Proptosis and blindness caused by meningioma in a patient treated with cyproterone acetate

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Background Cyproterone is a derivative of progesterone with antiandrogenic, antigonadotropic and progestagenic activity. High-dose preparations are indicated for use in the treatment of prostate cancer (200-300 mg per day) and in the treatment of hypersexuality (50-600mg per day). Cyproterone blocks the binding of dihydrotestosterone (DHT) to prostatic cancer cells and exerts negative feedback on hypothalamic-pituitary axis by inhibiting luteinizing hormone (LH) secretion leading to decreased testosterone production. Lower-dose (2mg) cyproterone acetate (CPA) is available for use in women in combination with ethinylestradiol (0.035mg) for the treatment of severe acne and hirsutism. The suspicion that long term treatment with high daily doses of CPA could be responsible for the development of meningiomas was reported in 2008 by Froelich et al. He described multiple meningiomas in 9 female patients treated with CPA (50mg per day). Six patients were followed radiologically for a period exceeding 5 months (8 to 81) before treatment withdrawal. A significant increase in tumor size and/or the development of new lesions was observed in all cases.¹

A large, controlled, population-based study using data from The Health Improvement Network UK primary care database confirmed a significantly increased risk of meningioma in male patients taking high-dose CPA. However, these risk estimates were based on only four cases of meningioma. There was no significant association between meningioma and low-dose CPA use in female patients.²

Nevertheless, the hypothesis that the exposure to high dose CPA increases the risk of meningioma is also supported by another large retrospective cohort study performed in a Spanish primary care database (BIFAP). Among 2474 users of high dose CPA four meningioma cases were identified, resulting in an incidence rate which was significantly higher than that observed among the non-users and among users of low dose CPA. After adjusting for age and gender, patients exposed to high dose CPA showed an increased risk of meningioma of 11.4 (95% CI 4.3-30.8) as compared to non-users.³

Case report We describe the clinical findings in a patient who has been treated with CPA 100mg per day for 23 years to reduce his aggressive sexual drive. The 42-year old male patient is known with mental retardation due to perinatal asphyxia. He was referred with slowly progressive unilateral proptosis and blindness. Best corrected visual acuity was 6/10 in the right eye and no light perception in the left eye. We noted an obvious proptosis and exodeviation of his left eye (Fig 1). Fundoscopy was unremarkable in the right eye and showed optic atrophy in the left eye (Fig 2). MRI of the brain revealed 11 meningiomas. One large meningioma located in the anterior temporal lobe extended into the orbit and caused proptosis and compression of the optic nerve leading to blindness of the left eye (Fig 3). The patient had been treated with a high dose of CPA (100 mg per day) for more than 20 years. As written above there is a link between long term use of this drug and the development of meningiomas. The treatment with CPA was discontinued as literature suggests a regression of meningiomas after discontinuation of the drug. On a MRI follow-up 5 months after cessation of CPA, a regression of the largest meningiomas with a maximum of 10.7mm was noticed (Fig 4 and 5).

Take Home Message
- Always ask about general health and drug intake
- Consider the potential risk of a meningioma in patients receiving CPA
- Patients with existing meningioma or a history of meningioma should not be prescribed high-dose (>25mg/day) CPA. This warning does not apply to medicines that contain low-dose CPA
- Withdrawal of CPA may induce regression of existing meningiomas.

References