Introduction

Meningiomas account for approximately 30% of all primary intracranial tumors, and the majority are benign. The growth rate is variable in these tumors, and after radiographic diagnosis a large proportion of meningiomas frequently plateau in size and either stop growing or grow very slowly.\(^1\) Asymptomatic solitary meningiomas are therefore typically managed with clinical and radiographic follow-up.

The relationship between meningiomas and sex hormones is well known, and a growing number of reports have illustrated regression of meningiomas after hormonal withdrawal.\(^2\)–\(^4\) Regression after intratumoral hemorrhage has also been reported,\(^5\) whereas spontaneous regression is probably extremely rare.\(^6\)

Here, we report regression of a meningioma associated with \(\alpha_1\)-blocker treatment for benign prostatic hyperplasia (BPH), a drug that has previously not been linked directly to regression of meningioma. The patient did not present with, or went through, intratumoral hemorrhage, which would explain the regression.

Case Report

A 59-year-old male patient had experienced slight memory problems and unspecific visual disturbances. Neurological examination revealed no focal deficits. The initial magnetic resonance imaging (MRI) showed a lateral sphenoid wing meningioma on the right side with a maximum diameter of 43 mm, and the estimated tumor volume was 29.9 cm\(^3\) (\(\text{Fig. 1A–C}\)). The tumor showed all typical characteristics of a meningioma including extra-axial location, contrast enhancement, and dural tail. There was minimal peritumoral edema. The tumor was considered an incidental finding, the surgery was not recommended and the patient was followed with serial MRI. The first control MRI after 12 months demonstrated that the tumor was reduced by 50% to 14.8 cm\(^3\) (\(\text{Fig. 1D–F}\)). On the second MRI after 24 months the tumor had shrunken further to 10.0 cm\(^3\) (not shown). On the last MRI after 37 months the tumor was reduced further to 6.7 cm\(^3\), that is a reduction of 78% from the initial volume (\(\text{Fig. 1G–I}\)). The tumor volume measured from serial MRI is plotted in \(\text{Fig. 2}\).
The patient did not receive any steroid medication before or during the follow-up. He had not been treated for any malignant disease. During the follow-up, however, the patient was treated with an α₁-adrenoceptor antagonist (tamsulosin) for BPH.

**Discussion**

Data regarding the natural history of untreated meningiomas have been published in several studies, but evidence-based guidelines for treatment of patients with small meningiomas are still lacking. In patients selected for observation, Sughrue et al found that 51% of untreated meningiomas < 2.5 cm in diameter remained stable, 22% increased in size, and 27% decreased in size during a median follow-up period of 42 months. In our case, the meningioma was treated with tamsulosin, a drug that has been shown to reduce tumor volume in patients with BPH. After 12 months, the tumor volume had decreased to 14.8 cm³. After 37 months, the tumor volume had further decreased to 6.7 cm³.

**Fig. 1** T1 weighted with gadolinium MRI findings in our patient. (A–C) At diagnosis (October, 2010) showing a right-sided typical sphenoid wing meningioma with a maximum diameter of 43 mm and an estimated tumor volume of 29.9 cm³. (D–F) After 12 months (October, 2011), the tumor volume was reduced to 14.8 cm³. (G–I) After 37 months (November, 2013), the tumor volume was reduced further to 6.7 cm³. MRI, magnetic resonance imaging.

**Fig. 2** The tumor volume measured from serial MRI. MRI, magnetic resonance imaging.
Regression of Intracranial Meningioma during Treatment with α1-Adrenoceptor Blocker

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Regression of a meningioma has been reported in an 80-year-old male patient with BPH following change of medication from chlormadinone acetate (a progestin steroid with antiandrogen and antigonadotrophic effect) to naftopidil (α1-adrenoceptor antagonist).2 The cessation of the progestogen receptor agonist was interpreted as the explanation for the effect on tumor, but in light of the present case report, we propose that the observed regression could as well be due to the introduced α1-blocker or a combination of the two drugs.

The α1-receptor is a mediator of contraction in smooth muscles, and can be found in skin, sphincters, gastrointestinal tract, nerves, and brain. Stimulation of the receptor regulates growth and proliferation of various cells. α1-blockers are used in the treatment of BPH, heart failure, and hypertension. A possible explanation for an induced regression of meningioma by α1-blockade could be decreased effect of receptor activation that maintains growth and sustains the size of the tumor.15,16 Whether meninigomas express adrenoceptors, however, has not been extensively investigated. The first logical step would therefore be to perform receptor analysis to investigate whether meninigomas express adrenoceptors to any extent or other receptors that may represent targets for designed drug therapy. Biopsies from all patients operated for meningiomas at our hospital are stored and are available for later investigations. Some recent studies show that the α1-adrenoceptor antagonist naftopidil induces apoptosis in malignant mesothelioma cells by activating caspase-8 in association with upregulated tumor necrosis factor-α and increased Fasl secretion followed by the effector caspase-3.17 Studies of α1-adrenoceptor blockade and tumor treatment have mainly been done on prostate cancer, renal cell tumors, malignant pleural mesothelioma, and bladder tumors.18,19

Due to the high incidence of meningiomas and the large proportion of small tumors that do not grow, a relatively large group of patients are currently followed for incidental meningiomas without treatment. The encouraging observation in our patient warrants further appropriate evaluation of α1-adrenoceptor blockade in a prospective trial with accurate volumetric assessment in a preselected population with incidental meningiomas. Men above the age of 60 would for natural reasons be good candidates, but since α1-blockers have a low adverse effect profile a study group should not necessarily be that restricted. We are able to match our national drug registry with the cancer registry and thereby identify eligible patients.

This report of regression of an asymptomatic meningioma associated with α1-antagonist treatment is a reminder that treatment of incidental meningiomas must be based on thorough consideration of the patients medication history, especially in elderly men undergoing endocrine therapy for prostate disease and women treated for uterine cancer. Whereas surgery and occasionally radiation therapy are standard treatment for solitary meningiomas, these treatment modalities are not suitable for meningomatosis. The prospect of medical treatment is furthermore tempting in multiple meningiomas and recurrent disease, since surgery and radiation often are insufficient.

Conclusion

Although approximately 50% of incidentally diagnosed meningiomas do not grow, genuine spontaneous regression is extremely rare. However, a few cases of regression after progestative hormonal treatment withdrawal have been reported. Furthermore, regression of a meningioma has been reported in a male after changing the medication for BPH from progesterone agonist therapy to α1-blocker. We here report regression of a meningioma to 22% of the initial volume after 3 years during treatment with α1-adrenoceptor antagonist, indicating an association between the adrenoceptor blocking and the observed regression of the meningioma.

Addendum

After the last MRI (3-years follow-up), α1-blocker treatment was discontinued. The patient will be followed with serial MRI. If the meningioma should regrow, we have to consider putting the patient back on α1-adrenoceptor blocker or should we alternatively operate the tumor to study its receptor expression?

Note

An abstract of this case history was presented at the Annual Meeting of the Norwegian Neurosurgical Society; October 26, 2014; Norway.
References