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Original Article

Clinical characteristics of the patients with cavernous angiomas

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Abstract

Aim: Cerebral cavernous angiomas (CCAs) are a rare type of hamartoma characterized by a small sinusoidal vein without normal parenchyma. This study aimed to assess the radiological findings, clinical symptoms, and localization of CCAs and compare results with those in the literature.

Material and Methods: Patients with CCA who underwent surgery between January 2012 and January 2018 were retrospectively evaluated.

Results: Of the 41 patients with CCA, 24 (58.5%) were males and 17 (41.5%) were females. The patients were aged from 6 to 72 (mean: 36.75 ± 16.97) years. Moreover, 13 (31.7%), 6 (14.6%), 14 (34.1%), 4 (9.8%), and 2 (4.9%) patients presented with supratentorial lesions localized in the frontal, parietal, temporal, occipital, and thalamic regions, respectively. Two (4.9%) patients had cavernomas in the infratentorial area that contains the pons. No pathology was observed on brain computed tomography scan and magnetic resonance imaging (MRI) in the control examinations.

Conclusion: Surgical excision should be performed in individuals with cavernous angiomas that are symptomatic. Critically localized and asymptomatic cavernous angiomas can be monitored with MRI at regular intervals. Surgical treatment should always be considered since neurological deterioration may occur due to epileptic seizures and recurrent bleeding that do not respond to treatments.

Keywords: Angioma; Hamartoma; Epilepsy.

INTRODUCTION

Angiomas are vascular lesions, known as cavernoma, cavernous hemangioma, or angioma, in the central nervous system (CNS) and whole body. Cerebral cavernous angiomas (CCAs) are relatively rare, with a prevalence rate of approximately 0.4%–0.5% based on autopsy and magnetic resonance imaging (MRI) studies (1-4).

Cavernous angiomas can develop anywhere in the cerebral hemispheres and are covered with a single-layer endothelial cell, without neural tissue, vein, and artery involvement (5-7).

CCAs can be asymptomatic or can cause mass effect on peripheral brain tissues or symptoms of low-pressure bleedings. Hemosiderin ring develops due to extravasation of blood into the brain parenchyma causing irritation in sensitive tissues and seizures. CCAs commonly cause headache, bleeding, seizures, or focal neurological deficits (8-11). Most pediatric patients may be at risk of temporary bleeding for a short period of time, and an average rate of up to 2% per month was recorded (12,13). Thus, asymptomatic patients can be followed-up with MRI, whereas surgical removal of CCA is recommended in symptomatic individuals.

In this study, we aimed to present the clinical features of 41 cases diagnosed as cavernous angioma in our clinic.

MATERIAL and METHODS

A study was conducted in the neurosurgery clinic of a tertiary hospital. The local ethics committee approved this protocol. Patients diagnosed with cavernous angioma who underwent surgery between January 2012 and January 2018 were retrospectively assessed. The medical records of all patients who underwent surgery, regardless

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of age, were evaluated. A total of 46 patients underwent surgery during this period. Five patients with missing imaging findings were excluded. Computed tomography (CT) scan and MRI with contrast were performed preoperatively. In our clinic, angiography is generally not indicated in the evaluation of CCAs because these lesions are poorly visualized on angiography (12). In CT sections, these lesions are described as a well-defined collection of multiple rounded densities without a mass effect. MRI studies are specific, and hemosiderin deposition can be observed as a popcorn perspective with an associated bloom on susceptibility imaging (12). On the basis on radiological examinations, lesion characteristics, such as location, extension, and size, and diagnosis of CCA were identified. Cavernous angiomas were completely excised in all patients, and the Scopis Hybrid Neuronavigation System (Scopis GmbH, Berlin Germany) was used. A total of 41 patients were included. Moreover, 39 (94.1%) and two (4.9%) patients presented with cavernoma in the supratentorial area and posterior fossa, respectively. Age and gender; complaints of the patients; comorbidities; and location, size, and number of lesions on MRI were recorded. According to the MRI results, the Zambraski classification was used, as shown in Table 1 (1). The preoperative and postoperative Glasgow coma scale score of all the patients was 15.

