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Imported cysticercosis in Spain: A retrospective case series from the +REDIVI Collaborative Network

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ABSTRACT

Background: Neurocysticercosis (NCC) is the most common parasitic neurological disease worldwide and a major cause of epilepsy. Spain is the country reporting the highest number of NCC imported cases in Europe.
Methodology: Retrospective case series of NCC patients registered in the +REDIVI Network from October 1, 2009 to July 2018. A specific questionnaire, including clinical and diagnostic characteristics, was created and sent to the collaborator centers.
Results: 46 cases were included in the analysis. 55% were male, mean age of 40 years. 95.6% were migrants. The median duration since migration from an endemic area was 10 years. Predominant nationalities were Ecuadorians (50%) and Bolivians (30.4%). Frequent locations were parenchymal (87%), subarachnoid (26.1%) and intraventricular cysts (10.9%). Serological analysis was performed in 91.3%, being 54.8% positive. Most prevalent clinical manifestations were persistent headache (60.9%), epilepsy (43.5%) and visual changes (13%). Patients were mainly treated with albendazole (76.1%), corticosteroids (67.4%), and anticonvulsionants (52.2%). 82.5% had a favorable clinical outcome.
Conclusions: Most NCC cases were long-standing migrants. Few clinical differences were observed depending on the cysticerci location. The treatment was often not according to current recommendations, and no uniform criteria were followed when it came to the therapeutic regimen. NCC case management in Spain (including clinician awareness and laboratory capacity improvements) needs to be strengthened.

1. Introduction

Cysticercosis is a parasitic infection caused by the larval stage of the pork tapeworm *Taenia solium*. Neurocysticercosis (NCC) refers to cysticercosis involving the central nervous system (CNS), including the brain parenchyma, meninges, ventricles, basilar cisterns, sulci, gyri, spine, and retina [1]. People are infected by ingestion of the eggs shed by a tapeworm carrier [2].

One of the most complex traits of NCC is its great clinical heterogeneity. This parasitic disease is associated with a variety of signs and symptoms depending on the number, size, stage, and location of the cysticerci as well as the host's immune response [3,4]. Symptoms include headaches, seizures, hydrocephalus, meningitis, dementia, and other signs of space occupying lesions. On the other hand, *cysticerci frequently* cause *asymptomatic* infection and persist for many years [5].

NCC is the most common parasitic neurological disease worldwide and the greatest cause of acquired epilepsy. According to the World Health Organization (WHO) estimates (2017), the total number of people suffering from NCC, including symptomatic and asymptomatic cases, is between 2.56 and 8.30 million [6]. Infections are common in Central and South America (excluding Chile, Uruguay, and Argentina), parts of the Caribbean (notably Haiti), Indian subcontinent, most of Southeast Asia (Laos), part of China, many regions of non-Muslim sub Saharan Africa, and regions of Eastern Europe [7].

NCC poses a serious health hazard for people living in areas of high endemicity. Increased tourism and international business affairs have also rendered people from non-endemic areas more susceptible to acquire this parasitic disease [8,9]. Imported cases to non-endemic countries often result in delays in diagnosis, are expensive to treat, and can sometimes cause secondary local transmission [10,11].

In the last decades, NCC is becoming more common in Europe because of increased migration and travel. In Spain residual transmission of cysticercosis still persist. It is also the country reporting the highest number of imported cases of cysticercosis in Europe [5]. A recent study showed that the NCC burden is even higher than previous estimates, probably because it hosts the largest number of migrants coming from Latin America in Europe [12]. Despite the recent advances, large gaps in practical knowledge about the disease epidemiology still exist. This study is aimed at describing the demographic, clinical, radiological, and laboratory features of patients diagnosed with NCC registered in the Spanish + REDIVI Collaborative Network.

2. Methods

Retrospective case series of patients diagnosed with NCC and registered in the +REDIVI Collaborative Network from October 1, 2009 to July 2018. This national network includes 25 centers which share a common online database where new cases of imported infectious diseases are prospectively registered. +REDIVI includes migrants (person living in Spain but born in any other country), visiting friends and relatives (VFR)-migrants (migrant traveling back from the country of birth after visiting friends and relatives), VFR-travelers (the person who travels back from his/her first-degree relative's country of birth) and travelers (conventional international tourists returning from travel).

