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CLINICAL, RADIOLOGICAL AND CEREBROSPINAL FLUID PRESENTATION OF NEUROCYSTICERCOSIS

A PROSPECTIVE STUDY

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SUMMARY — The wide clinical spectrum of neurocysticercosis has led to many attempts at clinical, radiological, CSF and other classifications. Based on an objective review of the relevant literature and on a prospective study of 42 patients with active neurocysticercosis, a new classification is proposed, based on clinical, tomographic, magnetic resonance and CSF evidence of viability of cysts. The first step is to define whether the disease is active or not. Inactive disease may be parenchymal calcifications or hydrocephalus. Active disease may be intraparenchymal, extraparenchymal or mixed. Statistical analysis of 42 cases with active disease shows intraparenchymal disease to occur in younger patients, perhaps more frequently in females, and to have a better prognosis than extraparenchymal of mixed disease. The latter appears to have the worst prognosis. Therapeutic implications are that only active disease warrants etiological therapy. There remain doubts about the best therapy for some infrequent subtypes of extraparenchymal and mixed disease.

Apresentação clínica, radiológica e no líqüido cefalorraquidiano da neurocisticercose: estudo prospectivo.

RESUMO — O amplo espectro clínico da neurocisticercose deu espaço a muitas tentativas de classificações clínicas, radiológicas e de LCR, entre outras. Baseados em revisão objetiva da literatura relevante e em estudo prospectivo de 42 casos de doença ativa, nova classificação é proposta com base em evidências clínicas, tomográficas, de ressonância magnética ou LCR indicando viabilidade de cistos. O primeiro passo é estabelecer se a doença é ou não ativa. Doença inativa pode ser representada por calcificações intraparenquimatosas ou hidrocefalia. Doença ativa pode ser intra ou extraparenquimatosa, ou mista. Análise estatística de 42 casos com doença ativa demonstra que doença intraparenquimatosa ocorre em um grupo mais jovem, talvez mais no sexo feminino, e tem melhor prognóstico que doença extraparenquimatosa ou mista. Doença mista parece ter o pior prognóstico. Implicações terapêuticas são que somente doença ativa deve receber tratamento etiológico. Permanecem dúvidas sobre a melhor conduta em algumas formas infreqüentes de doença extraparenquimatosa ou mista.

Neusocysticercosis is the result of the invasion of the central nervous system (CNS) by larvae of Taenia solium. Oral ingestion leads to cysticercosis when embryos cross to the blood stream and reach body tissues. The hexacanth embryo evolves to Cysticercus cellulosae or to Cysticercus racemosus [1,2]. Larvae show great preference for muscle, brain and cerebrospinal fluid (CSF) cavities due to extensive blood supply, including of the choroid plexi [31]. Between 60 and 92% of patients

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have parasites in the CNS parenchyma or CSF cavities, more frequently in cerebral hemispheres, ventricles and subarachnoid spaces around the brain [16]. The frequency of parasite location in brainstem, cerebellum, spinal cord or canal may have been underestimated by the poor resolution of computed tomography (CT) as compared to magnetic resonance imaging (MRI) in these areas [2] (Radvany and Marie, personal communication). Once established the parasite evolves through vesicular, colloidal, granular-nodular and calcified stages in approximately 2-5 years [11,18]. Signs and symptoms of neurocysticercosis may be related to mass effect of the evolving parasite and to its epileptogenic effect on the brain parenchyma. There may be arteritis close to the location of the parasite and meningeal irritation due to release of cyst material in CSF. Hydrocephalus may be secondary to cyst impactation in foramina, to acute or chronic ventricular inflammatory changes [1,2,4,16,17]. These pathophysiological mechanisms may operate concomitantly, in various combinations, or still in combination with other mechanisms recently demonstrated by MRI [2] (Radvany and Marie, personal communication). Prognosis of neurocysticercosis is related directly to the success of therapeutic manouvres to erradicate live parasites, which must be assumed to be multiple even when CSF, CT or other x-ray imaging methods demonstrate only one cyst [4,23]. Initial findings of MRI corroborate this point of view [4] (Radvany and Marie, personal communication). Prognosis is also related to the degree of success of therapy directed towards decreasing the effects of inative parasites on brain parenchyma, and of chronic meningeal and ventricular changes which take place in some patients late in the disease [11,22,23]. Therapy of neurocysticercosis may be divided in etiological, when it attempts to erradicate live parasites, or symptomatic when it attempts to alleviate consequences of active or inactive parasites on brain parenchyma, CSF dynamics and meninges [2,6]. Etiological therapy is restricted to the presently available «cysticidal» agents. Praziquantel has been extensively evaluated for a number of years [2,3,5,6,24]. Albendazole has been evaluated preliminarily [12]. There is much indirect evidence that praziquantel is more efficient in brain parenchyma than in CSF cavities [22,29]. Surgical excision of cysts a widely used procedure across neurosurgical departments, cannot be considered etiological as it removes single or at the most few cysts [2,3,5]. Surgical excision of large parenchymal cysts or of intraventricular cysts, CSF shunting procedures, diuretics and steroids are the available alternatives of symptomatic therapy. Epilepsy is a common complication of neurocysticercosis and is treated accordingly [2].

