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REVIEW ARTICLE

Neurocysticercosis in Western Europe: a re-emerging disease?

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Abstract The objective of the study was to estimate the magnitude of neurocysticercosis in Western Europe and to determine the pattern of disease expression in the region. Review of patients with neurocysticercosis diagnosed in Western Europe from 1970 to 2011. Abstracted data included: demographic profile, clinical manifestations, form of neurocysticercosis, and whether the disease occurred in immigrants, European international travelers, or Europeans who had never been abroad. A total of 779 patients were found. Of these, only 28 were diagnosed before 1985. Countries with more reported patients were Portugal ($n = 384$), Spain ($n = 228$), France ($n = 80$), The United Kingdom ($n = 26$), and Italy ($n = 21$). Information on citizenship status, clinical manifestations, and forms of the disease was available in only 30–40 % of patients. Immigrants accounted for 53 % of cases, European travelers for 8 %, and non-traveler Europeans for 39 %. Immigrants/European travelers were most often diagnosed during the new Millennium, presented most often with seizures, and had less frequently inactive (calcified) neurocysticercosis than non-traveler Europeans. The prevalence of neurocysticercosis in Western Europe may be on the rise. The pattern of disease expression is different among immigrants/European travelers than among non-traveler Europeans. It is possible that some patients had acquired the disease as the result of contact with *Taenia solium* carriers coming from endemic countries. Much remains to be learned on the prevalence of neurocysticercosis in this region.

Keywords Cysticercosis · Neurocysticercosis · Western Europe

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Introduction

> "For every case of cysticercosis immediately diagnosticable there are a large number which will defy diagnosis for years" LIEUTENANT-GENERAL SIR WILLIAM PORTER MACARTHUR The British Medical Journal, December 21, 1935.

Taeniasis and cysticercosis have been associated with Europe for Centuries. Indeed, the occurrence of swine cysticercosis was a common knowledge among the ancient Greeks who considered these animals as impure. Also, the first human cases of neurocysticercosis were described in Europe during the Renaissance and, during the second half of the nineteenth Century, German investigators recognized cysticerci as the larval stage of *Taenia solium*, describing the life cycle of this tapeworm [1]. By 1912, the prestigious *Handbuch der Neurologie* included a chapter on *Cysticercosis cellulosae* that listed more than 100 references, mainly from Germany, France, and Italy [2]. Indeed, cysticercosis was highly prevalent in Western Europe by the end of the nineteenth Century. When meat inspection became compulsory in Germany, hygienic swine breeding developed. As a result, the rate of cysticercosis in pork carcasses and human autopsied brains dropped progressively until it was considered extinct in Germany during the first decade of the twentieth Century. The German scenario reflected that of Central Europe

where, after a transient increase in prevalence following the end of World War I, human and swine cysticercosis practically disappeared.

In countries of Eastern Europe, cysticercosis remained endemic during the twentieth Century. In Warsaw, 1.2 % of admissions to a neurosurgical center up to 1949 were due to neurocysticercosis, and 132 cases were identified at the same institution from 1936 to 1961 [3, 4]. From 1935 to 1970, a total of 181 patients with neurocysticercosis were admitted to a neurologic service in Bucharest [5]. From that time, it is presumed that neurocysticercosis continues endemic in Eastern Europe but, with the exception of sporadic reports, the information that comes from these countries is limited [6–9].

A natural epidemiological scenario that took place in The United Kingdom after the return of soldiers from the Far East helped to understand the dynamics of infection. Early in the twentieth Century, the members of the British Army and the Royal Air Force were sent on duty to India for defined periods of time. Back home, hundreds of soldiers had neurocysticercosis-related epilepsy [10, 11]. Most important, it could be recorded the onset of neurological symptoms according to their date of return to a cysticercosis-free country by that time, and it was noticed that most patients had their initial seizure between 2 and 5 years after return, suggesting a long asymptomatic stage. Some additional patients were family members of these soldiers but had never been in India, suggesting locally transmitted disease from a household contact with neurocysticercosis that was also infected with *T. solium* [11]. This outbreak of neurocysticercosis, where the date of infection could be traced, gave us an invaluable lesson on the natural history of this disease.

A second European outbreak of neurocysticercosis is currently happening in Spain (and probably in other countries of Western Europe) due to the massive immigration of people from Africa and South America that took place during the past two decades. While neurocysticercosis remained endemic in Spain during the second half of the twentieth Century [12], its prevalence was reduced to 4.3 % per 100,000 inhabitants by 1989, with cases mainly confined to rural areas [13]. However, together with the growing number of immigrants, more than 100 "urban" cases have been recognized during the past decade [14, 15]. Human cysticercosis must be considered a disease mostly transmitted from person to person, and the role of infected swine is to perpetuate the infection. While swine husbandry is currently considered adequate in Western Europe [16], the hundreds of *T. solium* carriers entering to these countries every year—acting like *Trojan horses*—could be continuously increasing the endemic nature of cysticercosis without the need of infected swine.