A data collection sheet is filled out online and a unique identifier code is automatically generated for each new episode. A coordinating center is in charge of database management and quality assessment as well as ensuring proper compliance with a pre-defined protocol. Further information on + REDIVI methodology has been published elsewhere [13,14].

2.1. Case definitions

2.1.1. Neurocysticercosis (NCC)

Diagnosis of NCC is frequently a challenge since histological demonstration of the parasite is not feasible in most cases, clinical manifestations are non-specific, most neuroimaging findings are not pathognomonic, and immune diagnostic tests are often faced with problems related to poor sensitivity or specificity. In this study, the NCC diagnosis was performed according to the accepted diagnostic criteria described at *Del Brutto* et al. [15]. The previous proposal for diagnosis of NCC, based on four categories of diagnostic criteria: absolute, major, minor, and epidemiologic [16], was replaced by the latest revised diagnostic criteria, based on two principles: neuroimaging studies are essential for the diagnosis of NCC, while clinical and exposure data only provide circumstantial evidence [17].

Definitions for the state and location of the cyst have been made accordingly to the literature. The location of the parasite in the CNS and

its expansion toward the inside of the brain parenchyma or toward the subarachnoid and ventricular spaces is a major determinant of its process of evolution and the subsequent clinical manifestations [1,18].

Viable (vesicular) cysts: Are well-defined, rounded cystic structures with fluid within the cyst that are isointense with CSF on computed tomography (CT) imaging and do not enhance after the administration of contrast, with minimal or no surrounding inflammation. The tapeworm scolex can be frequently visualized as an internal asymmetric nodule within a cyst referred to as "hole with dot" sign.

Transitional (colloidal) cysts: Are cystic structures with poorly defined borders and enhance after the administration of contrast, and commonly surrounded by edema. On CT, the cyst will appear as isointense fluid with ring enhancement of the lesion, whereas MRI will reveal cyst fluid which is isointense, ring enhancement on post-contrast T-1 weighted images, and lack of a scolex.

Inactive (granular) cysts: Are cystic structures transformed into a small nodular lesion. CT and MRI demonstrate enhancement of the nodular lesion after contrast medium administration. Calcified cysticerci are clearly visible on CT as nonenhancing hyperdense nodules. Patients with calcification on CT scan can have intermittent or persistent perilesional brain edema.

Cerebral edema: Perilesional edema appears as a bright signal using MRI FLAIR or T2 imaging. It is almost always accompanied by enhancement around the cyst on the T1-weighted images postgadolinium.

Parenchymal NCC: Are those lesions located within the brain cortex outside of the ventricles and the subarachnoid space (out of the spine, eye, etc). Small cysts partially embedded in the parenchyma but growing toward the subarachnoid spaces behave as intraparenchymal rather than as subarachnoid cysts.

Subarachnoid NCC: Are those most typically located in the Sylvian fissure or basal cisterns. Cysts are proliferative, lack a scolex in many instances, and are referred to as racemose cysticercosis. Hydrocephalus is the most common complication, due to chronic arachnoiditis resulting in the occlusion of foramina of Luschka and Magendie, and the parasite's mass effect on the ventricular system. Those cysts located within the cortical sulci are generally small in size that behave similar to parenchymal brain cysts.

Ventricular NCC: Are those located in the ventricles and/or basal cisterna. Many intraventricular and cisternal cysts are isodense and isointense to CSF, it may be the presence of ventricular deformity, distention, and associated hydrocephalus that suggests intraventricular cysts on CT. Degenerating cysts results in acute or chronic inflammation leading to CSF flow obstruction and hydrocephalus. Obstruction of CSF flow can be intermittent due to floating mobile cysts.

2.2. Data collection and statistical analysis

A specific questionnaire, including basic demographic information, signs and symptoms, radiological patterns, laboratory test results, treatment strategies, and patients' clinical outcome was created and sent to those collaborator centers that reported NCC cases to + REDIVI during the study period.