Classification of neurocysticercosis — The spectrum of neurocysticercosis with regard to its clinical, CSF, radiological, surgical and pathological aspects has prompted investigators to use numerous classifications or descriptions for forms of the disease which may appear to be specific entities. Many of these attempts were carried out before the advent of CT, when surgery was necessary to establish the nature of a mass lesion identified by angiography or ventriculography. Terms such as tumoral, edematous [13] or pseudotumoral [10] have been used to describe intracranial hypertension. Convulsive [25] and epileptic [28] apparently refer to those patients that present with epilepsy, although it is not clear whether other symptoms or signs may have been concomitant. In one of the largest series published, including 500 cases studied between 1956 and 1979, Takayanagui and Jardim [28] were satisfied that all cases could be classified as epileptic, hypertensive, meningitic, psychic or apopletic forms. Loo and Braude [16] circumvented the problems by classifying their 23 patients in groups I, II and III, as defined earlier by Stepien and Chorobski [27]. Group I (7 patients) appears to have been the tumoral form of Facure et al.[13], group II the «encephalitic» form of Rodriguez-Carbajal et al.[21], and group III to include all other possible presentations specially those with hydrocephalus and basal leptomeningitis. The latter has been referred to as the racemose form. One of the few specific syndromes to emerge from a review of the clinical spectrum of neurocysticercosis [2] has been called «acute encephalitic» [7,9,21,27], «acute edematous» [20] and «cysticercus encephalitis» [17] or received yet other denominations. Other investigators have chosen not to attempt classifications and to describe patients by symptoms, signs and findings on ancillary investigations [19]. As a whole the attempts referred have not taken into account the concepts of inactive forms or of disease activity with relapses and remissions. Similarly, factors related to prognosis and therapy were not considered. Sotelo et al.[23] attempted to address this question in a study of 753 patients evaluated between 1977 and 1982. They failed to overcome a basic drawback of their predecessors, the overlap in clinical, radiological, CSF and pathological observations. Some 30% of their patients appeared to have active and inactive disease concomitantly. As emphasized in the same publication, «in clinical trials, well-defined forms of neurocysticercosis are prerequisites for the precise evaluation of results» [23]. The lack of

even gross definitions of cysticercosis has led to much confusion with regard to the effects of treatment, for example praziquantel. In a recent symposium in São Paulo (Spina-França et al., personal communication) there was no agreement on the benefits of such therapy, while a partially controlled study has demonstrated its effect on intraparenchymal neurocysticercosis [24].

Our approach has evolved over a few years [2-4] in an attempt to simplify and include concepts of disease activity as defined by clinical, imaging or CSF means. Our objective has been to develop a classification which provides clinicians and investigators with data of clear diagnostic, prognostic and therapeutic relevance. Table 1 shows the proposed classification. Inactive and active refer to etiological disease process, i.e., to forms in which there are demonstrated or presumed unviable and viable parasites, respectively. The inference is that inactive forms warrant symptomatic treatment while active forms are indications for etiological (i.e. «cysticidal») therapy.

