Background

Although the availability of next generation sequencing and detailed endocrine tests may have increased the likelihood of reaching a diagnosis in boys with XY DSD, it has also led to challenges in interpretation of results.

Objectives

To examine the range of endocrine and molecular genetic variation in a group of boys undergoing evaluation for XY DSD.

Methods

Boys with XY DSD who were evaluated and discussed at the DSD Diagnostic Board in Glasgow from 2016 to 2019 were included. Sequence variants were classified according to ACMG guidelines and Class 3 variants of uncertain clinical significance (VUS) were divided into 3A and 3B, depending on whether the phenotype was consistent or not, respectively.

Results

N=124
Median (Range) or N (%)
Age (years) 0.87 (0.17,95)
External Masculinization Score (EMS) 8.25 (2, 12)
Positive Family History of DSD 34 (27)
Parental Consanguinity 8 (%) Associated Malformations 60 (55)
Recognised Genetic Syndrome 13 (11)

Table 1. Clinical Characteristics

Figure 1. Endocrine assessment results

Table 2. Range of endocrine investigations

Figure 2. Comparison of phenotypes of XY DSD boys with or without family history of DSD, associated malformations, endocrine abnormalities and between subgroups of endocrine abnormalities identified

No significant differences in phenotypes between those in whom family history of DSD and associated malformations were present or not, between boys with normal and abnormal endocrine investigations were found

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Table 3. Range of genetic investigations

The appearance of external genitalia seems to be unrelated to the presence of genetic abnormality

Conclusions

The extent of undermasculinisation in boys with DSD seems to be unrelated to the presence of molecular genetic or endocrine abnormalities. The increased use of NGS, needs to be coupled with rigorous and standardised processes for interpretation of results.

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2015)*

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