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Presentations and Outcomes of Patients with Disorders of Sexual Development (DSD) in a Tertiary Paediatric and Adolescent Gynaecology (PAG) Service

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Introduction

Adolescence is a unique period of human development during which complex medical conditions may present. Disorders of sexual development are rare and can present with range of clinical presentations, and most tertiary centres would only see a few new cases each year. PAG is a highly specialised area and DSDs present a complex management situation, with specialist gynaecological, endocrinological, surgical, and psychological support vital.

The study was designed to analyse common presentations of patients with DSDs in adolescence, age at presentation, age of diagnosis, karyotype, mullerian structures, gonadal histology and management.

Results

24 adolescents with DSD were identified from the PAG database. 6 adolescents had classical congenital adrenal hyperplasia (25%). 8 adolescents (33%) had androgen insensitivity syndrome (AIS), with 5 cases being partial (PAIS) and 3 complete (CAIS). 4 adolescents (17%) had Swyer syndrome (46XY DSD). The remaining cases included a 46XXp Turners variant (1), ovotesticular 46XY DSD (1), mixed gonadal dysgenesis 46X0/46XY (2), 5-alpha reductase deficiency 46XY (1) and 17-beta HSD3 deficiency 46XY (1).

The most common reasons for referral were primary amenorrhea, hormone replacement, and vaginal dilation and the average age initial review 17 years, 3 months. 5 adolescents were unaware of their diagnosis prior to referral and assessment, with 13 diagnosed in infancy with ambiguous gentalia or hernia.

Gonadectomy was performed in all cases, except in the Turner's variant. In CAIS, bilateral gonadectomies were most often done at infancy. Dysgerminoma was diagnosed in two cases with Swyer syndrome, with involvement of oncology for chemotherapy and one required further surgery.

Methods

The study was a retrospective review of adolescent females ages 8 to 18 years with DSDs presenting to the Queensland PAG Service, Brisbane Australia over the last 10 years. Data was collected with patient consent using electronic records and paper charts. HREC ethics approval was obtained.

Conclusion

This study highlights that some DSDs may not be detected until adolescence and involves highly complex and multidisciplinary management. Management through PAG service included gonadectomy, pubertal induction and oestrogen replacement where indicated, vaginal dilatation, and psychological counselling. It is essential that PAG specialists be familiar with patients with DSD, and competent to assess, treat, and counsel these highly complex cohort of individuals in a multidisciplinary team.

Table 1: Description of commonly encountered Disorders of Sexual Differentiation (DSD).

Most common DSDs	Chromosome	Characteristics
Turner's Syndrome	45XO	Short webbed neck, low set ears, short stature, amenorrhoea, cardiac malformations, streak gonads, uterus present
Classical Congenital adrenal hyperplasia	21-hydroxylase deficiency	Excessive androgen production, salt losing crises. Genetically female: ambiguous genitalia, clitoromegaly, fusion of labioscrotal folds, no testes, normal ovaries and uterus Genetically male: penile enlargement, early axillary and pubic hair, tall stature
Complete androgen insensitivity syndrome	46XY	Phenotypically female, external female genitalia, shallow vaginal cavity, no uterus, undescended testes
Partial androgen insensitivity syndrome	46XY	Ambiguous genitalia, primary amenorrhoea, clitoromegaly, no uterus
Mixed gonadal dysgenesis	45X/46XY mosaicism	Variable – partial virilization, ambiguous genitalia, majority phenotypically male
XY gonadal dysgenesis (Swyer's)	46XY SRY mutations	Female genitalia, streak gonads, uterus present, infertility
Ovotesticular disorder	46XX/46XY, 46XX, 47XXY	Ambiguous genitalia, ovarian and testicular tissue

Table 2: Characteristics of DSD cases (excluding cases of congenital adrenal hyperplasia)