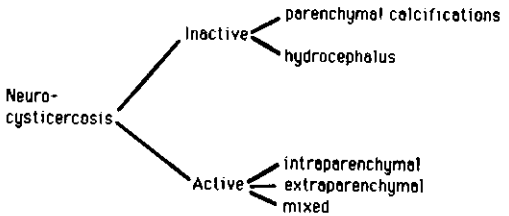

Table 1 — Classification of neurocysticercosis according to a prospective study of 42 patients with active disease and to published cases of inactive disease. Socalled miliary racemose and basal leptomeningeal neurocysticercosis are considered as other active forms.

METHODS

In the periods of January 1983 to August 1984 and January 1985 to May 1986 all patients admitted to the Clinical Neurology Unit at Hospital Nossa Senhora das Graças with a diagnosis of active neurocysticercosis were included in prospective studies of the efficacy of new therapeutic regimens with praziquantel [3,5]. Active disease was defined by detection of viable cysts in brain parenchyma (intraparenchymal form) or in CSF cavities (extraparenchymal form) as viewed by CT, or detection of the typical CSF reaction [14]. Patients in whom both evidence of disease activity in CSF and on CT found were labeled the mixed form. Specifically excluded from this study were patients with multiple calcifications in the cerebral parenchyma and patients with chronic hydrocephalus, without parenchymal cysts or CSF inflammatory reaction.

On admission history and physical examination were carried out according to a previously determined schedule by at least 2 certified neurologists. CTs were obtained in all patients on admission following standardised procedures, before and after intravenous contrast injection, in the same scanner (EMI 1010), by a neuroradiologist unaware of clinical data. CSF was obtained by lumbar puncture or upon insertion of ventriculoperitoneal shunts and CSF was analysed according a standardised routine which included cell counts, determination of sugar and total protein, syphilis immunology, complement fixation test for cysticercosis, preparations for fungi and Koch bacilli. EEG, chest x-rays, full blood counts, erythrocyte sedimentation rate, serum creatine and sugar were determined. Patients included in the second study period also underwent determination of bilirrubin, liver transaminases, alkaline phosphatase and urine analysis as part of a prospective clinical trial of a novel therapeutic regimen of praziquantel. Patients were followed clinically, by CSF and CT at 6 monthly intervals after initial evaluation and treatment. Results were analysed by Student's t-test and χ^2 test with Yates correction.

RESULTS

Of the 42 patients included in the present study 19(45%) had the mixed intra and extraparenchymal form of neurocysticercosis. Twelve patients (29%) had the intraparenchymal and the remaining 11(26%) had the extraparenchymal form. There was a trend towards

the mixed and extraparenchymal forms to include more males, as well as towards the group with the mixed form having a longer history ($p > 0.05$). Intraparenchymal neurocysticercosis was present in a younger age group ($p < 0.01$, table 2).

	Mixed	Intraparenchymal	Extraparenchymal
Age (m ± sd, years)	35 ± 14	24 ± 14*	30 ± 14
Age (range, years)	2 - 62	6 - 51	5 - 54
Male sex	12	5	7
Length of history (m ± sd, months)	54 ± 88	21 ± 55	20 ± 50
Number	19	12	11

*Table 2 — Age, sex, length of history and number of patients with mixed, intraparenchymal or extraparenchymal forms of active neurocysticercosis. m, mean; sd, standard deviation; *, significantly different from the other two groups.*

Analysis of symptoms and signs on examination at presentation of the three different forms of active neurocysticercosis (Table 3) indicated that intraparenchymal and mixed forms have somewhat similar pictures, epilepsy being the symptom found in 100% and 68% of cases respectively, followed by headache respectively in 33 and 58% of the patients. In the mixed form psychiatric features (32%), nausea and vomitting (16%) and double vision (11%) followed in frequency at presentation. In the intraparenchymal form psychiatric features were found at presentation in 17%. Symptoms at presentation in the extraparenchymal form were radically different. Headache was found in 91% and nausea and vomitting in 54%. Epilepsy and psychiatric features were found at presentation in only 1 patient each. The frequency of headache was greater in the extraparenchymal than in the intraparenchymal group ($p < 0.05$). The frequency of epilepsy was greater in the intraparenchymal than in the extraparenchymal form ($p < 0.001$) and in the mixed than in the extraparenchymal form ($p < 0.01$). Nausea and vomitting were more frequent in the extra than in the intraparenchymal group ($p = 0.05$). Physical examination was normal in 42% in the mixed

