



Surgical versus conservative treatment in patients with cerebral cavernomas and non refractory epilepsy

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ABSTRACT

Purpose: The optimal therapy of patients with cerebral cavernoma (CCs) and new onset epilepsy, sporadic seizures, or non well established refractory epilepsy is still not clear. The aim of this study was to compare the incidence of seizures in patients with CCs both operated and non operated, in order to obtain more information on the correct management of these patients.

Materials and methods: We studied retrospectively 43 patients with non refractory epilepsy secondary to CCs. Twenty-six of them (60.5%) underwent surgery and made up the surgical group, and 17 patients were treated medically and constituted the medical group. Seizure frequency and other clinical variables were compared between both groups.

Results: At two years, out of the 26 operated patients, 19 (73%) remained seizure free, 4 (15%) had less than a seizure per month, and one patient (4%) had more than one seizure per month. At five years, 15 patients of the surgical group remained for analysis. Of them, 11 (73.3%) were seizure free, and 4 (26.7%) had less than one seizure a month. In the medical group, 12 out of 17 patients were seizure free (70.6%). There were no significant differences between the two groups ($p = 0.2$ and $p = 0.3$, respectively). Seven patients had postoperative neurological sequelae.

Conclusion: Surgical treatment of patients with non refractory epilepsy due to CCs did not significantly reduce the likelihood of seizures when compared to medical treatment. It must also be considered that surgery carries serious risks. A prospective and randomized study must be carried out to further clarify our findings.

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1. Introduction

Cerebral cavernous malformations are hamartomatous vascular lesions of the brain with an approximated prevalence of 0.2–0.9% – shown by necropsy and/or magnetic resonance imaging (MRI) studies.^{1,2} They constitute nearly 10% of all vascular cerebral malformations.³ The annual bleeding rate has been estimated to be between 0.2% and 3% per person per year of exposure.^{2,4–7} Seizures are the most common clinical presentations in supratentorial cavernomas. Seizures are probably provoked because cavernomas have a tendency to microhemorrhage into adjacent brain tissue resulting in surrounding hemosiderin and gliosis, predisposing to epileptogenicity.⁸ The literature documents several studies of

patients with well established refractory epilepsy secondary to cerebral cavernomas where surgery of the cerebral lesions resulted in high rates of seizure freedom.^{9–12} However, there are no prospective randomized studies comparing surgical and conservative treatments for this type of patient. Therefore, it is still unknown if resection of the lesion is the optimal treatment for patients with cavernomas and new onset epilepsy, sporadic seizures, or non well established refractory epilepsy. The aim of this study was to compare clinical evolution in terms of seizure frequency of patients with cerebral cavernomas operated and non operated in order to obtain more information on the optimal management of these patients.

2. Materials and methods

2.1. Patients

We initially recruited retrospectively 54 patients with cerebral cavernomas and epilepsy from our clinical database.

Abbreviation: ILAE, International League Against Epilepsy.

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Inclusion criteria in this study were: (a) at least, one epileptic seizure (before surgery in patients operated); (b) presence of supratentorial cavernoma, single or multiple, determined by computed tomography (CT) or MRI; and (c) at least, one year of follow up. All patients underwent a CT or MRI scan. Exclusion criteria were the presence of well established refractory epilepsy, defined by the recent proposal of ILAE for refractory epilepsy as failure of two adequate and well tolerated treatments in mono or bitherapy¹³ before surgery. After being diagnosed of cavernoma, most patients were first sent to a neurosurgical service, so surgery was in most cases indicated by a neurosurgeon. Then, a lesionectomy or an extended lesionectomy was performed if the cavernoma was located in a non eloquent region. Surgery was undertaken on 19 patients because of seizures and 7 because of hemorrhages. None of the patients studied had a complete presurgical epilepsy evaluation. Only one patient was monitored through cortical mapping during surgery.

There were a number of reasons why some patients were only given medical treatment: because of the excellent control of their epilepsy, the location of the cavernoma in an eloquent area or because the patient declined surgery.

