

# Awareness is the key!

## Heavy delay in diagnosis of 17-Hydroxysteroid-Dehydrogenase III deficiency (17HSD3D) and other insights and conclusions from a cohort of ten 17HSD3D patients in Germany.

Jakob Meinel<sup>1</sup>, Nadine Grossmüller<sup>1</sup>, Annette Richter-Unruh<sup>1,2</sup>

<sup>1</sup> Paediatric Endocrinology, MVZ Dr. Eberhard & Partner Dortmund, Germany

<sup>2</sup> Paediatric Endocrinology and diabetes, University Children's Hospital Münster, Germany

### background and objective

17-Hydroxysteroid-Dehydrogenase III deficiency (17HSD3D) is a rare genetic disorder that leads to disorders of sex development (DSD) in 46,XY patients. Phenotype at birth ranges from unsuspecting female genitalia to micropenises. Besides molecular genetic testing no reliable lab parameters have been established for pre-identifying patients through basal steroid-levels or hCG-testing. This bares the risk of under-, mis- or late diagnosis. Many patients only appear conspicuous during adolescents due to virilisation and amenorrhea. Further, little research has been performed on psychological wellbeing, gender identification and gender related behaviour of affected patients. We aim to share insights from our cohort of 17HSD3D patients in these fields of interest.

### method and patients

Blood hormone levels from 10 17HSD3D patients from Nordrhein-Westfalen, Germany were collected for signs of possible patterns in steroid profiles. Information on time to diagnosis was drawn from case histories. Semi-structured interviews with patients and parents were performed for information on psychological wellbeing and their gender identity. Patients and parents were interviewed individually to avoid adulteration.

### results

Mean age at diagnosis of DSD and 17HSD3D were 4,3 and 10,9 years respectively. Five patient's steroid profiles were determined before gonadectomy and commencement of hormone therapy and thus could be considered for evaluation, resulting in sample size too small to draw definitive conclusions. It remains noteworthy that all patients with gonads showed androstendion and estrone levels above tanner-related reference values. This may be approached in further research. Basal testosterone/androstendione-quotient was below 0,62 regardless of gonadectomy.

### references

<sup>1</sup> Lee PA, Houk CP, Ahmed SF, Hughes IA; International Consensus Conference on Intersex organized by the Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology. Consensus statement on management of intersex disorders. International Consensus Conference on Intersex. Pediatrics. 2006 Aug;118(2):e488-500.

<sup>2</sup> German Society of Urology (DGU), German Society of Pediatric Surgery (DGKCH), German Society for Pediatric Endocrinology and Diabetes (DGKED). S2k-Leitlinie Varianten der Geschlechtsentwicklung. Association of the Scientific Medical Societies in Germany. 2016 Jul; AWMF-Registry Number 174/001.

Thus far 5 semi-structured interviews were conducted, 3 are still pending and 2 patients did not wish to be interviewed. All 5 were declared as female at birth. 2 now identify themselves as male and 3 as female. However, 2 female-identifying patients showed male gender related behaviour and were less confident about their gender. One male-identifying patient continues to struggle with his gender, after his gender reassignment was commenced during early adolescence.

### conclusion

This highlights the relevance of gender neutral upbringing of 46,XY 17HSD3D patients to allow development to both male and female gender. Yet only in 2 patients the parents have not made a definitive gender assignment and leave this decision up to their child. These are the 2 patients now identifying as males. We advocate that gender reassignment should be deferred until 18 years for a more deliberate decision to be possible. Allowing for the fact that gender identity can change throughout development. An average 6-year delay between diagnosis of DSD and 17HSD3D emphasizes the need for increased awareness among physicians as well as clear diagnostic procedures for 17HSD3D to allow for swifter diagnosis thus reducing burden for patients and family through the limbo of unclear etiology. It also shows that 17HSD3D is taken too little notice of and could mean that many cases remain undiscovered. In addition, timely detection is beneficial due to increased cancer risk among patients and thus allowing for early monitoring of gonads.<sup>1</sup> Our interviews showed that only 2 out of 5 had received counseling by a psychologist, though recommended by guideline.<sup>2</sup> The other 3 however seemed contempt with their current situation and did not feel the need for counseling. Further, our interviews showed that patients may have gender dysphoria before diagnosis of DSD, thus physicians should consider DSD and hence 17HSD3D in these patients too. For this awareness is the key.