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Multiple cavernous hemangiomas of the orbit: separate occurrence within a 24-year period

Multipli kavernozni hemangiomi orbite – odvojeno pojavljivanje u toku dvadeset četiri godine

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Abstract

Background. Cavernous hemangioma is a frequent and the most common, primary, benign tumor of the orbit in adults. It is typically single and unilateral, considered not to recur after having been completely excised. Multiple orbital cavernous hemangiomas without signs of hemangiomatosis are rare. Multiple cavernous hemangiomas may recur after a complete excision and may exist with concurrent systemic tumors. Tumor recurrence is supposed to develop from vasculature that is present already in response to a proliferate stimulus. **Case report.** A 39-year old female with painless proptosis of the right orbit was found to have four orbital tumors. The first orbitotomy was performed in 1984 by excising four cavernous hemangiomas. Six years later, another, the fifth one cavernous hemangioma was totally excised from the same orbit. Nine years after the first operation, reorbitotomy was performed because of positive radiological and clinical signs of *de novo* tumor in the orbit. The operation did not confirm the tumorous tissue. The fourth orbitotomy was performed 24 years after the first operation and two cavernous hemangiomas were totally excised. **Conclusion.** This case show the possibility of cavernous hemangioma recurrence after a previously totally excised tumor, separated more than two decades. A very long follow-up of the patients operated for these benign tumor lesions is recommended.

Key words:
hemangioma, cavernous; orbit; neurosurgery; recurrence.

Apstrakt

Uvod. Kavernozni hemangiom je čest, primarni, benigni tumor orbite kod odraslih. Obično je jedan, unilateralan. Smatra se da ne recidivira kada se u potpunosti odstrani. Multipli kavernozni hemangiomi bez znakova hemangiomatoze su retki. Oni recidiviraju i mogu biti udruženi sa sistemskim tumorima. Izgleda da recidiv tumora nastaje iz vaskularne mreže koja već postoji pod dejstvom određenih stimulativnih faktora. **Prikaz bolesnika.** Kod 39-godišnje bolesnice sa bezbolnom proptozom, dijagnostikovana su četiri tumora u konusnom prostoru desne orbite 1984. godine. U toku prve operacije potpuno su odstranjena sva četiri tumora karakteristika kavernoznog hemangioma. Šest godina kasnije potpuno je odstranjen peti kavernozni hemangiom iz ekstrakonusnog prostora. Devet godina posle prve operacije izvršena je reorbitotomija zbog radioloških znakova *de novo* tumora u retrobulbarnom prostoru, desno. U toku operacije nije nađeno tumorsko tkivo. Još dva kavernozna hemangioma odstranjena su dvadeset četiri godine posle prve operacije iz iste orbite. **Zaključak.** Prikazana bolesnica pokazuje mogućnost pojave recidiva kavernoznih hemangioma i nakon prethodno potpuno odstranjenih tumora, u vremenskom intervalu od preko dvadeset godina. Sugeriše se dugotrajno praćenje bolesnika koji su operisani zbog ove vrste benignih tumorskih lezija.

Ključne reči:
hemangiom, kavernozni; orbita; neurohirurgija; recidiv.

Introduction

Cavernous hemangioma is a frequent and the most common primary, benign tumor of the orbit in adults. It is typically single and unilateral, considered not to recur after having been completely excised [1]. Multiple cavernous hemangiomas (MCH) are rare and may exist with concurrent systemic tumors [2–4]. Multiple cavernous hemangiomas may occur simultaneously or separately by long intervals [1]. The orbital muscle cone lateral to the optic nerve is most frequent location of MCH. Discrete multiple tumors could appear in the apex region and cause "orbital apex syndrome" [5]. The

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tumor is presumed to be a low-flow malformation or hamartoma that are present from birth and enlarging later in life. Some authors consider cavernous hemangioma as a high-flow lesion with direct antigrade flow to the venous side [6]. Interestingly, these tumors are isolated from the orbital vascular system and, therefore, do not enlarge with Valsalva maneuvers [7]. A complete excision of MCH is usually possible and surgical morbidity is low [8–10]. Multiple cavernous hemangiomas may recur after complete microsurgical excision [10, 11].

Recurrence suggests that lesions develop from vasculature that is present already in response to a proliferate stimulus [1, 12]. Serial computed tomography (CT) documented a long period of slow growth, followed by a shorter interval of arrest, with eventual involution of tumor and relief of proptosis [13]. A combination of clinical signs and magnetic resonance imaging (MRI) is highly sensitive and specific for the diagnosis of orbital cavernomas. In the presence of visual deterioration clearly attributable to the tumor immediate surgery is recommended, while lesions producing solely exophthalmos can be safely followed by observation. An acute worsening of the visual function in a child due to multiple cavernous hemangiomas in the single orbit has been described [10, 14, 15].

