Letter to Editor/Carta ao Editor

Neurocysticercosis: a new trend in SUDEP research?

Neurocisticercose: uma nova tendência em pesquisas de SUDEP?

Fulvio Alexandre Scorza[1], Ricardo Mario Arida[2], Philipe Ribeiro Furtado de Mendonça[1], Esper Abrão Cavalheiro[1] and João Pereira Leite[3]

Dear Editor:

Epilepsies constitute one of the most common serious brain disorders and have no geographic, social, or racial boundaries; they occur in men and women and affect people of all ages, although more frequently affecting young people in the first 2 decades of life and people aged >60 years. Worldwide, there are at least 50 million people who have epilepsy, and many of these have seizures that are refractory to treatment with the currently available therapies[1]. From all of the effects of the epilepsies, perhaps the most concerning is sudden unexpected death in epilepsy (SUDEP).

Unfortunately, very little progress has been made in preventing the occurrence of SUDEP and, in addition, SUDEP is rarely discussed among neurologists and scientists. As we know, ~1 in 1,000 patients with chronic epilepsy will die suddenly, unexpectedly, and without explanation each year[2]. Furthermore, epilepsy is associated with a 2- to 3-fold increase in mortality compared to the general population, and SUDEP is the most important direct epilepsy-related cause of death[3]. To date, a wide range of factors for SUDEP have been assessed, including refractoriness of the epileptic condition, occurrence of generalized tonic-clonic seizures, antiepileptic medication (polytherapy with antiepileptic drugs), young age, duration of the seizure disorder, early onset of epilepsy, and winter temperatures[4]. Knowledge of the risk factors underlying SUDEP could guide investigations into its pathophysiologic mechanisms[5]. In this context, understanding the mechanisms underlying SUDEP may lead to the identification of previously unrecognized risk factors that are more amenable to correction[6]. Although different mechanisms may play separate roles in different cases, the 2 major domains that are involved in SUDEP are autonomic, i.e., cardiovascular, and respiratory[6]. In brief, respiratory compromise, such as increased lung weight, pulmonary congestion, or edema, appears frequently in postmortem examinations of SUDEP victims[5]. From a cardiovascular point of view, it is very probable that cardiac changes during and between seizures play a potential role in SUDEP[4].

In recent years, significant progress has been made in identifying some of the associated risk factors for SUDEP, the clearest of which are uncontrolled epilepsy and a history of generalized tonic-clonic seizures[6]. Conversely, it is important to note that it remains to be elucidated which factors make an individual more susceptible to this outcome than another with comparable epilepsy severity. Following this reasoning, a very interesting recent paper, reporting a case of SUDEP in a patient with a solitary cysticercosis lesion in the cerebral cortex[7], inspired us to propose a new hypothesis concerning SUDEP. Approximately 40 million people who have epilepsy live in countries with poor resources, and the major cause of this higher rate of epilepsy is related to the presence of endemic parasitic diseases such as neurocysticercosis (NCy). The clinical features of NCy are sufficiently well recognized and may present with almost any neurological manifestation. An enormous number of case reports have described every possible sign or symptom; however, the vast majority of cases present as either headaches (due to intracranial hypertension) or seizure disorders. Classically, NCy is a major contributor to the burden of seizures and acquired epilepsy in developing countries but is also becoming a health concern in developed countries[8]. For example, in the United States, Wallin and Kurtzke showed that over the past 2 decades, NCy was found in 10% of patients who had seizures and were evaluated in an emergency department in Los Angeles and in 6% of patients in New Mexico, qualifying NCy as an important emerging infection[9]. The treatment modality available to individuals with NCy for preventing or decreasing the severity and number of seizures is anti-epileptic drugs.

To our knowledge, there are very few reports describing the association between sudden death and NCy[10–12]. For example, in 1997, Ndhlovu described a case of sudden death that turned out to be an unexpected case of NCy. The author calls attention to the fact that most doctors expect cerebral NCy to present with seizures and have forgotten its other clinical manifestations[10]. Verma and colleagues reported a rare case of sudden death in an apparently healthy asymptomatic young adult male who was involved in a vehicular accident and died almost instantaneously due to the rupture of cysticerci cysts during trauma[11]. More recently, Llompart Pou and coworkers reported an acute case of a native woman from Peru who had cephalalgia that rapidly worsened and caused sudden and unexpected death[12]. In brief, the authors reported that the patient came to the emergency room complaining of severe headache for the previous 6h. On arrival, she acted strangely, although no seizure activity was noted and she had not been taking medication. She was placed under observation, and almost 2h later she presented with cardiorespiratory arrest and died after 20 min of cardiopulmonary resuscitation[12].