Descriptive statistics, mean ± standard deviation, and number and percentage were used to analyze demographic data, clinical data, and radiological classification, respectively.

RESULTS

Of the 41 patients with CCA, 24 (58.5%) were men and 17 (41.5%) were women. The patients were aged 6–72 (mean: 36.75 ± 16.97) years. Moreover, 13 (31.7%), six (14.6%), 14 (34.1%), four (9.8%), and two (4.9%) patients presented with supratentorial lesions localized in the frontal, parietal, temporal, occipital, and thalamic regions, respectively. Two (4.9%) patients had cavernomas located in the infratentorial area that contains the pons. Only one female patient had multiple frontal lesions, whereas all other patients had a single lesion. In the preoperative period, 23 (56.9%), 15 (36.5%), two (4.9%), and seven (17.1%) patients had headache, seizures, cerebellar dysfunction (pons cavernoma), and focal neurological deficits, respectively. Table 2 presents age, sex, comorbidities, localization of lesion, and size of lesion. Cavernous angiomas were completely excised in all patients. Only three patients had subarachnoid hemorrhage. The patients were followed-up for 3 months to 6 years. Based on the control examinations of our cases, epilepsy, headache, and neurological deficits improved. The frequency of seizures decreased in two patients with cranial lesions. In ten patients, seizures did not recur again. No new pathology was found on brain CT scan and MRI in the control examinations. Figure 1 presents T2-weighted MRI images of the left frontal cavernoma that was transcortical excised by neuronavigation system.

Table 1. Zabramski classification (1)

	MRI Findings	Pathological Findings
Type 1	T1: Hyperintense center T2: Hyper-/hypointense core and hypointense surrounding rim	Subacute hemorrhage. Macrophages with hemosiderin and gliotic brain tissue around the lesion
Type 2	T1: Irregular/split center T2: Irregular/split core and hypointense surrounding rim	Local hemorrhage and thrombotic areas at different time points. Hemosiderin accumulation in the peripheral tissue, calcification in the gliosis and large lesions
Type 3	T1: Iso-/hypointense T2: Hypointense core and hypointense surrounding rim GE: Hypointense	Hematoma in the chronic stage. Hemosiderin accumulation within and around the lesion
Type 4	T1: Challenging to detect/not visible T2: Challenging to detect /not visible GE: Hypointense punctuate lesion	Telangiectasia

T1 and T2: T1- and T2-weighted magnetic resonance images; GE: gradient-echo sequences

Table 2. Demographic characteristics of the patients, location and size of the cavernous angiomas, and Zambraski classification