Neurocysticercosis in Western Europe has been overlooked for decades because it was considered rare. By the turn of the new Millennium—as part of a workshop on cestode zoonoses—Overbosch et al. [17] presented roughly estimates on the prevalence of this condition in the region and concluded that much remains to be learned on the actual burden of the disease. The recent creation of the Cysticercosis Working Group in Europe [18] is a good start to accomplish the goal to control the disease before it becomes a serious public health problem, as it is the case of the Southwestern US, a region that was almost free from neurocysticercosis some decades ago, and that nowadays, has become highly endemic [19].

The main purpose of this study is to present a review of the Western European literature on neurocysticercosis over the past 40 years, to estimate the magnitude of the disease in the different countries, to determine whether the number of autochthonous cases is increasing, and to illustrate the pattern of disease expression in the region.

Methods

A literature search of neurocysticercosis in Western Europe from 1970 to 2011 was performed using the electronic database of MEDLINE (National Library of Medicine, Bethesda, MD). Key words "*cysticercosis*" and "*neurocysticercosis*" were combined with the name of each of the Western European countries. Limits and language restrictions were not applied to the search; instead, abstracts, clinical notes without an abstract, and letters to the editor were reviewed to identify potentially eligible articles. Thereafter, a manual search that included the author's files as well as the list of references of cysticercosis books, position papers, and selected articles was reviewed, and relevant information was requested to colleagues and cysticercosis experts.

Selected studies were those including original data on patients with neurocysticercosis (either case reports or series of patients) evaluated within the Western European territory from 1970 to 2011. The work of European investigators outside the Continent, and duplicated publications were excluded. Articles separately reporting different aspects of the same series of patients (i.e., clinical manifestations in one paper and neuroimaging findings in other) and those combining previous published case reports or small case-series into a larger study were included in the analysis to gather additional information, but patients were counted only once. Authors were contacted when doubts remained after data revision and to request hard-to-find papers.

Besides the year, the country of origin of the publication and the number of cases, abstracted data of selected articles included (whenever possible): age and gender of reported patients, the specific form of neurocysticercosis (as shown

on neuroimaging studies), clinical manifestations, and whether the disease occurred in immigrants, international travelers, or European citizens who had never traveled abroad.

Results

The search identified 499 papers, of which 143 met inclusions criteria [20–162] Ninety-four of the 143 selected articles were single case reports, 33 were small series of less than 20 patients, and only 16 articles described larger series of patients. There was an important increase in the number of publications over the years (Fig. 1). Most articles came from Spain, France, Italy, The United Kingdom, Portugal, and Germany. After reviewing data—and counting only once those patients spited into separate publications—a total of 779 patients were identified (Table 1). Of these, only 28 were evaluated before 1985. By far, the countries with more reported patients are Portugal ($n = 384$) and Spain ($n = 228$), with the main difference that most patients from Portugal were evaluated from 1988 and 1992 in a single center, while patients from Spain were reported from all over the country and mainly in the past few years. France ($n = 80$) is another country with an important number of reported patients, followed by The United Kingdom, Italy, and Germany. In the remaining countries, there is either no data, or the reported number of patients is five or less.

The only field study conducted in Western Europe was performed in a rural village located in Northeastern Portugal. In that small community-based survey, four (5 %) out of 81 inhabitants had antibodies against cysticercus antigens in serum, and one of them had neurocysticercosis on CT scan [118]. In such village, all pigs were seronegative, suggesting that neurocysticercosis was not acquired by contact with locally infected taenia carriers [118]. There

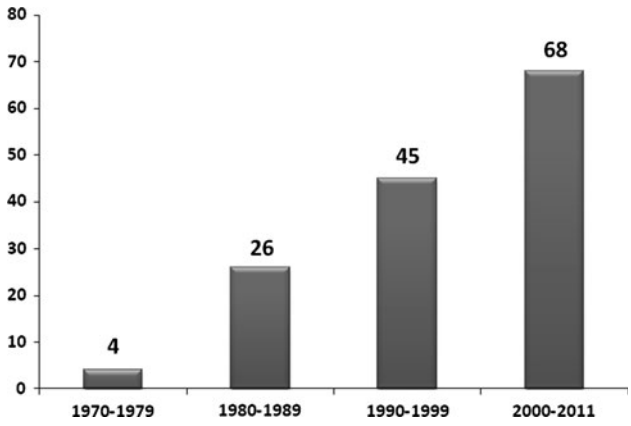

Fig. 1 Steadily increasing number of publication on patients with neurocysticercosis diagnosed in Western european countries

