Clinical Management of Youth with Gender Dysphoria in Vancouver

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Objective To describe patient characteristics at presentation, treatment, and response to treatment in youth with gender dysphoria.

Study design A retrospective chart review of 84 youth with a diagnosis of gender dysphoria seen at BC Children's Hospital from 1998-2011.

Results Of the 84 patients, 45 (54%) identified as female-to-male (FtM), 37 (44%) as male-to-female (MtF), and 2 (2%) as natal males who were undecided. Median age of presentation was 16.9 years (range 11.4-19.8 years) and 16.6 years (range 12.3-22.5 years) for FtM and MtF youth, respectively. Gonadotropin-releasing hormone analog treatment was prescribed in 27 (32%) patients. One FtM patient developed sterile abscesses with leuprolide acetate; he was switched to triptorelin and tolerated this well. Cross-sex hormones were prescribed in 63 of 84 patients (39 FtM vs 24 MtF, $P < .02$). Median age at initiation of testosterone injections in FtM patients was 17.3 years (range 13.7-19.8 years); median age at initiation of estrogen therapy in MtF patients was 17.9 years (range 13.3-22.3 years). Three patients stopped cross-sex hormones temporarily due to psychiatric comorbidities (2 FtM) and distress over androgenic alopecia (1 FtM). No severe complications were noted in patients treated with testosterone or estrogen.

Conclusion Treatment with gonadotropin-releasing hormone analog and/or cross-sex hormones, in collaboration with transgender-competent mental health professionals, is an intervention that appears to be appropriate in carefully selected youth with gender dysphoria. Long-term follow-up studies are needed to determine the safety of these treatments in this age group. *(J Pediatr 2014;164:906-11)*.

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"Transgender" is an umbrella term used to identify individuals whose gender identity does not conform to conventional gender roles of either male or female.[1] More specifically, a transgender female (male-to-female [MtF]) is a natal male who has a gender identity that is female; conversely, a transgender male (female-to-male [FtM]) is a natal female who has a gender identity that is male.[2] The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* has replaced "gender identity disorder" with "gender dysphoria." Gender dysphoria in adolescents and adults (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* 302.85) is defined as "incongruence between one's experienced/expressed gender and assigned gender … causing clinically significant distress and impairment in social, school or other important areas of functioning."[3] Gender dysphoria will often remit in the majority of prepubertal children; however, in most gender dysphoric adolescents, it will not.[4] The prevalence of adolescent-onset gender dysphoria is not known, and there are limited accurate assessments of prevalence of transgenderism in adults in North America. However, the prevalence of adults seeking hormonal or surgical treatment for gender dysphoria is reported to be 1:11 900 to 1:30 400 in the Netherlands.[5] The etiology of gender dysphoria remains poorly understood, but there is increasing evidence of a biologic and/or genetic component.[6-8]

The Amsterdam Gender Identity Clinic developed guidelines and protocols for the diagnosis and clinical management of children and youth with gender dysphoria.[9,10] In pubertal children (ie, having reached Tanner stage 2 or 3) with a confirmed diagnosis of gender dysphoria, pubertal suppression with gonadotropin-releasing hormone analog (GnRHa) therapy is suggested. This is seen as the first step toward transitioning to the perceived gender and allows the patient more time to determine whether a full physical transition is in his or her best interest. Cross-sex hormones (androgens for FtM and estrogens for MtF individuals) are then gradually added to induce the physical changes of the desired gender. This treatment approach is supported by published guidelines from the World Professional Association for Transgender Health[11] and the Endocrine Society[1] related to the diagnosis and treatment of gender dysphoria in children and adolescents.

BCCH	British Columbia Children's Hospital
BCTCCG	British Columbia Transgender Clinical Care Group
FtM	Female-to-male (transgender male)
GnRHa	Gonadotropin-releasing hormone analog
MHP	Mental health professional
MtF	Male-to-female (transgender female)

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The objective of this retrospective study was to describe a Canadian cohort of transgender youth from our program at the Endocrinology and Diabetes Unit at British Columbia Children's Hospital (BCCH) with respect to patient characteristics, clinical management, and response to treatment.

Methods

The BCCH Transgender Program consists of a pediatric endocrinologist, an endocrine nurse clinician, and a social worker who work in partnership with mental health professionals (psychiatrics and psychologists) from the community, allowing for a cohesive "clinic without walls" experience that delivers medical care (ie, GnRHa and cross-sex hormone therapy) and psychosocial support to this population. This medical team was integrated into the British Columbia Transgender Clinical Care Group (BCTCCG) in 2003, with the establishment of resources and written provincial guidelines for transgender youth and adults.[12] Almost all patients are first evaluated by a mental health professional MHP from the BCTCCG who is trained and competent in the diagnosis and management of gender dysphoria in youth. Patients are subsequently referred to the BCCH clinic for medical therapy, usually at the initiation of puberty, as deemed appropriate by the MHP.

