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Androgen Insensitivity Syndrome - A 10 year Experience

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OBJECTIVE - To analyse the diagnosis and management of androgen insensitivity syndrome from January 1992 to December 2001. METHOD - Ten cases of androgen insensitivity syndrome identified by detailed clinical, cytogenetic and hormonal evaluation from January 1992 to December 2001 were analysed with reference to their clinical presentation, management and outcome. RESULT - Complete androgen insensitivity syndrome was diagnosed in seven individuals, two of whom were sisters. All presented at puberty with primary amenorrhea and female phenotype. They were managed successfully by psychological counseling, gonadectomy and hormone replacement therapy with graded vaginal dilatation. Laparoscopic gonadectomy was done in the two sisters. Incomplete androgen insensitivity syndrome was diagnosed in three individuals who presented with virilization at puberty. Feminizing genitoplasty was done in all. Only one case required vaginoplasty. All were followed up with detailed psychological counseling. Satisfactory vaginal length could be achieved in all patients. Five women (three of complete variety and two of incomplete variety) subsequently got married and are having successful coitus. Significant recession of hirsuitism, change of voice and breast development were noted in the three cases of incomplete androgen insensitivity syndrome two years after surgery. CONCLUSION- Excellent quality of life can be achieved in individuals with androgen insensitivity syndrome by a combination of psychological counseling, individualized surgery and hormone replacement therapy.

Key words: androgen insensitivity, gonadectomy, genitoplasty

Introduction

Androgen insensitivity syndrome (AIS) is defined as female or ambiguous phenotype in a 46 XY male with normal testes and normal testosterone production and metabolism", Genetic defects of human androgen receptors can cause a wide spectrum of AIS, ranging from phenotypic females in complete AIS to ambiguous genitalia in incomplete or partial AIS to male infertility in minimal AIS[2]. More than 250 mutations of the androgen receptor gene have been identified", Incidence of complete AIS is 1 in 20,000 while that of incomplete AIS is 1 in 62,000[4]. These are rare conditions but extremely distressing to the concerned individuals requiring expert handling. Management should include detailed psychological counseling not only to determine the sexual mentation but also to help these individuals to cope with their problems. In view of a high incidence of gonadal malignancy associated with dysgenetic gonads; gonadectomy is advocated. The incomplete AIS individuals require a feminizing genitoplasty in addition to a gonadectomy.

The complete AIS generally presents at puberty with primary amenorrhea. However, the incomplete variety may present at birth as ambiguous genitalia or at puberty with virilization. Timing of gonadectomy is controversial but feminizing genitoplasty is done at the time of diagnosis to prevent any conflict of gender identity.

Material and Methods

Ten cases of AIS were identified by detailed clinical, cytogenetic and hormonal evaluation from January 1992 to December 2001. All individuals presented at puberty with primary amenorrhea. There were seven cases of complete AIS and three of incomplete AIS who presented with virlization in addition to primary amenorrhea.

Table I summarizes the clinical presentation and investigations done in these cases.

Results

All cases presented at puberty. Age ranged from 14 to 26 years. Incomplete variety presented about 2 years earlier

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Table I. Clinical Presentation and Investigations.

	Complete AIS n=7	Incomplete AIS n=3
Age range	16 - 26 yrs	14 - 18 yrs
Primary amenorrhoea	Present	Present
Virilization	Absent	Present
External Genitalia	Female	Male
Brest development	Present	Absent
Testes	Abdominal 5 Absent 1 Completely descended 1	In scrotum and inguinal canal
Vaginal canal	Present in all	Present in all except one
Psychologist evaluation	Female sexual mentation	Female sexual mentation
Karyotype	46 XY	46 XY
Serum Testosterone	Normal male levels	Normal male levels
Serum FSH & Serum LH	Increased	Increased
Pelvic ultrasound	Uterus and ovaries not identified	Uterus and ovaries not identified
Histopathology	5 - immature testicular tissue 1 - testicular tissue with ovary like stroma (Inl patient no gonadal tissue could be identified at laparoscopy	2 - atrophic testes 1 - testicular tissue with sertoli cells