is more information on the prevalence of neurocysticercosis among neurologic patients attending specialized centers. That information, however, mainly came from Portugal and Spain. In the former, neurocysticercosis represented the 0.66 % of 35,000 CT scans performed at Santo Antonio Hospital (Porto) from 1983 to 1992, [124] and the 0.12 % of 30,000 CT scans at Santa María Hospital (Lisbon) from 1987 to 1992 [127]. In Spain, neurocysticercosis was the cause of 0.8 % of space-occupying brain lesion evaluated at the Neurosurgical Service of Xeral Hospital (Vigo) from 1983 to 1986 [77] and 0.1 % of neurologic patients seen at Doce de Octubre Hospital (Madrid) up to 1988 [85]. More recently, a mean of two new patients with neurocysticercosis per year has been evaluated during the past decade at Gregorio Marañón Hospital, a sanitary center that covers a population of 637,000 individuals living in Southeastern Madrid [75]. The only study attempting to determine the prevalence of neurocysticercosis in France was conducted in the Southeastern region of the country more than 20 years ago, where the authors found 29 cases over a 10-year period [147].

Information on the citizenship status is available in 371 (48 %) patients. Of these, 197 were immigrants from endemic countries and 174 were European citizens. History of traveling to endemic areas could be obtained in 31 of the latter, meaning that (at least) 143 individuals acquired the disease within the Western European territory (Table 2). For European travelers, there are few or unreliable details

Table 1 Western European countries with reported cases of neurocysticercosis (1970–2011)

Country	Number of publications	Reported patients
Austria	2	2
Denmark	3	3
Finland	1	1
France	27	80
Germany	11	12
Greece	4	6
Italy	15	21
Norway	1	4
Portugal	11	384
Republic of Ireland	1	1
Spain	45	228
Sweden	1	1
Switzerland	5	6
The Netherlands	2	4
United Kingdom	14	26
Total	143	779

No reported patients from Andorra, Belgium, Iceland, Liechtenstein, Malta, Monaco, and San Marino. Luxembourg had one reported patient but was not included as the original publication could not be found [164]

Table 2 Available data of patients with neurocysticercosis diagnosed in Western European countries (1970–2011) according to their citizenship status

Citizenship status (data available in 371 patients)	Evaluated in the new millenium (data available in 371 patients)	Patients with seizures (data available in 320 patients)	Patients with inactive disease (data available in 304 patients)
European non-travelers ($n = 143$)	17.5 % (25 of 143)	60.4 % (67 of 111)	30.4 % (41 of 135)
European travelers ($n = 31$)	58 % (18 of 31)	83.3 % (25 of 30)	–
Immigrants ($n = 197$)	73.1 % (144 of 197)	69.8 % (125 of 179)	15.3 % (22 of 144)

on the time spent aboard or the specific sojourn region. For non-European citizens, information on the time elapsed between immigration and the appearance of clinical manifestation is only described in 56 patients, and varied widely from 1 month to more than 20 years (mean 67.2 ± 64.5 months). Most of the 197 immigrants from endemic areas came from South America ($n = 112$) and Africa ($n = 45$), the former being most often diagnosed in Spain, and the latter in France and Portugal. Asian immigrants ($n = 16$), particularly from the Indian Subcontinent, were more often diagnosed in The United Kingdom. When comparing the citizenship status according to the year of diagnosis, we found that most immigrants and European travelers were diagnosed during the new Millennium. In addition, combined data from age and citizenship (available in only 281 patients) showed that Europeans with no history of travel abroad were older (mean age 51.9 ± 13 years) than European travelers (35.6 ± 15.5 years) and immigrants (31.2 ± 10.6 years).

Neurocysticercosis was fortuitously discovered (asymptomatic) in 186 patients (180 Portuguese, five Spaniards, and one Swiss). Information on the specific clinical manifestations was available in 506 of the 593 remaining patients with symptomatic disease. Of these, 368 (76 %) had seizures, 64 had evidence of intracranial hypertension, 35 presented with focal neurologic deficits, 23 complained of headache, 13 had progressive cognitive decline, and the remaining three patients had sudden death while in the emergency room. Information on the clinical manifestations according to the citizenship status was obtained in 320 patients. Immigrants and European travelers developed more often seizures than non-traveler European citizens (71.8 vs. 60.4 %).

