysticercosis patients from the National Institute of Mental Health and Neurosciences (1980–2010)

Age/ Sex	Parasite stage	Clinical symptoms	Radiological localization	Hydrocephalus/ arachnoiditis	Treatment		Clinical outcome
					Pharmacological	Surgical	
50/F	Damaged (S)	Right lower limb weakness	L4, EM, ID	No/yes	ABZ	L	Improved
16/F	Damaged (S)	Left leg monoparesis	T11, IM	No/no	None	LE	ND
35/F	Damaged (S)	Paraparesis	T12–L1, EM, ID	No/no	ABZ	LE	Totally recovered
45/M	Damaged (S)	Quadriparesis, spasticity	CMJ, IM	No/no	None	LE	ND
ND	Damaged (S)	Spastic paraplegia	T2, IM	No/no	None	LE	ND
16/M	Vesicular (S)	Paraparesis, urinary retention	L1, IM	No/no	None	LE	ND
39/M	Vesicular (S)	Paraparesis, hypothesis	T12, IM	No/yes	None	LE	ND
28/M	Damaged (S)	Asymmetric paraparesis	T1–T2, IM	No/no	None	LE	ND

Parasite stage: *S* solitary, *M* multiple

Radiological localization: *CMJ* cervicomedullary junction, *EM* extramedullary, *ID* intradural, *ABZ* albendazole

Surgical: *L* laminectomy, *LE* laminectomy plus excision of parasites, *ND* data non-available

Table 3 Differences between Mexican and Indian spinal cysticercosis patients

	Mexican ($N = 19$)	Indian ($N = 8$)	P
Age (years)	47.9 ± 14	32.7 ± 11	**0.01**©
Gender			
Women	11 (58 %)	3 (37.5 %)	0.66®
Men	8 (42 %)	4 (50 %)	
Parasite stage			
Vesicular	12 (63 %)	2 (25 %)	0.08®
Degenerative (calcified, colloidal)	6 (33 %)	6 (75 %)	
Number of parasite			
Solitary	7 (37 %)	8 (100 %)	**0.003**®
Multiple	12 (63 %)		
Topography of lesion			
Cervicomedullary or cervical	5 (26 %)	1 (12.5 %)	0.55®
Thoracic	7 (37 %)	5 (62.5 %)	
Lumbar	3 (16 %)	2 (25 %)	
Compartment location			
Extramedullary	18 (95 %)	2 (25 %)	**0.006**®
Intramedullary	1 (5 %)	6 (75 %)	
Treatment			
Surgical	2 (11 %)	6 (75 %)	**0.002**®
Pharmacological (ABZ, Corticosteroids) or Combined (surgical and pharmacological)	17 (89 %)	2 (25 %)	

Statistical differences between groups are in bold

© Two-tailed Student's t, ® χ^2 test

of patients. Spinal parasitic lesion was solitary in 57 cases (42.8 %), and multiple in 43 (32.3 %); no information was available for the rest of cases. Brain cysticerci were simultaneously found in 18 patients (13 %), and subcutaneous cysticerci were reported in 5 (4 %).

The main clinical manifestations were motor or sensitive symptoms, in 104 cases (78.1 %); other symptoms included intracranial hypertension, in 24 cases (18 %); and no information was available for the rest of cases. Treatment consisted of surgical excision in 41 cases (31 %), combined surgical excision and cysticid treatment in 30 (22.5 %), and cysticid treatment alone in 14 (10.5 %). Clinical outcome was generally good, with 97 (72.9 %) surviving patients. A lethal outcome was reported for three patients, and there was no information for the rest. Neurological sequels were observed in 34 patients (25.6 %). The main differences in patient characteristics between both neurological centers and literature cases are summarized in Table 4.

Table 4 A comparison between the case series from our neurological centers and those previously reported

	Mexican neurological center ($N = 19$)	Indian neurological center ($N = 8$)	Literature cases ($N = 133$)	P
Age	47.9 ± 14	37.3 ± 13.3	36.3 ± 16	**0.01**©
Gender				
Women	11 (58 %)	3 (37.5 %)	54 (41 %)	0.6®
Men	8 (42 %)	4 (50 %)	59 (45 %)	
Clinical symptoms				
Motor or sensitive	19 (100 %)	8 (100 %)	95 (72 %)	**0.0001**®
Other			7 (5 %)	
Parasite stage				
Vesicular	12 (63 %)	2 (25 %)	73 (55 %)	**0.0001**®
Degenerative (calcified, colloidal)	6 (33 %)	6 (75 %)	41 (31 %)	
Number of parasite				
Solitary	7 (37 %)	8 (100 %)	82 (62 %)	**0.005**®
Multiple	12 (63 %)		50 (38 %)	
Compartment location				
Extramedullary	18 (95 %)	2 (25 %)	73 (55 %)	**0.0001**®
Intramedullary	1 (5 %)	6 (75 %)	49 (37 %)	
Mixed			5 (4 %)	

Statistical differences between groups are in bold

© Anova test, ® χ^2 test

In a sub-analysis considering only Latin-American ($N = 65$) and Indian ($N = 38$) cases from the literature, we found clear differences in parasite location. Extramedullary parasites predominated in Latin-American patients (82 % of cases), while intramedullary location predominated in Indian patients (63 %), $P = 0.0001$. With respect to the number of parasites, multiple parasites predominated in Latin America (80 % of cases) while single parasites were prevalent in Indian cases (74 %), $P = 0.0001$.

