

Regression of Giant Olfactory Groove Meningioma and Complete Visual Acuity Recovery after Discontinuation of Cyproterone Acetate

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Abstract

Purpose: To report on the medical management of meningioma with compression of the optic chiasm associated with the use of cyproterone acetate (CA).

Case Report: A 65-year-old woman who was being treated with CA presented with a recent decrease in visual function, leading to discovery of a giant olfactory groove meningioma with compression of the optic chiasm. CA was discontinued immediately, and her visual function improved dramatically. At 13 months, in addition to a significant improvement in visual and neurocognitive symptoms, the tumor volume was reduced by 50%.

Conclusion: In meningiomas associated with CA, treatment cessation may result in prompt improvement in symptoms and a reduction in tumor volume, even if the tumor is large and causing neurologic impairments.

Keywords: Compression; Cyproterone Acetate; Medical Treatment; Meningioma; Optic Apparatus

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INTRODUCTION

The relationship between meningioma and female sex hormones has been clearly demonstrated, but the underlying mechanism remains unclear. Progesterone receptors are strongly expressed in about two-thirds of meningiomas, but little is known about their precise role in tumorigenesis. We have previously reported

the association between cyproterone acetate (CA),^[1] a progesterone agonist, and development of de novo meningioma as well as an increased growth rate. We have observed that the volume of most meningiomas is reduced following discontinuation of the drug.

Although the link between CA and growth of meningiomas has been clearly identified, the medical management of these meningiomas, especially when there is a mass effect and associated neurologic impairments, has never been documented.

Here we describe a patient in whom we decided to apply a “discontinuation and scan” strategy, based on our recently acquired knowledge, despite the large

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size of the tumor and a significant mass effect causing neurologic symptoms.

CASE REPORT

A 65-year-old woman was referred to a neurosurgeon for a consultation because of a recent decrease in visual acuity (VA), which leads to the discovery of a giant olfactory groove meningioma with compression of the optic chiasm [Figures 1 and 2a and b]. The patient complained of a one-year history of asthenia and problems with attention. An ophthalmic examination revealed a decrease in VA in the right eye (20/50) and left eye (20/40). Dilated fundus examination and color fundus examination showed a normal optic disc in both eyes, i.e., no edema or atrophy of the optic disc. No routine color vision test was performed to complete the assessment of the optic nerve function.

Initial visual field testing showed an incomplete temporal hemianopsia and a bilateral blind spot enlargement [Figure 1]. Magnetic resonance imaging (MRI) confirmed our suspicion of an olfactory groove meningioma measuring 69 cm³ and a sphenoidal planum meningioma measuring 69 cm³ was identified. She had been treated with CA for hyperandrogenism for 15 years. The treatment was immediately discontinued.

Ophthalmic monitoring and repeat MRI were scheduled, with planning for surgical intervention in case of further visual decline. After administration of a steroidal anti-inflammatory drug for 15 days, repeat ophthalmic

examination revealed a dramatic improvement in the patient's visual function with normalization of VA in both eyes (20/20) and improvement in her visual fields [Figure 1]. A MRI performed 5 weeks after cessation of CA showed a slight reduction in tumor volume from 69 cm³ to 65 cm³.

In view of the favorable initial clinical evolution, the observation period was extended with close imaging and ophthalmic monitoring. The patient's VA remained normal and a subsequent improvement in her visual fields was documented [Figure 1]. Optical coherence tomography was repeated 3 months after the first examination and showed a slight bilateral decrease in temporal retinal nerve fiber layer thickness. This decrease remained stable one year after the first examination. The initial neurocognitive symptoms also regressed significantly and the patient's work skills improved.

MRI performed 5 and 13 months after cessation of CA confirmed a clear and long-lasting reduction in tumor volume, with a decrease from 69 cm³ at baseline to 35 cm³ on the final MRI performed at 13 months [Figures 3 and 2c and d].

DISCUSSION

This case highlights the causal role of CA in the growth of meningioma as well its successful medical management despite a mass effect and obvious neurologic impairment. Development and growth of de novo tumors has

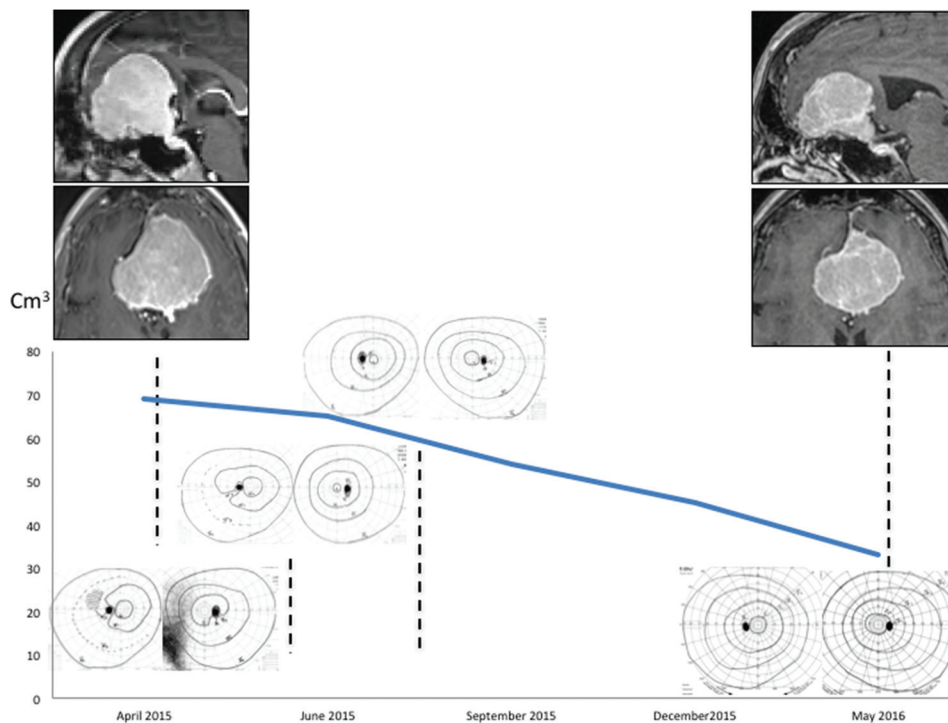


Figure 1. Evolution of tumor reduction and recovery of visual acuity.

