SHORT REVIEW

Symptomatic meningioma induced by cross-sex hormone treatment in a male-to-female transsexual

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Abstract Transsexuality is defined as a strong conviction of belonging to the opposite sex in individuals without any physical intersex condition. Cross-sex hormone therapy is an important component of medical treatment of transsexuals but it is not exempt from adverse effects.

We report a case of a meningioma in a male-to-female transsexual patient treated with estrogens and cyproterone acetate for the past 4 years. He claimed recently severe headache and visual impairment. Blood tests showed normal results. A contrast-enhanced magnetic resonance imaging (MRI) scan revealed a mass in the tuberculum sellae consistent with a meningioma. Treatment was discontinued and tumor resection was performed. Histologic diagnosis confirmed strongly progesterone receptor-positive and estrogen negative meningioma. After surgery, the patient rejected the possibility of continuing with the treatment of estrogens and cyproterone, and so triptorelin (GnRH agonist) was initiated. At 1-year follow-up the patient’s symptoms had ameliorated and a MRI scan revealed no recurrence of the tumor.

This is the third case reported in the literature of a meningioma after treatment with estrogens and cyproterone acetate. We consider extremely important a long-term follow-up observation of male-to-female transsexual undergoing cross-sex hormone therapy in order to detect as soon as possible the adverse effects that can be derived from this therapy.

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Meningioma sintomático inducido por tratamiento hormonal cruzado en un transexual hombre a mujer

Resumen El transexualismo se define como una fuerte convicción de pertenecer al sexo opuesto en aquellos individuos que no tienen ninguna patología intersexual. La terapia hormonal cruzada es un componente fundamental del tratamiento médico de los transexuales, pero debemos tener en cuenta que no está exenta de efectos adversos.

Comunicamos un caso de meningioma en un transexual de hombre-mujer tratado con estrógenos y acetato de ciproterona durante 4 años, que consulta por cefalea y alteraciones...
Introduction

Transexualismo es definido como una fuerte convicción de pertenecer a la otra corteza sin ningún otro tipo de intersex, y es un fenómeno multidimensional que requiere una aproximación multidisciplinaria.

El tratamiento de los sujetos transexuales es un desafío para los endocrinólogos, que deben trabajar en colaboración con profesionales de salud mental cuando tratan a estos pacientes. Para poder proporcionar una ayuda de acuerdo con las diferencias entre los patrones de vida y el género, se requiere un tratamiento endocrino que ha sido un componente importante de los tratamientos de transexualismo.

El acuerdo sociocultural de feminización en el tratamiento de transexuales con el tratamiento de transexuales recomendado el uso de estrógenos en combinación con un antiandrógeno para reducir los niveles de testosterona endógena. El estrógeno está generalmente administrado de manera oral como acetato de estradiol u otros esteroides de tipo estradiol. Ciproterona acetato, un medicamento antihormonal, es uno de los fármacos antihormonales más utilizados en Europa.

La administración de estrógenos en una combinación de fármacos antihormonales puede asociarse con un conjunto de efectos adversos, con frecuencia venosas trombosis, hiperprolactinemia y deterioro de los niveles de quimiorreceptores. La relación entre los fármacos antihormonales y los efectos adversos es menos predecible. Otros efectos adversos son específicos para las pacientes, como parestesias, que se consideran menos comunes. Aunque aún está siendo investigado, esta es la tercera vez que se realiza un estudio de casos de transexuales con tratamiento de transexualismo y efectos adversos asociados.

Case report

Un paciente de 35 años de edad fue remitido al departamento de endocrinología de nuestro hospital con síncope visual y dolor de cabeza. Había estado tomando extremos endocrinos con parches transdérmicos de estradiol (100 μg cada día) y ciproterona acetato (50 mg cada dos días) durante los cuatro años anteriores, sin ningún control médico. Ningún reasignamiento quirúrgico había sido realizado.

Campimetría reveló un déficit visual temporal y la prueba de campo visual de la retina en el ojo derecho. Las pruebas bioquímicas y hematológicas fueron normales. La resonancia magnética mostró un meningioma intracranal que se extrajo quirúrgicamente. La paciente mejoró en el seguimiento.