Patients were divided into two groups: (a) the surgical group – these were the patients that underwent surgery and were treated by lesionectomy or extended lesionectomy and (b) the medically treated group.

2.2. Methods

A variety of clinical variables were analyzed, such as age and gender, age at epilepsy onset, duration of epilepsy, age at operation, kind and frequency of seizures, localization and size of cavernoma, presence of hemosiderin surrounding the cavernoma before and after surgery. The primary endpoint was the seizure frequency of the operated and non operated patients. We also looked at the possibility of treatment withdrawal, and the presence of surgical sequelae, and cavernoma bleeding during the follow up.

2.3. Statistics

Statistical analysis was undertaken with SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA), and comparisons were performed using the Mann–Whitney *U* test.

3. Results

3.1. Demographic and clinical data

Out of the 54 patients recruited from our database, 11 were excluded from the analysis because of the presence of refractory epilepsy. Thus, the study was composed of 43 patients, aged between 23 and 74 years (mean, 47 years). Twenty-six patients (60.5%) were men, and 17 (39.5%), women. Mean age of seizure onset was 36 years (range 9–70 years). Localizations of the cavernomas in the brain were: 13 frontal, 13 temporal, 8 parietal, 8 multiple, and one patient had an occipital localization. The cavernoma was sized less than 2 cm in 19 patients (44.2%), between 2 and 6 cm in 23 (53.5%), and greater than 6 cm in one patient (2.3%). Hemosiderin deposits surrounding the cavernous angioma were detected by MRI in 30 cases (69.8%). Finally, 26 patients (60.5%) underwent surgery (lesionectomy in 22, and extended lesionectomy in 4). These 26 patients composed the surgical group, and the 17 non operated patients composed the medical conservative group. Comparison of principal demographic and clinical data of both groups is summarized in Table 1. There were no significant differences in the baseline clinical characteristics between both groups.

3.2. Seizure outcome

At two years, 19 out of the 26 operated patients (73%) remained free of seizures, 4 (15%) had a seizure frequency lower than a seizure per month, and only one patient (4%) had more than one seizure per month. At five years, 15 patients of the surgical group remained for analysis. Of them, 11 (73.3%) were free of seizures, and the other 4 patients (26.7%) had less than one seizure a month.

Table 1

Comparison of the principal clinical features between the surgical and the conservative treatment groups. There were not significant differences between two groups. Abbreviations: GTCS: generalized tonic-clonic seizures; CPS: complex partial seizures; SPS: simple partial seizures.

	Surgical group (n=26)	Medical group (n=17)
Age, mean	44,8 (range 23–65)	50,2 (range 7–74)
Gender	16 men (61%) 10 women (39%)	10 men (59%) 7 women (41%)
Localization of cavernoma	Temporal 7 (27%) Frontal 9 (34%) Parietal 6 (23%) Occipital 0 (0%) Multiple 4 (15%)	Temporal 6 (35%) Frontal 4 (23%) Parietal 2 (12%) Occipital 1 (6%) Multiple 4 (23%)
Size of cavernoma (cm)	<2 cm 11 (42%) 2–6 cm 15 (58%)	<2 cm 8 (47%) 2–6 cm 8 (47%) >6 cm 1 (6%)
Type of seizures	GTCS ± CPS-SPS 10 (38%) CPS 6 (24%) SPS 10 (38%)	GTCS ± CPS-SPS 8 (47%) CPS 5 (30%) SPS 4 (23%)
Age at onset	36,5 (range 9–63)	38,8 (range 13–70)
Hemosiderin on presurgical MRI	20 (77%)	10 (59%)
Indication of surgery	19/26 (73%): seizures 7/26 (27%) hemorrhage	–
Seizure frequency pre surgery	Isolated seizure 8 (31%) ≤3 seizures 10 (38%) Annual seizure: 3 (11%) ≥1 monthly: 5 (20%)	–
Epilepsy duration (pre surgery)	40 months (range 0–376)	–
Neurological deficit	2 (8%)	0

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