A descriptive analysis was performed in order to assess sex distribution, age, travel background, immunosuppression status, laboratory, and radiological findings, main presenting signs and symptoms and other relevant diagnoses, treatment and clinical evolution. Qualitative variables were expressed as relative and absolute frequencies, and quantitative data were expressed as median and interquartile range (IQR). 95% confidence intervals were calculated. The χ^2 test and Student's t-test were used when appropriate for comparison of categorical and continuous variables, respectively.

Ethics approval was obtained from the coordinating center's ethics committee and for all centers which requested it.

Table 1
Sociodemographic information of 46 NCC patients, +REDIVI, 1st October 2009–July 2018.

Variable		n	%
Sex	Male	26	56.5
	Female	20	43.5
Age group	**<30**	8	17.4
	30–44	22	47.8
	≥45	16	34.8
Country of origin	**Ecuador**	23	50.0
	Bolivia	14	30.4
	Guatemala	2	4.3
	Nicaragua	2	4.3
	Dominican Republic	2	4.3
	Peru	1	2.2
	Spain	2	4.3

3. Results

3.1. Sociodemographic and epidemiological characteristics

Information was provided for 47 out of 61 (77%) of NCC patients reported to + REDIVI by 11 collaborative centers. There was 1 patient who did not meet inclusion criteria, and thus excluded from the analysis.

Forty-six cases were included in the analysis. 55% were male. Mean age was 40 years (IQ range: 32–49). Forty-four NCC cases (95.6%) were migrants living in Spain for a median of 10 years (IQ range: 5.7–12). Predominant nationalities were Ecuadorians (50%) and Bolivians (30.4%). Eighteen of them (39.1%) had traveled to his/her country of origin during the last five years. 11% had other relative affected. The remaining two cases were Spanish travelers with long stage travel background to Sub-Saharan Africa and Asia in the previous years (Table 1).

3.2. Diagnosis

All patients were diagnosed by magnetic resonance imaging (MRI, n = 43) computed tomography (CT, n = 37), or both (n = 35). Serological test were performed in 91.3%. Cysticerci lesions were observed in 26 patients (25.6%), from which the presence of a scolex was identified in 9 patients according to the MRI reports.

Several cyst locations were identified; by neuroimaging there were 63 different locations in 46 patients. Parenchymal cysts were found in 40 (87%) cases, subarachnoid cysts in 12 (26.1%); intraventricular cysts in 5 (10.9%); ocular in 2 (4.3%) and, spinal in 1 (2.2%) case. Pure parenchymal location was observed in 67.4% of the patients. There was one patient that even combined four different locations (parenchymal, subarachnoid, spinal and ocular NCC) (Table 2).

58.7% of NCC patients had more than two brain lesions, 19.6% two lesions and 21.7% only one lesion. Most patients had 2 or more cysts at different stages. Within the 40 cases of parenchymal NCC, 23 patients had viable cysts, 22 calcified cysts and 2 solitary cysticercus granuloma.

Table 2
Neuroimaging. location of the lesions, +REDIVI, 1st October 2009–July 2018.

Location of the lesions by neuroimaging	n	%
Parenchymal NCC	31	67.4
Parenchymal and subarachnoid NCC	5	13.0
Subarachnoid NCC	3	6.5
Parenchymal, subarachnoid and intraventricular NCC	2	4.3
Intraventricular NCC	1	2.2
Ocular NCC	1	2.2
Parenchymal and intraventricular NCC	1	2.2
Subarachnoid and intraventricular NCC	1	2.2
Parenchymal, subarachnoid, spinal and ocular NCC	1	2.2

Cysts located in the subarachnoid space and/or the ventricles were most commonly in a transitional stage (Supplementary Table 1).

Cerebral edema was observed in 9 patients with parenchymal NCC, and in 1 patient with parenchymal and subarachnoid NCC (21.7%). Hydrocephalus was detected in every patient with intraventricular NCC (13.1%). Other less common findings (arachnoiditis, compression of the chiasma and lacunar infarct) were seen in the patient with complex parenchymal, subarachnoid, spinal and ocular NCC.

Serology blood test' results were available for 42 out of 46 patients (91.3%), out of which 23 were positive (54.8%), 18 negative and 1 doubtful. Tests for both antibody and antigen were applied in 9 patients (out of which 8 had positive results for Ab detection). Antigen detection was negative in all of them except for 1.

