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CASE REPORT

The Role of Radiotherapy in Familial, Multiple and Symptomatic Cerebral Cavernomas

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Abstract: Stereotactic radiosurgery is an effective and safe method that can help prevent the development of deep-seated or large-sized cavernomas. However, there are limited studies on familial, multiple and symptomatic cerebral cavernous malformations (CCM). The approach in these cases is not yet clear. This case is a CCM that can be confused with other brain masses and metastases, and contributes to the literature in terms of genetic transmission, management and treatment of cavernomas.

Keywords: cerebral cavernous malformation, radiotherapy, familial transmission

1 Introduction

Cerebral Cavernous Malformations (CCM) are rare vascular disorders with slow flow and capillary vessels that take on a berry-like shape [1, 2]. The pathogenesis is not clearly known. It constitutes 5-15% of all cerebrovascular malformations [1]. The temporal and frontal lobes are the most commonly affected areas. Approximately 10% are seen in the deep center of the brain and 20% in the infratentorial region [2–5].

CCM can be single or multiple in the brain. Most cases are sporadic (50-80%), with no family history [2, 3]. Single cavernous malformations are observed in 75% of sporadic cases and 8-19% in familial cases. Multiple cavernous malformations are observed in familial cases. Approximately 75% of patients have an affected family member. Multiple cavernous malformations are observed in only 10-25% of sporadic cases and mostly occur secondary to radiation [3–6].

CCMs are generally asymptomatic [1]. Approximately 15% of patients experience cerebral hemorrhage, epileptic seizures, focal neurological disorders, or headache [6, 7]. The occurrence of symptoms depends on the size and location of the lesion. Diagnosis is made with cranial MRI or CT. CT is less sensitive in detecting cavernous malformations. It has a characteristic popcorn-like appearance on MRI. The central region of the lesion contains hemorrhage products of different stages with heterogeneous density. The periphery of the lesion is characterized by surrounding iron deposits [7–9]. Currently, there are 3 treatment options available for CCM: microsurgical resection, Stereotactic radiosurgery (SRC), and conservative treatment [4–9]. The lack of knowledge of the basic pathophysiology of CCM and the inability to perform resection on cavernomas located in areas that are particularly difficult to access surgically make the treatment process and the development of new treatment applications difficult [1–3]. In this case report, it was discussed which treatment method should be chosen for a patient with symptomatic, familial and multiple cavernomas.

2 A case report

A 77-year-old male patient with no known comorbidity history was admitted to the emergency room due to fainting while at rest. His past medical history was unremarkable. It was learned that his son was followed up for cerebral cavernoma malformation in his family history. No pathological findings were detected in the physical examination. No right vulpian sign or nystagmus was detected in the neurological examination. Routine laboratory tests were normal. Non-contrast brain tomography revealed multiple hyperdense foci (hemorrhage? hemorrhagic metastasis?) in the brain. Contrast-enhanced cranial MRI revealed multiple lesions measuring 11 × 7 mm in the right posterolateral aspect of the medulla oblongata bulbus, 11 × 10 mm in the lateral neighborhood of the 4th ventricle in the left cerebellar hemisphere, 10 × 6 mm to

the right of the midline anteriorly in the pons, 9 × 8 mm to the right of the midline centrally in the pons, 8 × 9 mm in the anterior aspect of the left temporal lobe, 13 × 9 mm protruding into the lateral ventricle in the posterior neighborhood of the left caudate nucleus, 9 × 12 mm in the posterior neighborhood of the right lateral ventricle, 6 × 5 mm in the corpus section of the right corpus callosum, which were heterogeneously iso-hyperintense on T1A images, hypointense hemosiderin rings on the periphery on T2A images, and did not show enhancement after intravenous contrast material, and were evaluated in favor of cavernoma in the foreground. In addition to the lesions described, scattered multiple millimetric hypointense images not observed on standard MR images but identified on gradient echo sequences were also evaluated in favor of submillimetric cavernomas (Figure 1). The patient was consulted by the neurosurgery department and surgery was not considered. Antiepileptic treatment was started. The patient was referred to our outpatient clinic for stereotactic radiosurgery. In the examination, it was seen that the patient responded to antiepileptic treatment, there was no active bleeding in the brain and the symptoms regressed. The effects and side effects of the treatment to be given were explained. Since the patient accepted conservative treatment, radiotherapy was not considered. He was discharged with the recommendation of outpatient clinic control.