	Forms of neurocysticercosis					
	Extraparenchymal		Intraparenchymal		Mixed	
	n	%	n	%	n	%
Symptoms						
Epilepsy	1	9	11	92	12	74
Headache	10	83	5	42	10	53
Nausea + vomitting	8	73	2	17	4	21
Psychiatric disturbance	1	9	3	25	3	16
Double vision	0	0	0	0	3	16
Signs						
None	6	54	7	58	7	37
Papilloedema	2	18	2	17	4	21
Nuchal rigidity	2	18	0	0	3	16
Ataxia	0	0	1	8	3	16
Ocular	0	0	1	8	4	21
Pyramidal	1	9	0	0	3	16
Total	11		12		19	

Table 3 — Symptoms and signs on examination of 42 patients with active neurocysticercosis admitted to a prospective study. Ocular is nystagmus and/or 6th nerve paresis. Pyramidal is pathologically increased deep tendon reflexes and/or motor deficit.

form, 50% in the intraparenchymal form and in 45% in the extraparenchymal form ($p > 0.05$). Patients with the mixed intra and extraparenchymal form had the more florid signs with increased tendon reflexes (32%), bilateral papilloedema (16%), 6th nerve paresis (16%) and ataxia (11%). Signs in the intraparenchymal form were infrequent and included bilateral papilloedema (2 patients), ataxia (2) and nystagmus (1). Similarly infrequent were signs in extraparenchymal form, which consisted of bilateral papilloedema and increased tendon reflexes (3 patients each). Association of signs and symptoms were frequent. Three patients with the mixed intra and extraparenchymal form had epilepsy and intracranial hypertension at presentation, and 2 had epilepsy and a psychiatric syndrome. Two patients with the intraparenchymal form had epilepsy and intracranial hypertension and one had psychiatric symptoms along with intracranial hypertension, while 2 had epilepsy combined with psychiatric symptoms. In the extraparenchymal form, only one patient had epileptic seizures which were superimposed on signs and symptoms of intracranial hypertension. Combinations of symptoms occurred in 5 of 19 patients with the mixed intra and extraparenchymal form of neurocysticercosis (26%), in 5 of 12 patients with the intraparenchymal form alone (42%), and in one of 11 patients with the extraparenchymal form (9%, $p > 0.05$).

The clniical definition of forms of neurocysticercosis was looked at by considering the frequency of 10 definite signs or symptoms in each patient, i.e., epilepsy, headache, nausea and vomitting, psychiatric disturbances, double vision, papilloedema, nuchal rigidity, ataxia, increased tendon reflexes and oculomotor disturbances, the latter defined as nystagmus or 6th nerve palsy. The numbers of symptoms were respectively 2.27 ± 0.73, 2.16 ± 0.71 and 2.63 ± 1.3 (mean $\pm$ standard deviation) in the extraparenchymal, intraparenchymal and mixed patients. The frequency of prominent symptoms was greater in the mixed than in the intraparenchymal form ($p < 0.01$). CSF results (Table 4) isolated the intraparenchymal group from the mixed and extraparenchymal cases in a definitive manner,

CSF	Mixed	Intraparenchymal	Extraparenchymal
Cells (n)	36 ± 71	1 ± 1	72 ± 90
Mononuclear (%)	94 ± 13	75 ± 45	88 ± 21
Eosinophils (%)	2 ± 8	0	11 ± 21
Polymorphs (+)	3 ± 12	0	0.3±0.6
Protein (mg/dl)	65 ± 69	36 ± 19	53 ± 44
Glucose (mg/dl)	69 ± 23	67 ± 12	59 ± 14
Complement fixation test (% positive)	47	0	36
Total	19	12	11

Table 4 — Findings on examination of CSF of 42 patients with extraparenchymal, intraparenchymal or mixed forms of neurocysticercosis admitted to a prospective study.