Cerebrospinal fluid (CSF) serology was performed in 5 patients being only positive in one patient, who had also a positive serologic result in serum. Out of them, detection of antigen in CSF was carried out in 3 patients, all with negative results. Histological demonstration of the parasite from biopsy was carried out in two patients: one sample came from open biopsy while the other one was obtained through *endoscopic* third *ventriculostomy*. Both patients had subarachnoid NCC. Molecular biology (PCR) was performed in 3 patients (1 in biopsy and 2 in CSF); only the one performed in the biopsy sample was positive.

3.3. Clinical characteristics

The most frequent clinical manifestation was a persistent headache (60.9%), followed by epilepsy (43.5%) and visual changes (13%). Half of the patients with epilepsy presented as generalized tonic-clonic seizures (Table 3).

The presence of comorbidities were recorded for 15 NCC patients, the most frequent being Chagas disease (n = 4), diabetes (n = 2) and hypothyroidism (n = 2). Two NCC patients were considered immunosuppressed (an HIV patient and a patient with Guillain-Barré syndrome both taking corticosteroids).

8.7% of patients (n = 4) were asymptomatic; all were incidentally diagnosed during: HIV follow up, study of hyperprolactinemia, and occupational cervical trauma. The fourth one was the sister of another + REDIVI NCC patient. Two of the four patients presented with viable parenchymal cysts (both with two lesions, one of the patients with one of the lesions in the subarachnoid space). The other two patients had calcified parenchymal NCC (with multiple lesions).

As expected, differences in clinical manifestations were observed considering the location of the cysticerci. All patients with intraventricular NCC had persistent headache, while epilepsy was found only in patients with parenchymal NCC and/or subarachnoid NCC. Asymptomatic patients mainly had parenchymal NCC (Supplementary Table 2).

3.4. Treatment and clinical evolution

Overall, 76.1% (n = 35) patients were treated with albendazole, 67.4% with corticosteroids, and 52.2% with anticonvulsionants. All patients with transitional and/or viable intraparenchymal NCC, subarachnoid NCC, and other combined forms were treated with albendazole and corticosteroids. There were 8 patients that were treated with both albendazole and praziquantel (not related to any specific clinical classification). Most common anticonvulsant was Levetiracetam (n = 19) (Supplementary Table 3).

Clinical evolution was favorable in 39 (82.5%) patients, unknown in 2 patients (lost follow-up) and not favorable in 5 patients. Patients with adverse outcomes were aged 30–44 (n = 4) and above 45 (n = 1) years. The reasons were: a) valve replacement needed one year after the initial ventriculo-peritoneal shunt; b) ventriculostomy for post-NCC hydrocephalus; c) Generalized tonic clonic seizures do not improve despite the treatment; d) persistent migraine; and e) persistent vertigo.

Of the patients with cystic parenchymal lesions (n = 40), 80% were treated with albendazole, 70% received corticosteroids and 20% received both albendazole and praziquantel. Information on following imaging studies was provided in 21 patients, out of which 85.7% showed resolution. 15 patients had just calcified lesions. Nevertheless, 6 and 2 were retreated with albendazole or praziquantel, respectively.

12 patients had subarachnoid NCC (including 8 with parenchymal NCC and 3 with ventricular NCC). All were treated with albenzadole and 9 received antiepileptic drugs. Clinical outcome was not favorable in 20% of patients with subarachnoid NCC.

Patients with persistent headache (n = 28) were mainly treated with albendazole (75%), corticosteroids (60.7%) and antiepileptic drugs (39.3%). Clinical evolution was mainly satisfactory (82.1%). Of the patients with seizures, 80% (n = 16) were treated with antiepileptic drugs, primarily levetirazetam (50%). Clinical progress was favorable in 85%; only one patient had recurrent seizures after two years of follow-up.

Surgery was performed in 7 patients (3 open surgery, 2 ventricular-peritoneal shunt, 1 endoscopy and 1 ocular cystectomy). All intraventricular NCC (n = 5) went under surgery. The other 2 patients had ocular NCC and parenchymal and subarachnoid NCC with important mass effect, respectively. There were 7 patients who received neither medical nor surgical treatment. 2 patients with calcified parenchymal NCC received antiparasitic drugs.