Discussion

Taenia solium cysticercosis is acquired by humans and pigs (the intermediary hosts) by ingesting the eggs released to the environment through human stools. Humans (the definitive hosts) developed the intestinal tapeworms (taeniasis) by eating meat-containing cysticerci [79].

Although uncommon, spinal cysticercosis seems to show clear differences, particularly in the radiological and clinical pictures, in cases from different geographical regions, as it is the case for brain cysticercosis [9]. In the Mexican population, brain cysticercosis is presented usually with multiple cysts in the ventricles or in the subarachnoid space of the base (extraparenchymal NC) [1, 11]. One single degenerated cyst has been reported only in pediatric population in Mexico [80, 81], as well as in the non-symptomatic open population [82]. In contrast, solitary calcified or colloidal cysticerci (parenchymal) predominate among Indian patients [2, 10].

Interestingly, we found that 31.5 % of Mexican SC patients had a previous history of NC SAB. The thoracic level was the most frequently involved, and multiple parasites predominated (68.4 % of patients). These data contrast with a recent Peruvian article, which reported lumbar as the most frequently involved region; in addition, 60.7 % (17 patients) presented NC SAB, and only one case of SC with concomitant brain parenchymal parasites [83]. With regard to the Indian SC patients, there was no antecedent of NC in any case. The thoracic level was the most frequently involved (62.5 %). All cases showed solitary, intramedullary lesions. A recent review on intramedullary cysticercosis also reported the thoracic level and solitary lesions as the most frequent finding [84].

With regard to treatment, 89 % of Mexican patients received a combined treatment (surgical and pharmacological), while surgical procedure alone predominated in Indian patients (75 %). It should be noted that surgical procedures do not warrant an important clinical improving, as we observed in Mexican patients: only two patients showed a complete clinical recovery.

Multiple factors may underlie the differences in infection intensity among adult SC patients observed in our study; for example, a possible lesser susceptibility to the infection in Indian patients, a lower infectivity of Indian *T. solium* variety, and/or differences in the infective pressure

or the characteristics of the inflammatory response between both groups of patients.

Supporting the relevance of host genetic factors in the radiological SC profile, a polymorphism of the matrix metalloproteinase-9 was recently reported as related to varying symptomatology of calcified NC [85]. Similarly, two polymorphisms of the TLR-4 receptor were also found associated with epilepsy in NC patients with parenchymal cysts [85]. Furthermore, since the Asian *T. solium* genotype prevails in India [86], differences in parasite genetics with respect to the African-American phenotype prevailing in Mexico may also be involved. Whatever be the case, the variations in the traits of SC found in this study highlight the relevance of systematically exploring the differences between both *T. solium* genotypes and their impact on the parasite affinity to the CNS [87].

On the other hand, the observed differences between intra- and extramedullary SC locations may be a consequence of different routes for the parasite to reach the spinal compartment. Most extramedullary cysticerci in Mexican patients could have spread from the cerebral subarachnoid space. Both the high incidence of brain subarachnoid parasites in the Mexican population [1, 11] and the simultaneous occurrence of cerebral subarachnoid NC in 30 % of SC patients may support this possibility [88]. In contrast, intramedullary parasites, mostly observed in Indian patients, are probably due to hematogenous invasion. Possible differences in adhesion molecules or other membrane markers may be involved in the differential oncosphere traffic, a hypothesis with merit to be explored.

The literature review showed that cysts in extramedullary locations usually involve the thoracic cord (36 %), followed by the cervical and the lumbar cord, and no differences were observed with regard to sex. This relation was more evident in the Mexican patients. On the other hand, most SC cases reported in the literature exhibited solitary cysts; this feature was similar to the Indian patients. The highest number of SC cases was observed in America (69/133), followed by Asia (43/133). The countries with more reported cases were Brazil (48) and India (36). Clear differences regarding topography (intramedullary/extramedullary) and number of (single/multiple) parasites between Mexican and Indian patients were observed, and these differences were also found in a sub-analysis of Latin-American and Indian patients from the literature.

Changes in the worldwide epidemiology of cysticercosis could be explained by the frequent travel and intercontinental migration; for example, immigration from Mexico and South America to the United States (mainly to the Southwestern and New York areas), and from India to countries in the Arabian peninsula (Kuwait, Saudi Arabia, and Qatar) makes this a global problem, no longer limited to the traditional endemic areas [89]. In this comparative study, both groups had low mortality, but 16/18 patients in the Mexican group showed limited improvement of symptoms or no improvement at all, in spite of the treatment (surgical and pharmacological). This stresses that SC is an important cause of morbidity in NC patients, comparable to cerebral parenchymal or intraventricular lesions, which are the main causes of symptomatic epilepsy, cognitive decline, high intracranial pressure, and focal neurological deficits in poor countries.

Despite the limitations of our retrospective study, it reports for the first time differences in the radiological and clinical profile between Asian and Latin-American patients with cysticercosis located at the spinal cord. Some worldwide features that point to differences in the frequency of this rare location of the parasite are also presented.

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Compliance with ethical standards

Conflict of interest The authors declare that no conflict of interest exists.

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