Information on the specific form of presentation of neurocysticercosis could be gathered in 491 patients (including some patients with asymptomatic disease). Of these, 376 (77 %) had parenchymal brain cysticercosis, 60 had subarachnoid cysticercosis, 20 had ventricular cysts (most often located in the IV ventricle), 11 had spinal cord lesions, and 27 had mixed forms of the disease with involvement of the brain parenchyma and the subarachnoid space. Parenchymal brain cysticercosis included single or multiple cystic or ring enhancing lesions in 190 patients, and calcifications alone in 186 patients (some patients with active parenchymal brain lesions also have calcifications). Correlation of the specific form of neurocysticercosis with the citizenship status (possible in only 304 patients) showed that non-traveler European citizens had more inactive neurocysticercosis (parenchymal brain calcifications) than immigrants and European travelers (30.4 vs. 13 %).

Discussion

This review of the literature suggests that the prevalence of neurocysticercosis is increasing in some Western European countries to the point that this parasitic disease may become a public health problem in the next few years, at least in Spain. Also, the profile of diagnosed patients has changed. While in the 1970s and 1980s, neurocysticercosis was usually recognized in old or middle-aged European citizens living in rural villages (with no history of traveling aboard), nowadays the disease is most often diagnosed in young immigrants from endemic areas as well as in younger European citizens (travelers or not) living in urban centers. It is possible that a number of the rural cases of neurocysticercosis reported from Spain during the 1970s and 1980s, represented people who acquired the infection trough taenia carriers who get infected locally, as many of them live in farms where pig husbandry was deficient [13]. The endemia in Portugal during those years could also be related to poor husbandry. However, most of the Portuguese patients with neurocysticercosis were reported from urban centers (Lisbon and Porto) and not from rural areas, as it was the case of Spain [25, 121–127]. Moreover, the endemia of neurocysticercosis in Portugal was temporarily related with the massive return of Portuguese people from their African colonies (Angola, Mozambique) after their independence. So, it is also possible that a number of these patients acquired the infection while living abroad, and then became symptomatic after returning to Portugal.

While the information is incomplete, valuable data could be obtained on some differences in the pattern of disease expression of neurocysticercosis between immigrants/European travelers and non-traveler European

citizens (Table 2). In general terms, the former present more often with seizures and have less chance to have inactive disease (as a probable reflection of more recently acquired infections).

As previously noted, swine husbandry is currently considered adequate in Western Europe [16]. However, the hundreds of *T. solium* carriers entering to these countries every year could be continuously increasing the number of human cases of cysticercosis without the need of infected swine. Needless to say, the illegal migrational status of many of these persons complicates even more the access to household contacts of neurocysticercosis patients in the search of the *Taenia* carrier. On the other hand, most European doctors have assumed that when this parasitic disease occurs in an immigrant it is because the infection had been acquired at their country of origin. While that is probably true, it must not be forgotten that a common social phenomena observed after mass population movements is that family members usually join pioneer immigrants some years after their settlement aboard, So, it is also possible that, in a given immigrant, the disease was acquired while already living in Europe through a recently arrived relative infected with *T. solium*. This hypothesis is supported by the fact that some immigrants have developed symptoms related to relatively fresh infections, i.e., single-enhancing lesions, more than 20 years after being living in Europe. In almost all of these cases, it has not been investigated the presence of taeniasis in the patient's close environment. Also, there is scarce published information on whether taenia carriers have been compulsorily searched among household contacts of European citizens with neurocysticercosis who have not traveled abroad. In this regard, it must be remembered the lesson given—almost 20 years ago—by the neurocysticercosis outbreak that occurred in the Orthodox Jewish community in New York City, where domestic employees recently immigrated from Latin America were found to be *T. solium* carriers, infecting people for whom they worked through a non-hygienic handling of food which, in turn, allowed the acquisition of the disease through the fecal-food-oral route [163].

While this review presents, for the very first time, evidence on the increasing magnitude of neurocysticercosis in Western Europe, it has the limitation that data have not been completely reported, and important information could have been missed. Also, there must be a number of patients reported in local—non-accessible—journals, which are now part of the so-called "lost science". Moreover, there are no large-scale field studies attempting to determine the real number of infected individuals in rural or urban centers or multicenter hospital-based studies to evaluate the percentage of neurocysticercosis cases among neurologic patients attending specialized medical centers. Therefore, exact numbers on the prevalence and incidence of this disease in Western Europe cannot be given but, on the basis of the experienced gathered from countries that were free of the disease and that are now endemic, it is plausible that we are just seeing the tip of the iceberg, and that many more cases have passed undiagnosed or non-reported.

Conflict of interest None.

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