Presentation	Karyotype	Mullerian Structure	Gonads, histopathology	Final diagnosis	Management
Cloacal exstrophy	46XY	No uterus	Gonadectomy. Histopath: testes.	Ovotesticular DSD	Repair coacal exstrophy and gonadectomy as child. Vaginal Dilatation and HRT.
Primary amenorrhoea	46XXp-	Small uterus	Streak ovaries, not excised	Turner variant	COCP.
Ambiguous genitalia birth	46XY	No uterus or cervix, rudimentary vagina. Small inguinal testes.	Gonadectomy. Histopathology: Immature testes.	PAIS	Gonadectomy and feminizing genitoplasty 1 year age. Vaginal dilatation.
Primary amenorrhoea	45XO/46XY	Absent uterus, cervix, and ovaries.	None	Mixed gonadal dysgenesis	Vaginal Dilatation.
Primary amenorrhoea	46XY	Subseptate small uterus	Gonadectomy. Histopath: streak gonads	46XY DSD Swyer Syndrome	Laparoscopic gonadectomy and bilateral salpingectomy adolescence. Pubertal induction and HRT.
Ambiguous genitalia birth	45XO/46XY	Small uterus, cervix	Gonadectomy. Histopath: testes.	Mixed gonadal dysgenesis	Gonadectomy and genitoplasy as infant. Pubertal induction and HRT. Vaginal Dilatation.
Ambiguous genitalia birth	46XY	No uterus or cervix	Gonadectomy. Histopath: testes.	PAIS	Gonadectomy and reconstructive surgery as infant. Pubertal induction and HRT. Vaginal dilatation.
Primary amenorrhoea	46XY	Small uterus	Gonadectomy. Histopath: streak gonads	46XY DSD Swyer Syndrome	Laparoscopic gonadectomy and bilateral salpingectomy adolescence. Pubertal induction and HRT.
Primary amenorrhoea, inguinal hernias, deep voice	46XY	No uterus	Gonadectomy. Histopath: testes.	5 alpha reductase deficiency	Gonadectomy and surgical creation neovagina in adolescence. Pubertal induction and HRT. Vaginal dilators.
Ambiguous genitalia birth	46XY	No uterus	Gonadectomy. Histopath: testes.	PAIS	Gonadectomy and surgical creation neovagina as child. Pubertal induction and HRT. Vaginal dilatators.
Ambiguous genitalia birth	46XY	No uterus	Gonadectomy. Histopath: testes	PAIS	Gonadectomy and feminizing surgery age 2yo. Pubertal induction and HRT. Vaginal dilatation.
Primary amenorrhoea	46XY	Rudimentary uterus	Right gonad: testes Left: Gonadoblastoma and germinoma	46XY DSD Swyer Syndrome	Laparoscopic bilateral gonadectomy and bilateral salpingectomy. No chemotherapy. Pubertal induction and HRT.
Inguinal hernias	46XY	No uterus or cervix	Gonadectomy. Histopath: testes.	17-beta HSD3 deficiency 46XY	Bilateral orchidectomy and hernia repair aged 12. Pubertal induction and HRT. Vaginal dilatation.
Inguinal hernias	46XY	No uterus or cervix	Gonadectomy. Histopath: testes.	CAIS	Bilateral gonadectomy and hernia repair in infancy. Pubertal induction and HRT. Vaginal dilatation.
Bilateral inguinal hernia	46XY	No uterus, vaginal remnant	Gonadectomy. Histopath: testes.	PAIS	Bilateral gonadectomy. Pubertal induction and HRT. Vaginal dilatation.
Primary amenorrhoea	46XY	Small uterus and cervix present	Ovary, left streak Ovarian dysgerminoma + gonadoblastoma (Stage1c)	46XY DSD Swyer Syndrome	Laparoscopic bilateral gonadectomy and bilateral salpingectomy. Bilateral salpingectomy + bilateral gonadectomy. Chemotherapy. COCP.
Bilateral inguinal hernia	46XY	No uterus	Gonadectomy. Histopath: testes.	CAIS	Bilateral gonadectomy 6 months. Pubertal induction and HRT. For vaginal dilatation when mature.
Inguinal hernias	46XY	No uterus	Gonadectomy. Histopath: testes.	CAIS	Bilateral gonadectomy and hernia repair 2 years. Pubertal induction and HRT. Vaginal dilatation.

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