Considering the facts described above, the major question now is whether there is any possible relationship between NCy and the occurrence of SUDEP. As exact knowledge regarding this association

1. Disciplina de Neurologia Experimental, Universidade Federal de São Paulo, São Paulo, SP. 2. Departamento de Fisiologia, Universidade Federal de São Paulo, São Paulo, SP. 3. Departamento de Neurologia, Faculdade de Medicina, Universidade de São Paulo. Ribeirão Preto, SP.
Address to: Dr. Fulvio Alexandre Scorza. Disciplina de Neurologia Experimental/ UNIFESP. Rua Botucatu 862, Edifício Leal Prado, 04023-900 São Paulo, SP, Brasil.
Phone: 55 11 5549-2064; 55 11 5573-9304
e-mail: scorza.nexp@epm.br
Received in 13/07/2011
Accepted in 30/09/2011

is lacking, some possibilities could be evaluated. Considering that NCy is a major cause of acquired epilepsy in Latin American countries and that the main risk factors for SUDEP are associated with poorly controlled seizures, our research group is in agreement with Professor Natasha Holmes and colleagues in proposing that because of the high prevalence of seizures in NCy, SUDEP may also play a large role in this disease[7]. Overall, experimental, epidemiological, and clinical studies will help in precise evaluation of the possible and real association between NCy, seizure occurrence, and SUDEP. For future studies, we suggest increased efforts, mainly in countries where NCy is endemic, in order to correlate the clinical, morphological, and physiological features of NCy patients who suffered SUDEP. In conclusion and despite some progress, SUDEP remains a significant clinical problem. Unfortunately, as all of the risk factors, mechanisms, and specific methods for preventing SUDEP have not been identified, exercising caution is prudent and necessary.

REFERENCES

1. De Boer HM, Mula M, Sander JW. The global burden and stigma of epilepsy. Epilepsy Behav 2008; 12:540-546.
2. Hirsch LJ, Hauser WA. Can sudden unexplained death in epilepsy be prevented? Lancet 2004; 364:2157-2158.
3. Duncan JS, Sander JW, Sisodiya SM, Walker MC. Adult epilepsy. Lancet 2006; 367:1087-1100.
4. Stollberger C, Finsterer J. Cardiorespiratory findings in sudden unexplained/unexpected death in epilepsy (SUDEP). Epilepsy Res 2004; 59:51-60.
5. So EL. What is known about the mechanisms underlying SUDEP? Epilepsia 2008; 49:93-98.
6. Nashef L, Ryvlin P. Sudden unexpected death in epilepsy (SUDEP): update and reflections. Neurol Clin 2009; 27:1063-1074.
7. Holmes NE, Iles LE, Danks RA, Korman TM. Neurocysticercosis Causing Sudden Death. Am J Forensic Med Pathol 2010; 2:117-119.
8. Velasco TR, Zanello PA, Dalmagro CL, Araújo Jr D, Santos AC, Bianchin MM, et al. Calcified cysticercotic lesions and intractable epilepsy: a cross sectional study of 512 patients. J Neurol Neurosurg Psychiatry 2006; 77:485-488.
9. Wallin MT, Kurtzke JF. Neurocysticercosis in the United States: review of an important emerging infection. Neurology 2004; 63:1559-1564.
10. Ndhlovu CE. An uncommon presentation of cysticercosis. Cent Afr J Med 1997; 43:207-209.
11. Verma SK, Agarwal BB, Agarwal G. Sudden death in neurocysticercosis by trauma. Forensic Sci Int 1998; 95:23-26.
12. Llompart Pou JA, Gene A, Ayestaran JI, Saus C. Neurocysticercosis presenting as sudden death. Acta Neurochir 2005; 147:785-786.