We presented a case of unilateral seven orbital cavernous hemangiomas occuring separatly within a period of 24 years.

Case report

A 39-year-old woman with painless proptosis of the right orbit that had started a year ago, was found to have four round tumors of the right orbit. They were located in intraconal intermedial space two, one in the superior extraconal and one in intraconal superlateral space. An original craniorbitotomy, "the drawer operation", with total excision of four tumors was performed in 1984 [16]. The histological findings confirmed a complete excision of four cavernous hemangioma. The dimensions of the tumors were in average 15 × 20 mm. The postoperative course was unremarkable with regression of proptosis and preservation of the normal vision function. Postoperative CT of the orbits showed no tumor.

Six years later the patient exhibited moderate weakness of the right superior lid. CT images showed tumor characteristics of cavernous hemangioma in supermedial intraconal space close to the bulb (Fig. 1A).

The orbitotomy was performed, and the tumor of the 12 mm in maximal diameter was completely excised and histologically confirmed to be cavernous hemangioma. The postoperative ophthalmologic findings revealed regression of upper lid weakness without tumor on postoperative MRI.

Three years after the second operation, the patient complained of the pain in orbital region. Examination revealed only a minimal increase of the right eye proptosis. Computerized tomography images showed the nonconclusive signs of tumor recurrence in medial intraconal space. We elected to follow up the patient in a short time interval. A few months later, the acute aggravation of visual function appeared. The patient exhibited progressive proptosis of the right bulb, double vision, lower vision acuity, and nonspecific periorbital pain. Computerized tomography images showed tumor-like lesion in the medial conal space. The third operation was performed in 1996. The histological findings of angiomatose tissue, without a clearly defined tumor tissue were found. In the postoperative course the proptosis completely reduced, but vision acuity preoperatively reduced on 20/25 of the affected eye persisted as well as pain. We lost patient for follow-up, after 1996.

The patient admitted again in October 2007. The most significant clinical sign was a marked protposis of the right eye. Exophthalmometry revealed an 8 mm proptosis on the right eye, lower vision acuity (20/30), corneal leucoma and paralysis of the upper lid. Computerized tomography and MRI showed two distinct tumors characteristic of cavernous hemangioma (Fig. 1B). The larger one was in infermedial space within muscle cone and smaller in extraconal supermedial space of the right orbit.

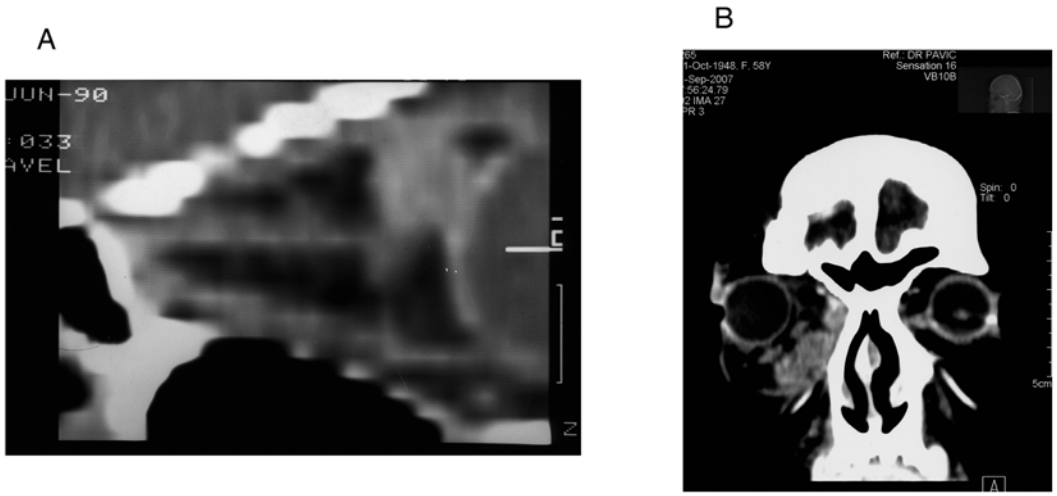

Fig. 1A – Computerized tomography of the orbit from 1990 showed fifth cavernous hemangioma; B – Magnetic resonance imaging from 2007 showed two cavernous hemangioma in the medial conal space

We proposed a new operation to the patient, emphasizing the possibility of further worsening of vision function after the operation, due to nonaccurate surgical timing. The fourth right orbitotomy was performed in 2007, and two tumors completely excised (Fig. 2A). Histological findings of the last two tumor samples confirmed blood-filled channels lined with endothelial cells and dense fibrous connective tissue - *septa* that were consistent with cavernous hemangioma for both tumors (Fig. 2B). Further aggravation of visual deficit occurred in spite of the complete preservation of the optic nerve and its vascular supply. The patient was discharged blind in the right eye.