4. Discussion

We present a retrospective serie of 46 NCC patients attended by clinicians from a Spanish clinical-epidemiological network during more than 8 years. This national network collects imported infectious pathology in travelers and immigrants. Contemporaneous NCC case series from London [19], Italy [20] or USA [21] have been recently published. To our knowledge, this is the first study reporting both clinical and diagnostic characteristics of NCC patients in Spain, the European country reporting the highest number of imported NCC [5,12].

4.1. Sociodemographic and epidemiological characteristics

Sex distribution was similar, with the age group 30–44 most commonly represented. Cysticercosis can affect men and women from infancy to old age, with a peak incidence at ages 20–50 years [11]. In this sense, our results are in accordance with published data.

Most NCC cases were *long*-standing migrants, mainly Ecuadorians and Bolivians. Overall, Ecuadorians and Bolivians represent the 26.8% and 3.6% of reported patients in +REDIVI, respectively. Neurocysticercosis was rare in developed countries up to the past few decades [10]. We know that cysticercosis affects the health and livelihoods of subsistence farming communities in developing countries of

Table 3
Clinical manifestations of NCC patients, +REDIVI, 1st October 2009–July 2018.

Clinical manifestations	n	%
Persistent headache	28	60.9
Epilepsy[a]	20	43.5
Visual changes	6	13.0
No symptoms (incidental finding)	5	10.9
Loss of consciousness	4	8.7
Stroke	4	8.7
Affection of the cranial nerves	1	2.2
Cognitive dysfunctions, psychiatric disorders	1	2.2
Other symptoms[b]	11	23.9

[a] **Number and Type of epilepsy:** < 3 seizures (10); ≥3 seizures (10); generalized seizures (10); focal seizures (7), generalized and focal seizures (1), absence seizures (1), status epilepticus (1).

[b] **Other symptoms (11 patients):** Radiculopathy (3), tinnitus (3), vertigo (2), eye pain with eyelid edema (1), nausea and vomiting (1), cervicalgia (1).

Africa, Asia and Latin America [7]. In a recent review, the estimated seroprevalence of anti T. solium antibodies was 17.4% in Africa, 13% in Latin America and 15.7% in Asia [22]. This seroprevalence might be even higher in rural settings. A study conducted in Ecuadorian endemic rural communities showed exposure to the parasite ranging from 25% to 40% [23].

Worldwide, the growing number of immigrants, increased tourism and international business affairs has increased the number of patients with cysticercosis in developed countries [7,8,10,24]. In our study, the origin of NCC cases may be due to the fact that Ecuadorians and Bolivians, together with Colombians and Peruvians, represent the biggest Latin American communities in Spain [25], particularly in big cities, where most + REDIVI reporting hospitals are located.

About two-thirds of reported NCC cases did not travel to their country of origin in the last five years. NCC latent period prior to the appearance of clinical symptoms is variable, with a median of 5 years (ranging 1–30 years) [26]. Infected people may remain asymptomatic for many years, not being aware of the potential risk to themselves [27].

4.2. Diagnostic imaging and parasitological diagnosis

NCC cysts were mostly parenchymal (>90% of the cysts) and subarachnoid. Cysts located in the subarachnoid space and/or the ventricles were generally in transitional stage. The invasive larvae of oncospheres enters the CNS through the bloodstream, initially invading the subarachnoid space, and then the cortex and the cortical-juxtacortical junction, where they develop into cysticerci [28]. Parenchymal NCC has been traditionally considered the second most common form of NCC, after the subarachnoid-cisternal form [29]. More recently, several reports on large series of NCC patients have shown that NCC has been frequently misclassified; with the parenchyma being the most frequent location [19,30]. Moreover, most current experts groups cysts over the gyri with parenchymal cysticerci, due to their clinical presentation, response to therapy, and difficulty of distinguishing cysts in the gyri from in the parenchyma radiographically [1].