since by definition patients with the intraparenchymal form could not had evidence of disease activity in the CSF at the time of presentation. CT (Table 5) isolated the extraparenchymal group from the intraparenchymal and mixed cases, as by definition there could be no evidence of disease activity in the brain, cerebellum or brainstem. There were 2 patients in this group with intraparenchymal calcifications, indicating that they had had, at some time in the past, intraparenchymal disease. One of these 2 patients had active epilepsy at the time of presentation, the only patient in this group with clinical evidence of intraparenchymal disease. Complement fixation test was negative in all cases of intraparenchymal disease, indicating that these patients had not had extraparenchymal disease in the recent past. In the mixed form of neurocysticercosis CT showed complex combinations of parenchymal and extraparenchymal abnormalities. Intraparenchymal cysts combined with other abnormalities were seen in 14(74%) of the 19 cases. In 9 cases (47%) there were calcifications indicating that some of the parasites were already at their final inactive biological stage. Three patients with intraparenchymal disease showed some evidence of extraparenchymal disease before clinical presentation, as suggested by hydrochephalus and ventricular asymmetry (Table 5). The so-called miliary, racemose and basal meningitic forms of neurocysticercosis were present in respectively 4, 2 and 2 cases, included in the presently advocated classification as all other cases.

CT scan	Mixed	Intraparenchymal	Extraparenchymal
Normal	—	—	6
IP cysts	4	5	—
IP cysts + other findings	14	7	—
Calcifications	9	5	2
Hydrocephalus	7	1	3
Ventricular asymmetry	4	2	1
Generalized edema	2	1	0
Total	19	12	11

Table 5 — Results of CT in 42 patients with extraparenchymal, intraparenchymal or mixed neurocysticercosis included in a prospective study. IP, intraparenchymal.

The prognostic value of the proposed classification was analysed by determining the clinical, CT and CSF remission and relapse rates in the 38 patients for whom data was available (Table 6). All patients irrespective of form of disease were treated according to three therapeuthic regimens, i.e., praziquantel in doses of 50 mg/kg/day for 15 days, 75 mg/kg/day for 15 days or 100 mg/kg/day for 10 days. Details are published elsewhere [2,3,5]. Symptomatic therapy in the form of ventriculoperitoneal shunting, steroids, diuretics and antiepileptic drugs was used as necessary. There was a trend towards worse prognosis in the mixed form than in the extraparenchymal forms as measured by the CSF remission rate ($p > 0.05$) and towards improved prognosis of the intraparenchymal form when compared to both extraparenchymal and mixed forms by clinical outcome ($p > 0.05$). The trend is supported by the need for ventriculo-peritoneal shunting procedures, which were carried out in 2 patients with the extraparenchymal and in 6 with the mixed form of neurocysticercosis. These warranted respectively 3 and 9 shunt reviews. Bacterial meningitis complicated 2 of the total of 20 shunting procedures. There were 2 deaths during follow-up. A patient with the extraparenchymal form died 29 months and another with the mixed form died 16 months after entering the study.

	Remission rate (last follow-up)			
Form of disease	CSF	CT	Clinical	Patients
Extraparenchymal	87 % (13 ± 9) *	—	50 % (13 ± 9)	8
Intraparenchymal	—	75 % (17 ± 6)	83 % (21 ± 6)	12
Mixed	40 % (17 ± 7)	66 % (17 ± 7)	61 % (20 ± 5)	18

Table 6 — Percentage of patients in remission as defined by CSF, CT or clinical examination. Remission was measured at last follow-up (months, mean ± standard deviation) after the initial therapeutic regimen of praziquantel ($p < 0.005$ Fisher's test).*

COMMENTS

Neurocysticercosis is a disease process somewhat similar to multiple sclerosis [15]. Its clinical presentation is varied and the clinical course marked by remissions and relapses related to immunological phenomena, verified by fluctuating CT and CSF evidence of inflammation. The degree and distribution of parenchymal inflammation is directly related to the presence of viable cysts. Meningeal inflammation as verified clinically and by CSF examination is related to the presence of viable cysts in the subarachnoid spaces [2,5]. Contrary to multiple sclerosis, in neurocysticercosis the antigen is relatively well identified. It may be one or many of the various components of one or more of the larval forms of Taenia solium. Cysticercus cellulosae in its vesicular stage [11] is viable and capable of inducing the typical immunological reaction observed in CT [18] and in CSF [14]. In its calcified stage Cysticercus cellulosae is not

capable of inducing immunological phenomena [2,18,20,23]. It is still unclear whether Cysticercus racemosus or the colloidal and granular-nodular [11] stages of Cysticercus cellulosae are immunologically competent.