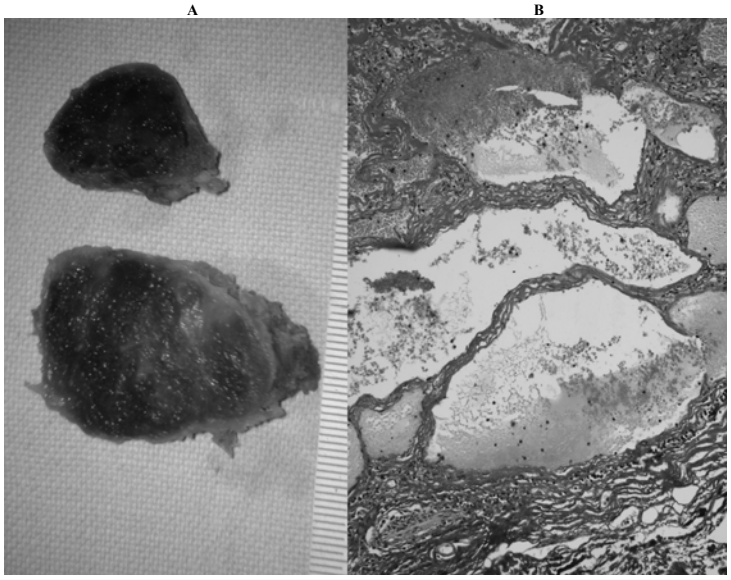

Fig. 2A – One half of two cavernous hemangiomas (small up and large down); B – Cavernous hemangioma: large endothelial-lined, blood-containing spaces separated by connective tissue septa. At the bottom the lesion has sharp demarcation from surrounding tissue (van Gieson, ×250)

Discussion

Cavernous hemangioma is easy to excise in the majority of cases, even primary multifocal found during the operation [4, 9]. The appearance and course of multiple unilateral orbital tumors separated by a long period of time raise questions about the mechanism of tumor growth, as well as the role of complete *vs* incomplete tumor removal. The clinical course of incomplete tumor removal without the recurrence and evidence of tumor slow growth even involution in nonoperated case underlines the significance of this hypothesis [1, 9, 12, 13]. The occurrence of multiple tumors recurrence in the single orbit after a total one-tumor excision fifteen years earlier is possible [11].

Orbital cavernous hemangioma expressed tumor growth factor bFGF (basic fibroblast growth factor) which can stimulate the growth of endothelial cells and vascular smooth muscle cells, suggesting that bFGF may participate in the growth of orbital cavernous hemangioma [17]. Tumor sex steroid receptors are present and may be related to the growth [18]. It is known that cavernous hemangiomas grow during pregnancy, suggesting a hormone dependant mechanism controlling the tumor growth [19].

The operative and histological findings and postoperative radiological investigation of the patient showed that the first four tumors were completely excised. It is unlikely that the fifth confirmed cavernous hemangioma was a result of recurrence due to tumors remnants. After a complete excision of the fifth tumor we came to a conclusion that it was a multiple cavernous hemangioma in the single orbit separated by a six-year period. According to the results of radiological and operative findings obtained through 1993 to 2007, the possibility of a multiple cavernous hemangioma recurrence from the small tumors, hiden in the inferomedial conal space, could not be excluded. The blindness of the right eye that occurred after the fourth operation, was probably of ischaemic origin, because the anatomical integrity of the optic nerve sheath was fully preserved.

After a period of 24-year-follow-up, four operations and seven unilateral cavernous hemangiomas of the single orbit totally excised, there remains a question whether the presented patient developed *de novo* multiple cavernous hemangioma separated by a long time intervals after previously totally tumor excised, or it was a case of multifocal tumor recurrence from remnants or small hide tumors. The role of tumor growth factor and sex steroid receptors seem to be very important.

Conclusion

The orbital cavernous hemangioma should be followed carefully for a long time, both after completely and incompletely excised and incidentally found tumors.

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