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Case report

Idiopathic intracranial hypertension in a pediatric transgender patient

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ABSTRACT

Purpose: Androgens given for gender affirmation have been implicated in the pathophysiology of idiopathic intracranial hypertension (IIH) in transgender patients. 10 cases of transgender adults with IIH have been published but this association has not been described in younger patients. Herein we describe the first case of IIH in an adolescent transgender patient.

Observations: A 17-year-old non-obese female-to-male transgender patient on subcutaneous testosterone since age 13 presented with a two-month history of transient visual obscuration and frontal headaches. Ophthalmological examination revealed Frisen grade 2 papilledema with preserved visual function. Lumbar puncture confirmed elevated opening pressure. Papilledema resolved with oral acetazolamide and reduction of testosterone therapy.

Conclusions and Importance: The use of cross-sex hormone therapy (CSH) for gender affirmation may increase the risk of IIH. Awareness of this association is important as the number of younger transgender patients seeking CSH is increasing significantly.

1. Introduction

Idiopathic intracranial hypertension (IIH) in adults is strongly associated with obesity and its incidence is four times higher in women than in men, at 7.7 versus 1.6 per 100,000, respectively.[1] The etiology of IIH is unknown and likely multifactorial. Even though the role of sex hormones in the pathophysiology of IIH is not completely understood, androgen excess in women is associated with IIH.[2] Specifically, women with IIH have increased serum testosterone and increased cerebrospinal fluid (CSF) testosterone and androstenedione. This pattern of androgen excess differs from the one seen in isolated obesity or obesity related to polycystic ovary syndrome, which shares many features with IIH,[3] suggesting that androgen excess may be an independent risk factor for IIH. Cross-sex hormone therapy (CSH), estrogen for transgender women and testosterone for transgender men, is used for gender affirmation. IIH has been reported in at least 16 adult transgender patients treated with CSH (Table 1),[4–13] whereas no cases have been reported in younger patients. Herein we describe the case of an adolescent who developed IIH while being treated with testosterone for a female-to-male (FTM) transition.

2. Case report

A 17-year-old non-obese female-to-male (FTM) transgender patient was referred to the pediatric neuro-ophthalmology clinic for evaluation of possible IIH because of a two-month history of transient visual obscurations and frequent generalised and frontal headaches that worsened with physical activity. He had no diplopia, tinnitus, nausea, or other symptoms of intracranial hypertension. He had undergone mastectomy at a younger age and had been treated with subcutaneous testosterone injections since age 13, which resulted in adequate masculinisation. His testosterone dose had been adjusted for age gradually, and 1 month before our exam it had been increased to 70 mg per week. The patient's body mass index was 25.8 kg/m^2, and he denied any recent weight gain. He was on no other medication. Ophthalmological examination revealed visual acuity of 20/20 in both eyes and normal color vision on Hardy-Rand-Rittler (HRR) plate test. The pupils reacted normally to light with no relative afferent pupillary defect (RAPD) and there was no sixth nerve palsy. The anterior segments looked normal on the slit lamp and fundoscopy revealed bilateral Frisen grade 2 papilledema. Optical coherence tomography (OCT) showed thickening of the peripapillary retinal nerve fiber layer (116 μm OD and 184 μm OS) and Humphrey 24-2 visual fields were normal. A head computed

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Table 1
Reported cases in the literature of idiopathic intracranial hypertension (IIH) in transgender patients.