Age (years)	Sex	Localization of lesion	Lesion size (cm)	Symptoms	Zambraski classification	Co morbidities
22	M	Frontal	1.7 × 1 × 0.9	Headache	0	
28	M	Frontal	0.9 × 08 × 1	Epilepsy	1	
44	M	Frontal	1.5 × 1 × 0.9	Headache	0	HT
51	F	Frontal	2 × 1.5 × 1	Epilepsy	0	HT
55	M	Frontal	1.5 × 1.9 × 1	Headache, epilepsy	2	CAD
11	M	Frontal	0.7 × 0.5 × 0.8	Headache	4	
24	M	Frontal	0.9 × 1.2 × 1	Neurological deficits, epilepsy	0	
56	M	Frontal	1.2 × 1 × 1	Neurological deficits	2	
28	M	Frontal	1.3 × 1 × 0.9	Epilepsy	0	
44	M	Frontal	1.5 × 1 × 1.2	Headache	2	
57	F	Frontal	1.7 × 1 × 1.2	Syncope	0	DM
12	M	Frontal	2 × 1.5 × 1.2	High intracranial pressure	0	
16	F	Frontal	1.6 × 1 × 1.2	Epilepsy	0	
50	M	Temporal	0.9 × 0.8 × 1	Headache, epilepsy	1	
33	F	Temporal	1.2 × 1.1 × 1	Headache	1	DM
26	M	Temporal	1.1 × 1 × 0.9	Headache	0	
12	M	Temporal	1.3 × 1.1 × 1	Epilepsy	0	
44	F	Temporal	1.6 × 1.2 × 1	Epilepsy	2	
25	M	Temporal	1.2 × 1 × 1.1	Headache	0	
33	F	Temporal	1.1 × 1.2 × 1	Headache	0	
46	F	Temporal	1.3 × 1.6 × 1.4	Headache	0	
19	F	Temporal	3 × 2 × 1.5	Neurological deficits, Epilepsy	2	
60	M	Temporal	1.4 × 1.2 × 1	Headache	0	CAD
53	F	Temporal	1.1 × 1.3 × 1.4	Headache	2	
30	F	Temporal	2.5 × 1.9 × 1.8	Epilepsy	2	
35	F	Temporal	1.4 × 1.3 × 1.2	Headache	0	HT
18	M	Temporal	1.4 × 1.1 × 1.2	Headache	2	
19	M	Parietal	1.2 × 1.3 × 1.1	Headache, epilepsy	0	
34	F	Parietal	1.1 × 1.2 × 0.9	Neurological deficits, epilepsy	2	
72	F	Parietal	1.2 × 1 × 0.9	Headache	2	
27	F	Parietal	1.1 × 0.9 × 1.1	Headache	0	
27	F	Parietal	2.2 × 2.1 × 1.9	Headache	2	
49	M	Parietal	2.1 × 2.2 × 2	Neurological deficits, epilepsy	0	HT
53	M	Occipital	1 × 0.6 × 1.1	Headache, epilepsy	1	
51	M	Occipital	1.1 × 1.3 × 1	Headache	0	HT
44	F	Occipital	0.4 × 0.6 × 1.2	Headache	3	
69	M	Occipital	2.2 × 2.8 × 2.9	Headache	0	
6	M	Thalamus	1.4 × 1.2 × 1.3	Epilepsy	2	
37	M	Thalamus	2.5 × 2.5 × 2.5	Headache	1	
60	F	Pons	0.4 × 0.3 × 0.6	Vertigo, imbalance	2	
46	M	Pons	0.5 × 0.4 × 0.6	Vertigo, imbalance	2	

F: Female; M: Male; HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease

DISCUSSION

The four main types of vascular malformations of the CNS are as follows: CCAs, developmental venous anomaly, arteriovenous malformation, and capillary telangiectasis (14). Cavernous angiomas, which account for 5%–13% of all cerebral vascular malformations, are developmental venous anomalies and vascular malformations (15,16). CCAs may not cause any symptoms and can be observed only on autopsy. Symptomatic CCA lesions most commonly occur with bleeding, seizures, or focal neurological deficits (8-11).

Intracranial cavernomas cause symptoms, such as low-pressure bleedings, that result in mass effect on the brain. Radiographic evaluation of suspected cavernomas begins with CT scan or MRI; by contrast, these lesions are poorly visualized on angiography (12,17). The accompanying nutrient artery and draining vein are usually not observed. These hamartomas occur due to the combination of large sinusoidal vascular spaces without muscular and neural tissues (18). Therefore, angiography was not recommended in the evaluation in our case series.

CCAs usually occur in middle aged women. The mean age of the study participants was 36.75 years, and 41.5% of patients were women. The mean age and gender distribution were similar to those in the literature (6,15).

Approximately 75% of cases of single lesions are sporadic; only 8%–19% were familial (1-4). By contrast, the presence of multiple cavernomas strongly indicates genetic inheritance. Approximately 75% of patients with multiple lesions were found to have relatives who also presented with such conditions (19). In patients with non-familial multiple cavernomas, the etiology is attributed to the secondary effects of radiation therapy (20,21). The occurrence of multiple CCAs and familial form is quite rare. In our case series, multiple lesions were observed in only one patient. Similar to our result, Çavuş et al. have shown the absence of multiple CCAs in 40 patients (5).