Around 80% of patients had 2 or more brain lesions. As expected, all patients with intraventricular NCC presented hydrocephalus in neuroimaging. Parenchymal NCC typically presents with seizures or headache, while ventricular NCC most often presents with obstructive hydrocephalus [1].

Serological results were positive in around half the NCC patients reported to + REDIVI, while neuroimaging findings were highly suggestive in all of them. NCC diagnosis is commonly based on neuroimaging studies (CT or MRI) and less often on confirmatory serologic testing [15]. In Spain, confirmatory human cysticercosis parasitological diagnosis is carried out by the National Microbiology Reference Laboratory (CNM in Spanish). The most commonly used commercial ELISA kits are available in some hospitals, but they use to cross-react with *Hymenolepis nana* and *Echinococcus granulosus*, which are common cestode infections. Moreover, their sensitivity and specificity may vary depending on the technique and nature of the antigen/s used. For commercial techniques, for example excretory/secretory antigen based-ELISA, the cut-off values are usually defined, but some laboratories modify them - according to their experience - since these antigens are usually quite sensitive but not very specific. Overall, these serological techniques are usually much more useful when applied to samples of cerebrospinal fluid (CSF) than of serum [31,32]. In the CNM, the lentil lectin-bound glycoprotein enzyme-linked immunoelectrotransfer blot assay (LLGP-EITB), which is the most specific serologic test [33], is performed as the serological reference standard for diagnosing NCC. Nevertheless, it may be negative in up to 30% of patients with only one degenerating cysticercus or calcified lesions [34]. Moreover, antibody can persist for a long time after the death of parasites, and thus a positive result in patients with calcified cysticercosis only do not indicate the presence of live parasites [32]. The HP10 Taenia monoclonal antibody-based ELISA and the Polymerase Chain Reaction (PCR) are also performed in the CNM upon request.

Detection of antigen in serum was negative in all serological positive patients except for one. The commercial ELISA assays available in Europe are not reliable [35,36]. Until now, the monoclonal antibodies assays seem to achieve reasonable sensitivity and specificity when using CSF samples, but not with their paired serum samples, due to false-positive reactions [36] The recently developed modified HP10 Ag-LFA detecting the T. solium metacestode HP10 antigen in serum might resolved this problem in the near future [33].

4.3. Clinical characteristics

Clinical findings are dependent upon the number, location, size, and stage/viability of cysts. The diversity of locations is believed to partly explain the range of NCC's clinical manifestations. Because there are frequently multiple cysts at various locations and stages, clinical symptoms can be varied and poorly understood [37].

In our study, the most frequent clinical manifestation was persistent headache, followed by epilepsy. According to several review papers, the percentages of NCC cases presenting with seizures and epilepsy varies from 70% to 90% [38,39]. However, there are several neurological disorders, less recognized as being linked to NCC, that can also occur [40]. Most probably, the availability of imaging technology in Spanish hospitals has facilitated the diagnosis of NCC in patients with a wider range of symptoms. In fact, 8.7% of patients were asymptomatic at the diagnostic time.

There was a considerably higher proportion of patients with parenchymal and/or subarachnoid NCC who presented with seizures/epilepsy as compared with patients with intraventricular NCC, probably related to the cysts specific localization.

4.4. Treatment and clinical evolution

No uniform criteria were followed when it came to the therapeutic regimen. NCC patients were mostly treated with albendazole, followed by corticoids and anticonvulsants. In NCC, the treatment duration and dosage depend mainly on the number, size, location and developmental stage of the cysts, their surrounding inflammatory edema, and severity of clinical symptoms or signs [17,41]. In this case series, antiparasitic drugs were used in all patients with viable intraparenchymal neurocysticercosis. All patients with intraventricular neurocysticercosis (IVN) in the lateral and third ventricles underwent surgery, although the surgical approach varied. Surprisingly, patients with subarachnoid NCC did not received prolonged therapy, as it is commonly recommended in the literature [17].