Patients included in this study met the following criteria: (1) at least Tanner stage 2 pubertal development (ie, breast development in natal females, testicular enlargement in natal males); (2) previous assessment by an MHP belonging to the BCTCCG; and (3) a confirmed diagnosis of gender dysphoria. All patients underwent a series of psychological tests, including the Utrecht Gender Dysphoria Scale,[13] the Piers-Harris Children's Self Concept Scale,[14] and the Gender Identity Questionnaire for Adolescents,[15] and most were receiving ongoing psychotherapy.

In total, 84 patients seen from January 1998 to December 2011 were included in this study. Of these, 45 natal females identified as male (FtM), 37 natal males identified as female (MtF), and 2 natal males were unsettled in their gender identity. Ethics approval was obtained from the University of British Columbia's Clinical Research Ethics Board.

The following data were obtained from the clinic notes: (1) age at first and most recent visit; (2) age at the start of GnRHa and of cross-sex hormone therapy; (3) natal sex; (4) perceived/affirmed gender; (5) Tanner stage at initial visit (breast for natal females, genital for natal males) and before initiating GnRHa and cross-sex hormones; (6) school grade level at first and most recent visit; and (7) medical and psychiatric comorbidities and complications related to medical treatment(s). Descriptive statistics were used. Data are reported as mean ± SD with 95% CIs and/or as a median and range. Differences between groups were assessed by Fisher exact test or χ^2 test where appropriate. A P value $\leq .05$ was deemed to be significant.

Results

Seventy-eight of the 84 youth (93%) had been assessed by ≥1 MHPs from the BCTCCG (2 psychiatrists and 3 psychologists in different locations in British Columbia) and were diagnosed with gender dysphoria before being seen in our clinic. The remaining 6 patients were seen in our clinic before they had been evaluated by an MHP, but they were not offered cross-sex hormones until they had completed mental health assessment. One of these patients did require therapy with a GnRHa to halt pubertal progression before assessment by an MHP. The median time from assessment by an MHP to the first visit to our clinic was 2.6 months (range 0 months to 7.4 years).

Consistent with other medical care in British Columbia, the majority of patients (68%) were referred to our clinic by their family physician or a walk-in clinic after being assessed by a psychologist; 25% were referred directly by a psychiatrist; and 7% were referred by a pediatrician or other subspecialist. The patient referral pattern roughly represented the geographical distribution of the province; only 1 patient was from out of province. The number of new referrals for gender dysphoria from 1998 to 2011 is shown in the Figure.

Initial Clinical Presentation

The characteristics of our patient population are summarized in Table I. Two MtF patients had disorders of sex development (Klinefelter syndrome and mild partial androgen insensitivity syndrome). At the first clinic visit, most patients were in school grades 8-10 (32%) or grades 11-12 (48%); 12% were in grades 5-7, and the remaining 8% were in college/university or no longer attending school.

GnRHa Treatment Approach

The median time between the first visit to our clinic and initiation of GnRHa was 0.2 month (range 0-3.2 months), with 12 of 27 patients (44%) receiving treatment at their first visit to our clinic. Of the 15 FtM patients receiving GnRHa, 14 transitioned to testosterone treatment during the observation period. Seven of these patients continued on GnRHa after starting testosterone; the other 7 patients discontinued GnRHa (after a median of 3.0 years, range 0.2-9.2 years). Five of the latter discontinued GnRHa at the time of hysterectomy and salpingo-oophorectomy, 1 discontinued GnRHa

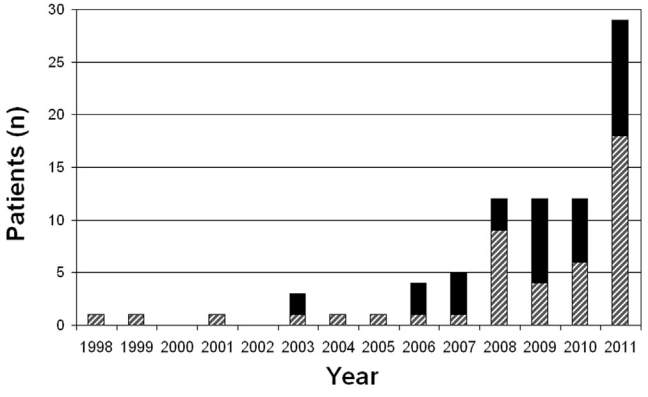

Figure. Number of new patients with gender dysphoria seen in 1998-2011. MtF, *black bars*; FtM, *hatched rectangles*.