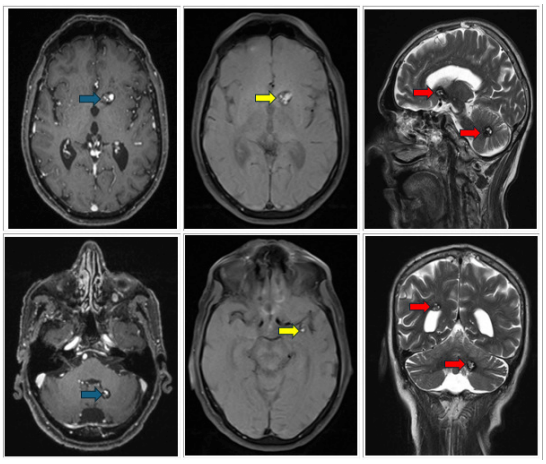

Figure 1 Red arrows: lesions with hypointense hemosiderin rings on the periphery on T2A images. Yellow arrows: lesions that appear heterogeneously iso-hyperintense on T1A images. Blue arrows: lesions that do not show enhancement on contrast-enhanced T1 images; they suggest cavernomas in the foreground.

3 Discussion

Surgery, radiotherapy and follow-up are recommended in the treatment of CCM. The decision on which of the available treatment options will be applied to the patient is made depending on a number of factors such as whether symptoms are seen or not, the presence of epilepsy, primary or recurrent hemorrhages, and neurological disorders [2–4]. Microsurgical resection is recommended if the lesion causing the symptoms is not located in the regions that provide important functions of the brain. In this way, existing epilepsy and future hemorrhages are also treated [3, 4].

Although microsurgical resection is the primary method in the treatment of cavernoma, the high risk of complications, especially in areas that are difficult to access with surgery, necessitates the need for other treatment options. In recent years, the rapid development of stereotactic radiosurgery methods has increased their use in the treatment of CCM. Stereotactic radiosurgery is preferred because it offers a treatment opportunity with a lower probability of developing neurological deficits in deeply located lesions close to important brain parenchymal areas. These are Gamma knife and linear accelerator (LINAC) beams. Both techniques include a large number of gamma rays and high-energy photons. The beams converge at a center of the cavernoma, thus delivering less dose to the surrounding tissue. Its disadvantage is that it takes up to 2 years to show its full effectiveness. It should not be forgotten that patients have a risk of rebleeding during this period [2, 5, 7–9]. There are many studies in the literature showing that this method is effective. However, there are a limited number of studies for familial, multiple and symptomatic CCM. The approach in these cases is not yet clear.

The potential risks that both surgical and radiosurgery treatments may pose necessitate the development of different treatment alternatives. In another treatment method, the conservative

approach, lesions are not directly intervened and lesion progression is left to its natural course [2, 6]. There are not enough studies in the literature on this subject, and when any negative situation occurs in patients, it is too late for early treatment, thus increasing the risk of permanent neurological damage in patients. In this case report, the approach to the treatment of a familial, multiple and symptomatic SCM case was discussed. The patient presented with an epileptic seizure, and there were numerous cavernomas located supra and infratentorially on the cranial MRI. There was no active bleeding complaint. It differs from the literature in these aspects. SCM is usually located supratentorially. Seizures develop in 23-79% of symptomatic supratentorial lesions. When compared to other parenchymal lesions with similar volume and location, cavernous malformations are twice as likely to present with seizures. Epilepsy is seen due to involvement in this region. In our case, infratentorial involvement was widespread as well as multiple supratentorial lesions.

As a result, there is currently no adequate treatment method for familial and multiple cavernomas. Stereotactic radiotherapy is an effective treatment method for symptomatic masses. However, new cavernomas may develop in the patient after treatment, either due to radiotherapy or the disease. In light of this information, studies that will shed light on the pathogenesis of the disease are needed to develop new methods for diagnosis and treatment.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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