Dear Editor,

Gender dysphoria (GD) is defined as a marked incongruence between one's experienced and one's assigned gender. It is characterized by a strong desire to get rid of one's primary and/or secondary sex characteristics and to have the primary and/or secondary sex characteristics of the other gender. Here, we present a case of a mother and daughter who were both diagnosed with GD.

The mother was diagnosed with GD at age 47. She was the only child and suffered from emotional, physical and sexual abuse by her mother. Although the father also physically abused her, she remembers him as a role model, as he was the only person offering affection and understanding. From the age of three, she started behaving like a boy. During later childhood and youth, the gender dysphoric feelings were repressed. After finishing high school, she started working as a maintenance technician at a psychiatric ward. She married at the age of 18. One year later she became pregnant, but after giving birth she felt no emotional connection with the baby-girl and could only manage the care for the child thanks to the support of her mother in law.

A diagnosis of GD was established in 2004. During the diagnostic phase, no genetic nor biologic abnormalities could be demonstrated. The karyotype was normal 46, XX. Shortly after the diagnosis, the client started with cross-sex hormone therapy. In 2006 he underwent bilateral subcutaneous mastectomy and endoscopic hysterectomy/ovariectomy. Metadoioplasty followed by the phalloplasty were performed in 2007 and 2009, respectively. In 2012, the sex reassignment surgery was completed with the placement of an erectile device and testicular prostheses. During this process, the client felt supported by his male partner, but their relationship ended in 2009. He had lost contact with his own mother since youth, and his father had died during the time of the diagnostic phase. Halfway transition, he was informed that his only daughter also experienced GD. As a parent, he struggled with guilt feelings but managed to handle these with the help of his psychiatrist.

The daughter was diagnosed with GD at age 31. She was also the only child. She remembered having a good relationship with her parents and had no traumatic childhood memories. Her father took no prominent place in her education, but she remembers a harmonious father-daughter relationship. GD became obvious from the age of eight.

During later youth, she suffered from psychological problems such as panic attacks and social phobia. After finishing hotel management training, she worked as an educator until she was 25. She stopped working because of psychological and orthopedic problems. In her twenties, she experienced forced sexual contacts with men. However, in her own sexual fantasies she wanted to be a man with a female partner. At the age of 27, she had a relationship with a bisexual woman. Currently, she has a female partner.

A diagnosis of GD was established in 2007, thus 3 years after the mother's diagnosis. During the diagnostic phase, no hormonal nor genetic abnormalities were found. She had a normal karyotype 46, XX. In 2008, cross-sex hormone therapy was started. Bilateral subcutaneous mastectomy and endoscopic hysterectomy/ovariectomy were performed in 2009. Because of a postoperative complication after the mastectomy further genital surgery was temporarily postponed. During transition, he felt supported by his family, although his father initially had a hard time accepting his decision. His parents divorced during the transition process.

He was informed about his mother's transition when she already was receiving cross-sex hormonal therapy and initially experienced a feeling of loss. However, since transitioning himself, their relationship has improved. Both father and son are doing well now.

It is estimated that about one-third of persons with GD has children. The question rises whether children of parents with GD are more likely to show GD themselves. The exact etiology of GD remains unclear although there is a tendency in the more recent literature to focus on biological aspects. With regard to biological factors contributing to the development of GD, research focused on brain structures and genetic factors. The existence of sexually dimorphic brain nuclei has been known for a long time. Several studies revealed that some of these nuclei in transsexuals resemble the nuclei in cis-gendered males and females. Furthermore, these nuclei are considered to be part of a complex network that influences the development of sexual behavior. It should be noted that only one female-to-male transsexual was reported in the referenced work.

According to neuroimaging studies that used gonadotropin-releasing hormone analogs to suppress puberty in adolescents with GD, the microstructure pattern of white matter, the gray matter volume of the putamen and cerebral activation patterns in GD persons before treatment seemed to share more features with those of the experienced gender than those of their natal sex. These findings have also been confirmed by neuroimaging studies in untreated transsexual
men, which showed that they share the pattern of white matter microstructure with those of the experienced gender.

With regard to genetic causes, only sporadic GD cases with chromosomal abnormalities have been found in the literature. A Belgian study showed that 97.55% of GD patients have a normal karyogram. Abnormal karyograms were more frequent in trans women than in trans men, 3.19% and 0.85%, respectively. Among the persons with abnormal karyograms, three had a Klinefelter syndrome, the other had abnormalities in their autosomal chromosomes. Five Lombardo et al. recently investigated the DNA of 30 transsexual women to detect molecular changes in well-known genes that influence sexual differentiation. However, no association with GD could be demonstrated. On the other hand, recent studies conducted in twins showed that genetic factors supposedly play a role in the development of gender identity. In a study of Heylens et al.7, 9 (39.1%) of 23 monozygotic female and male twins were found to be concordant for GD, opposed to none of 21 dizygotic twin pairs. Gómez-Gil et al.8 suggested that siblings of persons with GD show a higher chance to develop GD themselves. This chance seems to be higher in brothers of GD persons and in siblings of male-to-female transsexuals. In addition to these biological factors, the psychosocial context in which a child grows up may also play a role in the development of GD. A disturbed emotional parent-child relationship is considered a causative factor. The mechanism in the development of male-to-female GD would be a physically or emotionally absent father and an extremely involved mother. In trans men, the opposite situation is observed, with an unsatisfactory mother-daughter relationship and an intense relationship with the father. Based on a study, including 87 adult children of homosexual and transsexual parents, Cameron concluded that in homosexual but not in transsexual parents, a child's sexual orientation is influenced by the sexual orientation of its parents. In 1978, Green observed 34 children who stayed in touch with their transsexual parent after transition. None of them exhibited any clinically significant cross-gender behavior.

To our knowledge, this is the first case report about the presence of GD in a mother and daughter leading to hormone therapy and surgery in both. This report mainly focuses on psychosocial factors, but genetic factors cannot completely be ruled out as only karyotyping had been performed in this family.

AUTHOR CONTRIBUTIONS
TS, CV and GT performed the literature search and drafted the manuscript. GH and EDB revised the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS
All authors declare no competing interests.

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