The classification proposed here covers the clinical characteristics of fluctuating course and overlapping symptoms and signs, both related to multiple cysts at varying stages of their biological cycle at a given moment. The classification is one of etiological rather than clinical disease activity. Activity has been defined as the demonstration by CT or CSF evidence of the presence of intact parasites or of immunological reaction to them. At this stage greater precision about viability of the parasite is difficult because the inflammatory reactions demonstrated by CT or CSF in patients with racemosae, colloidal or granular-nodular cysticerci may be due to vesicular cysticerci not demonstrated by these methods. MRI, with its capacity to show cysticerci in greater detail, allowing visualization of the scolex [2], (Radvany and Marie, personal communication) may also be able to demonstrate all parasites in an individual, thus determining the biological stages of parasites in a given subject, as opposed to their immunological competence. As argued by Campos and Perpetuo [8] previous syndromic, pathological and radiological classifications of neurocysticercosis create unnecessary complexity and are by definition incomplete. As imaging methods advance pathological correlates become less relevant than when morphology and biology of parasites could not be ascertained by, for example, angiography, ventriculography or EEG. Radiological classifications based on CT [18,20] have given distorted ideas of the frequency of the various clinical presentations, for example over-rating the miliary (encephalitic or edematous) presentation of intraparenchymal neurocysticercosis. This has led at least one review to assume the CT data was clinically based [1]. Furthermore, in 3 of the major radiological studies available [18,20,21] there is no clear indication of clinical presentation, length of history, follow up, therapeutic procedures or CSF examination. Rodriguez-Carbajal et al.[21] concluded that 65% of their cases presented with the miliary (acute encephalitic, edematous) form, while Mazer et al.[18] and Minguetti and Ferreira [20] found approximately 20% in their large samples of patients for which there was no definition of etiological or immunological activity. In the present study of 42 patients with active neurocysticercosis only, there were 3 patients with miliary neurocysticercosis in the group with the mixed and one in the group with the intraparenchymal form of the disease, a percentage of less than 10%. This must be the more generally applicable frequency of this form since these 42 patients presented successively to a clinical neurology unit in a general hospital in an endemic area. Curitiba is in fact where the studies of Mazer et al.[18] and Minguetti and Ferreira [20] were carried out.

The argument of Sotelo et al.[23] who stated that «the most important feature for therapy of neurocysticercosis is analysis of the activity of the disease; immunodiagnostic tests and therapeutic decisions are different when the parasites are alive in comparison to cases where a previous infestation was eliminated by the host immune response and neurological deficits are due only to sequelae of granulomas and residual fibrosis», underlines much the same approach to diagnosis and classification as that of the present study. In their large sample of 753 patients inactive forms of neurocysticercosis were subclassified in parenchymal calcifications (57.6%) and hydrocephalus secondary to meningeal fibrosis (3.8%). Active forms were subclassified in arachnoiditis (48.2%), hydrocephalus secondary to meningeal inflammation (25.7%), parenchymal cysts (13.2%), brain infarction secondary to vasculitis (2.3%), mass effect due to a large cyst or cyst clumps (1.0%), intraventricular cysts (0.7%) and spinal cysts (0.7%). This classification leaves behind its archaic pathological, radiological or syndromic predecessors and applies concepts of disease activity based on parasite biological or immunological viability rather than on clinical activity of disease only. It does not, though, reach its stated objective of separating active from inactive cases. Approximately 27% of the patients had both active and inactive disease. It is difficult to envisage how this overlap in disease activity would make diagnostic or therapeutic decisions simpler. The study also failed to address the question of racemose neurocysticercosis, apparently including racemose with viable cysts. Basal meningitis was addressed much the same manner as in the presently proposed classification, i.e., active or inactive depending on CSF or CT demonstration of viable parasites or immune reaction [23].