Cavernous angiomas can be observed in any area of the CNS, most commonly in the cerebral hemisphere (80%). In particular, they can be observed in the subcortical region and frontal–temporal lobes in the cerebral parenchyma. Infratentorial involvement is rarely observed, although it may involve both sides of the tentorium (5,15,16). The most common location in the brain stem is in the pons (22). In our study, most cavernous angiomas (95%) were located in the supratentorial region, which is similar in the literature, and the majority of lesions (66%) were located in the frontotemporal region. Clinical symptoms include epilepsy in 50%–60% of cases, focal neurological deficits in 30% of cases, and headache in 25% of cases. In our study, headache and epilepsy were the most common symptoms with a rate of 36.5% and 56.9%, respectively, which is in accordance with data in the literature.

The frequency rate of bleeding in individuals with cavernous angiomas between weeks and years is 12%–80% (5,23,24). In our study, three (7.3%) patients presented with a history of bleeding. In general, CCAs are benign lesions that have minimal effects on brain circulation; therefore, several patients are clinically asymptomatic. However, in some special cases, CCAs may be markedly symptomatic; thus, attention must be paid to such cases.

Kang et al. have reported that hypertension was observed in 8.3% of patients (15). In our case series, the most common comorbidity was hypertension (5.12.1%). Patients who presented with hemorrhage have a long history of hypertension (5). However, in our study, patients with hypertension did not present with hemorrhage. These results may be observed in a relatively low number of patients.

Typical appearance on CT scan image includes a well-defined sum of multidirectional densities with small contrast enhancement, and no mass effect is observed. Calcifications are commonly observed (25,26). MRI studies have shown the characteristics of T1- and T2-weighted high-signaled areas in the center due to methemoglobin and low-signal areas due to calcification and fibrosis (8,27-30). In T2 sections, a heterogeneous density site at the center and a low-density area around the ring are typically observed (Figure 1) (31,32). Due to the presence of methemoglobin in the acute period of bleeding, a hyperintense image is obtained in both T1- and T2-weighted MRI sections. In the chronic period, the lesion is hypointense or isointense in T1-weighted MRI sections, and it can be challenging to identify (27,33). When an incidental, asymptomatic cavernous angioma is observed on brain MRI, a conservative approach is utilized, and annual MRI follow-up is performed. If multiple cavernomas are found during imaging, it can be caused by familial or post-radiation (34).

MRI findings show numerous images of CCAs, and the association of specific imaging features and prevalence rate of hemorrhage were described. A significantly higher rate of hemorrhage is observed in individuals with Zabramski type I and II cavernous malformations (32). In this study, 14 patients presented with Zabramski type II and five with Zambraski type I. Three patients with hemorrhage presented with Zabramski type II.

Microsurgical excision or stereotactic radiosurgery is applied for cavernous angiomas that cause severe bleeding and localization in sensitive areas (brain stem, motor cortex, etc.), persistent seizures, progressive neurological deterioration, and recurrent bleeding in nonsensitive brain regions. Surgical treatment results were remarkably satisfactory in most series. The mortality rate was around 0%, and persistent deficits were found in 4%–5% of patients (35,36). For postoperative permanent deficits in sensitive areas, such as the brainstem, the risk increases from 12% to 25%. In these areas, the lesions must be cautiously approached (37). There are controversies about the potential role of radiotherapy as a possible treatment option for cavernomas in high-risk locations, such as the brain stem or sensitive cortex (35,37,38). Radiosurgery reduces the risk of bleeding in

these patients by 4.5%–17.3%. By contrast, radiosurgery may lead to more complications, such as new permanent neurological deficits (16%), and a mortality rate of 3% was observed (38). The use of radiosurgery should be in accordance with the expected natural process of the lesion. Considering the risk of prolonged secondary injury due to radiation exposure, resection should be recommended as the first line therapy when possible (33,39). During clinic microsurgical excision in the present study, the Neuronavigation System was used for a high level of mechanical accuracy on deep localized small masses in surgical localization and for reducing craniotomy volume and morbidity related to craniotomy. Our results showed clinical benefits and minimal postoperative complications

Including relatively small number of patients and retrospective evaluation were the limitations of our study. Our preliminary results may be useful for prospective studies with larger patient numbers.