Case	Age	Gender	BMI	Hormone tx	Symptoms start	Treatment of IIH	Evolution
1 (12)	28	MTF	30.13	Estrogens, spironolactone	8 M post-tx start	Hold estrogen; change to sublingual estrogen + DMX 1 g/day	Resolved at 5 M
2 (12)	31	FTM	56.5	Testosterone	1Y post-tx cessation	DMX 1 g/day + resume testosterone	Resolved at 6 M
3 (5)	22	FTM	27.9[1]	Testosterone, progestin	Rapid onset post-tx start	Shunt	Resolved at 18 M
4 (6)	36	FTM	25.0	Testosterone	50 M post-tx start	DMX 1 g/day → 1.5 g/day, furosemide 20 mg/day, topiramate 25 mg/day, endovascular stent	Resolved at 1 M; atrophy without edema at 6 M
5 (7)	23	FTM	27.05	Testosterone	2W post-tx start	DMX 0.5 g/day + 50% decrease testosterone	Resolved at 5 M
6 (8)	22	FTM	<30	Testosterone	3W post-tx start	DMX 1 g/day with taper + change to long-action testosterone	Resolved
7 (9)	33	FTM	NA	Testosterone	<10 M post-tx cessation	DMX 1.5 g/day → furosemide 80 mg/day, topiramate 150 mg/day; fenestration OD	Improved at 1 M
8 (10)	39	MTF	>40	Estrogens, spironolactone	3-5Y post-tx cessation	DMX 2 g/day + fenestration OD	Improved subjectively at 1D, lost to follow-up
9 (11)	34	MTF	41.9	Estrogens, progestin	2.5Y post-tx start; 1 M post-op	DMX 1 g/day → 2 g/day → 2.5 g/day, topiramate 50 mg/day, therapeutic LP, fenestration OS	No symptoms at 2W; resolved + 50 lbs loss at 2 M
10 (4)	24	FTM	NA	NA	NA	DMX 1 g/day + 50% decrease testosterone	Resolved + increase testosterone at 2 M
11 (13)	23	FTM	29.1	Testosterone	11 M post-tx start	DMX 500 mg/day	Improvement at 5 M
12 (13)	29	FTM	35.0	Testosterone	19 M post-tx start	DMX 325 mg/day + topiramate	Persistence at 2 M
13 (13)	19	FTM	31.9	Testosterone	2Y tx, many months of symptoms	Topiramate	Improvement at 6 M
14 (13)	22	FTM	36.1	Testosterone	13 M post-tx start	DMX	Worsened at 1 M, lost to follow-up
15 (13)	23	FTM	44.0	Testosterone	15 M post-tx start	DMX 1 g/day + nortriptyline 75 mg/day	Improved over 2Y
16 (13)	25	MTF	NA	Estrogens	No symptoms, referral after 4Y tx	None	Stable at 3 M and 1Y

FTM = female-to-male transition, MTF = male-to-female transition, BMI = body mass index, tx = therapy, g = grams, mg = milligrams, lbs = pounds, OU = oculus uterque, OD = oculus dextrus, OS = oculus sinister, DMX = acetazolamide, D = day, M = months, Y = years, NA = not available/unknown.

tomography (CT) and angio-CT were also normal. A lumbar puncture confirmed elevated opening intracranial pressure (37.5 cm of water). The patient was diagnosed with IIH and started on oral acetazolamide 250 mg twice daily. Endocrinology was involved for management of hormone therapy. Testosterone was withheld the week of initial presentation and was subsequently tapered to 50 mg weekly. The headaches and optic nerve swelling improved progressively, allowing for cessation of acetazolamide 3.5 months later. On last follow-up, 10 months after initial presentation, the patient continued to receive 50 mg of testosterone per week and remained asymptomatic with no recurrence of papilledema.

3. Discussion

In recent years, the number of transgender adolescents seeking endocrine care has increased significantly. This is paralleled with societal acceptance of gender diversity[14] and the ample evidence that gender-affirmation treatment improves the mental health of patients with gender dysphoria, or distress caused by the incongruence between gender identity and gender assigned at birth.[15–17]

Our patient developed IIH while being treated with testosterone for FTM transition, like 70% of reported adults who developed IIH while undergoing affirming therapy (Table 1: cases 2–7, 10–15).[4–9,12,13] His IIH symptoms manifested 4 years after beginning testosterone treatment, which is in keeping with a widely variable duration between start of hormone therapy and onset of IIH symptoms in previously published adult cases, between a few weeks and 5 years (Table 1).[4–12] Of the previously reported adult cases, 8 were obese (Table 1: cases 1, 2, 8, 9, 12–15).[10–13] Our patient was not obese but was overweight. Even though androgen excess seems to contribute to IIH independently from obesity,[3] the latter remains an important confounding factor when analyzing the role of CSH in transgender patients with IIH.[18]

The exact role of testosterone in the development of IIH is unknown. However, given that men with androgen deficiency may have a higher risk of developing IIH, it has been proposed that IIH occurs at a level of circulating serum testosterone shared by women with androgen excess and men with androgen deficiency.[18] The presence of androgen receptors in the choroid plexus has been demonstrated in animal models.[19] Stimulation of those receptors by excess testosterone would result in increased CSF secretion in IIH.[2,3,20] Reflecting a trend that is likely to continue in years to come, monthly referrals to a pediatric transgender clinic in Northern California increased by over 500% between 2015 and 2018.[21] Awareness and reporting of the possible causal association between CSH and IIH, a potentially blinding condition, are important in view of the increasing number of young transgender patients seeking hormone-affirmation therapy.

Patient consent

Written informed consent for publication was obtained from the patient's legal guardian.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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