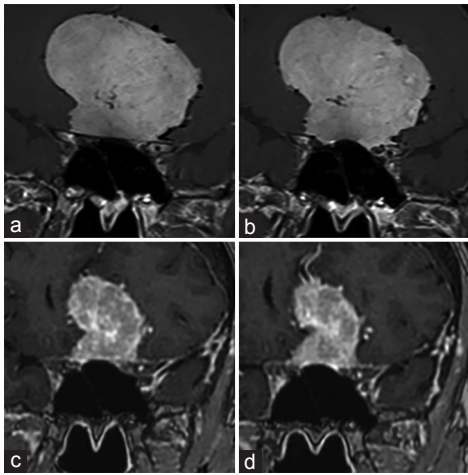


Figure 2. Coronal views focused on the optic apparatus. Relationship between both optic nerves and the tumor before withdrawal of cyproterone acetate (a and b) and 18 months later (c and d).

previously been observed in patients treated with CA.^[1-3] A reduction in lesion volume has been documented in most cases following discontinuation of CA^[1-3] and we have confirmed this phenomenon in our own case series of CA-associated meningiomas.^[1]

Despite the evidence of a link between treatment with CA and development of meningioma, we still encounter patients treated with the drug who require rapid neurosurgical intervention for severe visual impairment. Our present case was exposed to CA at its maximal dose (50 mg/day) for 15 years. The duration of CA exposure seems to be an important factor in the development of meningioma.^[4] Our experience in this patient suggests that there is a dose-response relationship between CA and development of meningioma and, interestingly, that associated neurologic impairments are reversible after cessation of CA.

The mechanisms by which CA promotes growth of meningioma are unclear. A positive effect on the proliferation of meningioma cells has been suggested^[5,6] as well as a vascular mechanism via increased angiogenesis.^[7] Lusis et al^[8] proposed that growth of meningioma could be more related to hemodynamic changes than to the direct action of progesterone on cell proliferation. In our patient, the rapid decrease in VA before the diagnosis improved dramatically after discontinuation of CA, and it could be assumed that a vascular mechanism was involved in this phenomenon. Interestingly, we noted a modification of the tumor signal after cessation of CA, especially on fluid-attenuated inversion recovery sequences [Figure 3]. Relatively limited peritumoral edema, generally associated with tumor growth, was observed around the tumor, indicating that the presence of severe edema is not necessary for rapid improvement. The meningioma in our patient showed only a very slight reduction in volume between the initial imaging

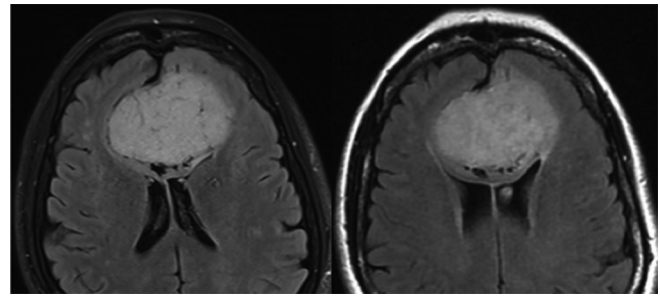


Figure 3. Signal modifications in fluid-attenuated inversion recovery sequences 6 weeks after discontinuation of cyproterone acetate.

and the second MRI performed at 6 weeks. Therefore, it seems very unlikely that contraction of the tumor alone could explain the rapid marked improvement in visual function. Unfortunately, we did not obtain baseline magnetic resonance perfusion sequences^[9] in this case; however, systematic use of these sequences could be useful for monitoring cases in the future and could help to validate the above hypothesis.

In our larger series of CA-associated meningiomas, we recommended surgical treatment of meningiomas that threaten the functional prognosis, which was the case for 2 patients included in the series.^[1] In the present patient, we initially opted for regular ophthalmic monitoring and to reserve surgery as a second-line option; the rapid recovery of her VA confirmed the appropriateness of this therapeutic strategy, although surgery would have been a viable option for this otherwise quite large tumor. During follow-up, we observed a slight bilateral decrease in temporal retinal nerve fiber layer thickness on optical coherence tomography, which was the result of a mass effect.

Patient awareness and collaboration were essential for regular observation of this lesion; surgical intervention would have been necessary otherwise. It is also important to take into account the consequences of sudden discontinuation of CA. Therefore, consideration should be given to the hormonal status of the patient, the indication for CA, the patient's tolerance of the symptoms of hyperandrogenism and their psychologic impact, and whether there is an alternative medical treatment available. In certain cases, when definitive cessation of CA is not well tolerated, a trial of dose reduction might be indicated. However, to our knowledge, no data have been published on such a strategy or its outcomes in terms of either meningioma or hyperandrogenism control rates.

In conclusion, in patients treated with CA who are diagnosed to have a meningioma, even when the tumor is large and presents with a mass effect and neurologic impairments, discontinuation of the antiandrogenic treatment may result in prompt improvement in symptomatology and a reduction in tumor volume.

Surgical treatment remains indicated when patient compliance is doubtful or close clinical and imaging monitoring cannot be implemented.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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