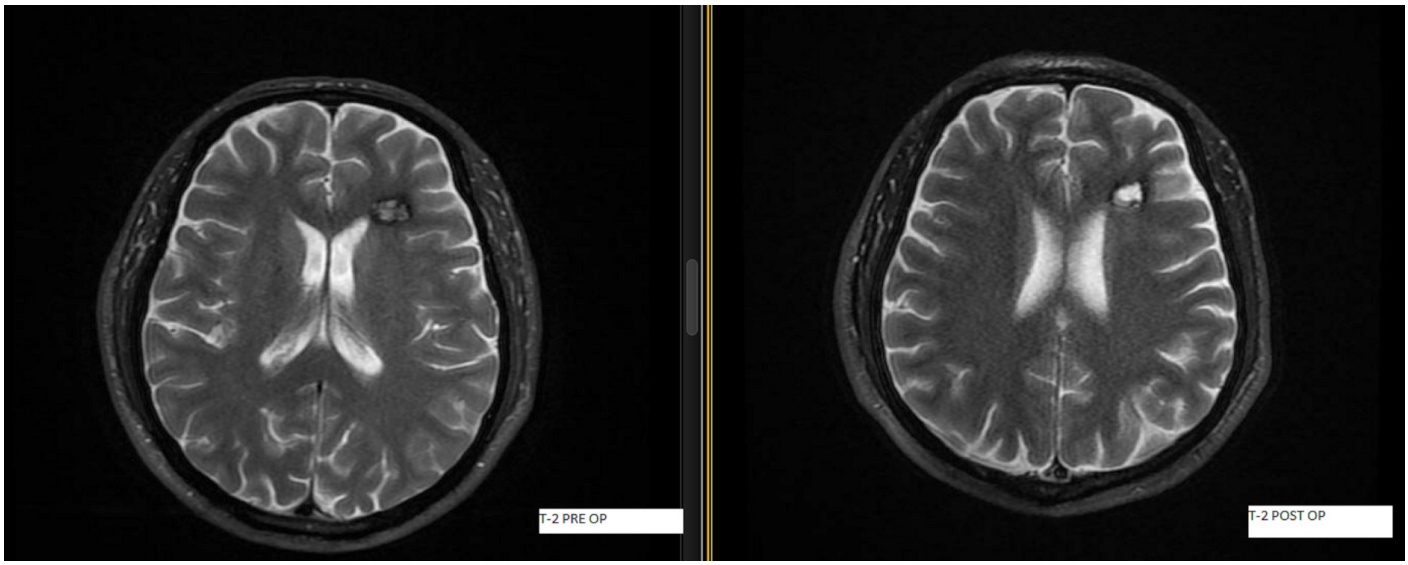

Figure 1. T2-weighted MRI images of the left frontal cavernoma that was excised by neuronavigation system

CONCLUSION

In conclusion, cavernous angiomas are rarely observed as vascular malformations that are more likely observed in the frontal–temporal lobes and localized in the subcortical region; they exhibit varying radiological features according to the amount and stage of bleeding products and calcification in the supratentorial area. Surgical excision should be performed in cavernous angiomas with or without symptomatic localization. Although cavernous angiomas with critical localization and those that are asymptomatic can be monitored with intermittent MRI, surgical treatment should be considered in these cases since severe neurological deterioration may occur due to recurrent bleeding.

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