Only 8 patients received combined antiparasitic therapy (albendazole + prazinquantel). According to the Guidelines for the clinical management of patients with NCC, recently published by the American Society of Tropical Medicine and Hygiene (ASTMH) and a panel of the Infectious Diseases Society of America (IDSA) [1], patients with >2 viable parenchymal cysticerci (VPC) should be treated with albendazole combined with praziquantel rather than albendazole monotherapy. This was not the case in our series (several patients with more than 2 VPC received albendazole monotherapy). These new guidelines also recommended adjunctive corticosteroid therapy in all patients treated with antiparasitic therapy, which was also not our case. Moreover, we do not know (or alternatively, we failed to capture) whether NCC patients underwent a funduscopic examination prior to anthelmintic therapy, as it is recommended by the ASTMH guidelines [1]. In the near future, we hope that these guidelines will help clinicians to follow a more homogeneous pattern.

Clinical outcome was favorable in most patients. According to several case series, calcified parenchymal NCC can resolve on imaging studies without being treated with antiparasitic drugs [42–44]. In fact, there have been a common debate over the usefulness and safety of

anti-cysticercal therapy in this NCC type of presentation [40]. Regarding viable NCC, up to date there is limited information on the clinical evolution of patients and its relation with the different type of treatment [1,42]. Clinical evolution of these patients with viable cysts seem to depend on a diversity of factors, such as the host immune response against the parasite, the extent of the disease or the country of living, among others [1,34,43].

5. Limitations and conclusions

The main limitations of the study are the retrospective design and the number of centers ascribed to + REDIVI, which potentially could bias the results. Some amount of bias might be the consequence of the non-representativeness of the sample. +REDIVI collect information from travelers and migrants, therefore cases of local transmission go unrecorded in this network. Nevertheless, in absence of a national surveillance system for cysticercosis, +REDIVI offer key information on imported cysticercosis for the following reasons: most of the big centers devoted to imported infections in Spain are included in the network. Also, the majority of these hospitals are located in cities with a high proportion of migrants. In the same way, even if the information regarding the diagnosis and treatment of NCC was collected retrospectively, the inclusion of cases in the database of +REDIVI is made prospectively.

In any case, our findings reported here have potential implications for public health. Data on the full range of clinical expression of NCC are scarce in the literature, although such data are essential to improve disease knowledge. On the other hand, there is no surveillance system for CC disease implemented in Spain, despite the recommendations given by the European Directive 2003/99/EC [45]. Even if most cases might be imported in Spain, human CC surveillance (including clinician awareness and improvements in laboratory capacity) needs to be strengthened. Finally, clinical management of NCC patients should be more uniform, which could be facilitated by the recently updated ASTMH guidelines. All these measures will result useful in both disease control and morbidity reduction.

Data statement

Due to the sensitive nature of this study, survey respondents were assured raw data would remain confidential and would not be shared.

Data not available/The data that has been used is confidential.

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CRediT authorship contribution statement

Zaida Herrador: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing - original draft, Writing - review & editing. **José A. Pérez-Molina:** Conceptualization, Investigation, Methodology, Project administration, Writing - original draft, Writing - review & editing. **César Augusto Henríquez Camacho:** Investigation, Methodology, Project administration, Writing - review & editing. **Azucena Rodriguez-Guardado:** Data curation, Investigation, Validation, Writing - review & editing. **Pau Bosch-Nicolau:** Data curation, Investigation, Validation, Writing - review & editing. **Eva Calabuig:** Data curation, Investigation, Validation, Writing - review & editing. **Angel Domínguez-Castellano:** Data curation, Investigation, Validation, Writing - review & editing. **María Asunción Pérez-Jacoiste:** Data curation, Investigation, Validation, Writing - review & editing. **M. Concepción Ladrón de Guevara:** Data curation, Investigation, Validation, Writing - review & editing. **Ana Mena:** Data curation, Investigation, Validation, Writing - review & editing. **Jose Manuel Ruiz-Giardin:** Data curation, Investigation, Validation, Writing - review & editing. **Diego Torrús:** Data curation, Investigation, Validation, Writing - review & editing. **Philip Wikman-Jorgensen:** Data curation, Investigation, Validation, Writing - review & editing. **Agustín Benito:** Methodology, Project administration, Writing - review & editing. **Rogelio López-Vélez:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Writing - original draft, Writing - review & editing.

Declaration of competing interest

The authors have no competing interests to declare.

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Appendix A. Supplementary data

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