The miliary form of neurocysticercosis, believed by many to be an acute disease process leading to death due to seizures and intracranial hypertension or to clinical resolution after therapy with steroids [2] poses further nosological problems. Generalised

cerebral edema with numerous ring-shaped contrast enhancing areas are seen on CT on presentation [2,21]. Upon clinical resolution a great number of parenchymal calcifications are seen [2,4,18,20,21]. The clinical and radiological picture as well as the clinical course and the subsequent appearance of calcifications suggest that each of the ring-shaped contrast-enhancing areas surround viable cysts which have invaded massively the CNS in an acute phase of the disease, as seen in many other parasitoses of the CNS such as malaria, african and american trypanosomiasis and schistosomiasis [2]. Very preliminary MRI data indicate that these small cysts may not be biologically viable as they appear not to have a scolex [2], (Radvany and Marie, personal communication). Pathological examination of brains in this acute phase does not appear to have been carried out sistematically [11,21]. The fact that those patients who survive the phase of severe intracranial hypertension and seizures recover fully in periods of 3 monthis to 3 years [2,7,9,18,20,21], and that not all patients develop multiple calcifications, remains to be explained in the light of pathological or MRI studies of larger series of patients.

The classification proposed here is unique in its methodological validation. Although the numbers are small they are representative due to the prospective standardised collection of data, with a specified study period. The location of the study at a clinical neurology unit is basic to avoid sampling bias towards more severe or towards more chronic cases, as observed respectively in neurosurgical or tropical disease department-based studies. Radiological series create bias similar to that of neurosurgical series, and do not offer appropriate clinical, CSF or follow-up data. Clinically based, prospective, consecutive series of active neurocysticercosis have been published infrequently and have not generally exceeded 100 cases [16,19]. The validity of the present classification has been demonstrated populationally since the intraparenchymal form was found in a significantly younger age group and perhaps more frequently in women. Semiological validity can be inferred from the possibility to predict that patients with epilepsy are very likely to have intraparenchymal or mixed forms, or that patients with headache, nausea and vomitting are most likely to have the extraparenchymal form. If headache, nausea and vomitting are accompanied by epilepsy or psychiatric disturbances, the most likely diagnosis will be the mixed form of neurocysticercosis. The separation of the three forms is quite clear on CSF and imaging methods. Therapeutically, ventriculoperitoneal shunting was needed in the mixed and extraparenchymal forms, but not in the intraparenchymal form. Although measurement of remission rates by CSF, CT and clinical methods failed to demonstrate statistical differences among the three groups, the need for shunting, shunt reviews and bacterial meningitis as well as the 2 deaths indicate the worse prognosis of the mixed and extraparenchymal forms of the disease.

Therapeutic implications of the classification proposed here are generally similar to those of Sotelo et al.[23], except that the draw-back of patients being at the same time carriers of active and inactive disease has been overcome. Demonstration of disease activity with intra and/or extraparenchymal neurocysticercosis appear to be clear indications for etiological therapy with specific parasiticidal agents. Some points remain obscure, such as the disagreement on whether the acute miliary form, the racemose form and some extraparenchymal presentations, specially intraventricular neurocysticercosis, should be treated etiologically [29]. The therapeutic parasiticidal effect of praziquantel has been demonstrated in a partially controlled study of intraparenchymal cases only [24]. Other available therapeutic manouvres are symptomatic and include surgical ressection of cysts when they are resistant to parasiticidal therapy or when they are very large and accessible in patients with critical intracranial hypertension. Intraventricular cysticercosis appears to be specially resistant to parasiticidal therapy [29]. Otherwise surgery is restricted to ventriculoperitoneal or other shunts [13,22]. Shunting is as common as its complications in these patients, with frequent revisions and placement of second, third or further shunts. Steroids, specially dexamethasone, have been used extensively in patients with cerebral edema demonstrated by CT [20]. Recently it has been suggested that dexamethasone may lower proziquantel concentration in the plasma by 50% [30]. The authors recommended that steroids should not be used routinely with praziquantel but rather be reserved for the intracranial hypertensive crises which may take place during praziquantel administration. Diuretics such as furosemide, manitol and glycerol are useful adjuncts in the therapy of intracranial hypertension. Other symptoms such as epilepsy warrant specific therapy [2].

Further subclassification of active neurocysticercosis in infarction due to arteritis, mass effect due to cyst size or clumps, arachnoiditis, hydrocephalus of varying origins,

intraventricular cysts and the inclusion of a spinal form without specification of its intra or extraparenchymal nature, as advocacted by many in the past and by Sotelo et al.[23] serves only to emphasize the well-known clinical, radiological and CSF pleomorphism of the disease. If one were to classify multiple sclerosis according to its multitude of clinical, biochemical, radiological and neurophysiological correlates, the classification would be endless rather than useful for prognostic or therapeutic purposes.

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