Consideramos muy importante el seguimiento a largo plazo de los pacientes transexuales porque, aunque son sometidos a este tratamiento, no podemos predecir qué efectos adversos pueden aparecer en el futuro.
Discussion

For transsexual patients, acquisition of the secondary sex characteristics of the gender with which they identify is an extremely important aspect of sex reassignment and for this change to come about it is necessary to employ sex steroids. In male-to-female transsexual patients, estrogens are used for feminization, while there are several treatments that can be applied in order to suppress androgenic actions. Cyproterone acetate is commonly employed by European endocrinologists. Other options are spironolactone, finasteride, medroxyprogesterone acetate and long-actin GnRH analogues. As regards progesterone, there is no evidence that its addition to cross-sex hormone treatment contributes to feminization, and it is not usually prescribed due to the many side effects it produces.4

Malignancies due to feminizing endocrine regimens in male-to-female transsexuals are not a common adverse effect, although estrogen administration has been related to breast cancer, prostate cancer, ovarian cancer and a few reports of prolactinomas.4,9 It has been hypothesized that the role of sex hormones in the development of intracranial meningiomas may explain the increased predominance of these tumors among women, and that the risk of developing one is higher among women with long-term use of contraceptives and postmenopausal women with a history of hormonereplacement therapy.4 The evidence suggests that progesterone contributes to the pathogenesis of a meningioma by influencing not only the development but also deenlargement of these tumors, since most of these grow during hormonal influx like pregnancy or the luteal phase of the menstrual cycle.4 What is more, most meningiomas express functional progesterone receptors, while estrogen receptors have been identified in approximately 10% of cases.

Cyproterone acetate is a synthetic progesterin that prevents androgens from binding to the androgen receptor, and has powerful antiandrogen properties. Given that it reduces further body hair growth and contributes to the feminizing effects of estrogens, even after gonadectomy, it is widely used in Europe in cross-sex hormone therapy for male-to-female transsexual patients. The dose required for achieving these effects is 50–100 mg daily. Other indications for this drug are inoperable prostate carcinoma (usually 200–300 mg a day) and severe signs of androgenization in women (androgen-related alopecia, hirsutism, seborrhea or acne). In 2008, Froelich et al. reported that cyproterone acetate in high doses over long periods of time could promote the development of meningiomas, since they found multiple meningiomas in 9 female patients treated with 50 mg a day of cyproterone acetate for different indications over a period of 10–20 years.4 In 2011, Cea-Soriano et al. reported a relationship between hormonal factors and meningiomas in a cohort study of 745 patients diagnosed with this type of tumor. They did not detect a significantly increased risk of meningioma among female users of low-doses of cyproterone acetate (50 mg or less a day), when compared with non-users, whereas said risk was significantly higher among male users of high-dose cyproterone acetate (more than 50 mg daily) when compared with non-users.9

Gil et al. in 2011 published the results of a retrospective cohort study performed using Spanish primary care database. They compared incidence rates of meningiomas in patients exposed to high-dose (50 mg or more a day) and low doses (50 mg or less daily) of cyproterone acetate (considered users) with those in non-exposed patients. They found that the incidence rate was significantly higher among users of high-dose cyproterone than in women receiving low doses and non-users.9

With all this evidence pointing to a role for progesterone in the development of meningiomas, it is of concern that male-to-female transsexuals are usually treated with progestins.

The first case of meningioma in a male-to-female transsexual was published by Gazzeri et al. in 2007 and concerned a 28-year-old male-to-female transsexual who had been receiving a feminizing endocrine regimen of 100 μg per day of ethinyl estradiol and 100 mg per day of cyproterone acetate for the previous 5 years. She developed a giant olfactory-groove meningioma with a histologic diagnosis that revealed a meningothelial meningioma that was negative for estrogen receptors and with a Ki–67 index of 5%. In 2010 Deipoli et al. reported another case of a 36-year-old male-to-female transsexual treated with 0.1 mg estradiol patches twice a week over more than 10 years and who developed an occipital meningioma that was strongly progesterone receptor-positive and estrogen receptor-negative.

We believe that the development of the meningioma in our patient was related to her cross-sex hormone treatment with cyproterone acetate, since a CT scan performed prior to her beginning this treatment showed normal results.9

Formal evidence from epidemiological prospective studies is lacking, however all the retrospective studies carried out to date have associated an increased risk of a meningioma with high doses of cyproterone acetate. This leads us to believe that a low dose may be a safer option for treatment of transsexual patients. In fact, we are currently treating patients with 25 mg a day of cyproterone acetate with very good antiandrogenic effects in the absence of any adverse reactions. An other reasonable option is the use of other antiandrogenic drugs such as spironolactone, which has less adverse effects, and to always consider sex reassignment surgery early on.

It is important to point out that this type of tumor does not cause an increase in any biochemical or hormonal values, which means that clinical findings are the ones that will make us suspect a meningioma.

To conclude, we report the third known case of a meningioma in a transsexual patient undergoing a feminizing regimen. The current number of published cases is very low, and so we hope that the present report will serve as guidance to clinicians, who should bear in mind the possibility of this type of complication when treating transsexual patients. Finally, as a result of our experience, we would suggest that hormone treatment be discontinued immediately when a patient receiving a cyproterone acetate regimen develops a meningioma.

Conflicts of interest

The authors have no conflicts of interest to declare.
References