at onset of puberty. The complete AIS individuals had a female phenotype with breast development and patent vagina. Gonads were intra-abdominal in most cases'". One case however had completely descended testes in the labia majora. Serum testosterone was normal to low. All underwent diagnostic laparoscopy. In one patient no gonadal tissue could be identified even after diagnostic laparoscopy. Gonadectomy was done in six cases. Laparotomy with gonadectomy was done in three cases while in two, who were sisters, this was done through the laparoscopic route. In one sister the gonads were lying free in the pelvis attached only laterally but in the other the gonads were attached to a median ridge. Removal of gonads was done by mobilization and dissection of gonads from the pelvic side walls and transection of the median ligament in the second sister. The procedure was completed in 15 minutes and was bloodless. Both patients were discharged after 24 hours. Histopathology of the gonads in one sister showed testes and in the second sister it revealed immature testicular tissue with ovary like stroma. The incomplete AIS individuals presented with virilization at puberty. They had male distribution of hair, hoarse voice, male habitus and no breast development. None of them had significant ambiguous genitalia at birth and had been brought up as females. Testes were descended completely or partially in all of them. In two cases only release of introital skin web was required to identify the 4 em long vagina. In one case there was no vagina identified and hence a McIndoe vaginoplasty was done. Feminizing genitoplasty comprised a gonadectomy, resection of crura, formation of clitoris and reconstruction of labia

minora with prepucial skin. Graded vaginal dilatation was advised post-operatively in all.

Satisfactory vaginal length could be achieved in all 10 patients. Successful coitus was achieved in five individuals who subsequently got married, of which two were of the incomplete AIS variety.

All were put on estrogen replacement therapy postoperatively. There was significant regression of hirsuitism, change of voice and breast development in the three cases of incomplete AIS two years after surgery. One girl with incomplete AIS is still schooling.

Discussion

Most reports in the literature of incomplete AIS are by pediatric surgeons. However, patients can present at puberty to the gynecologist as in our series.

In the series by Viner et al", 51 cases of AIS with 22 cases of incomplete AIS were identified. However, all presented with ambiguous genitalia at birth and 59% were raised as males. In our series, since there was no significant ambiguous genitalia at birth, all were raised as females.

Ahmed et al" reported a database in the United Kingdom of individuals with AIS, with 105 cases of complete AIS and 173 cases of partial AIS. All cases of partial AIS in the series again presented within one month of birth.

Velidedeoglu et aF also reported three sisters with incomplete AIS. However two of the sisters required vaginoplasty with neurovascular pudendal thigh flaps. Only one had adequate vaginal depth. We had good results with McIndoe vaginoplasty which is a simpler procedure. This woman is now married and is having satisfactory coitus.

Laparoscopic gonadectomy in complete AIS with abdominal gonads is a recent intervention. A 10 year medline search revealed only 12 cases managed by this route. The laparoscopic approach is minimally invasive, safe and more cosmetically acceptable replacement for laparotomy":".

Androgen insensitivity syndrome, although very rare, is extremely distressing to the concerned individuals and requires expert and sympathetic handling. Patients can be helped to achieve an excellent quality of life as a female by a multispeciality approach includinag gonadectomy, surgical correction, and detailed and repeated psychological counseling along with estrogen replacement therapy. Laparoscopic gonadectomy is an acceptable alternative to laparotomy and should be used as far as possible. Future research towards uterine and ovarian transplantation may help them to achieve reproductive potential.

In view of the poor anatomic and functional results of genital reconstructive surgery and consequent psychological problems, children with AIS should be raised as females.

References

1. Terry W. Hensle. Genital anomalies. In : Gillenwater JY, Grayback JT, Howards SS et al. eds. Adult and Pediatric Urology. 3rd ed. St. Luis. *Mosby Inc. 1996;2529-48*

2. Yong EL, Tut TG, Ghadessy FS et al. Partial Androgen Insensitivity and correlation with the predicted three dimensional structure of the androgen receptor Hegrand binding domain. *Molcell Endocrinol 1998;37:47-50.*

3. Okabe T, Nawata H.Pathogenesis of Androgen Insensitivity Syndrome. *Nippon - Rinsho* 1998; 56: 1881 - 6.

4. Griffith JE, Wilson JD. The syndrome of androgen resistance. *New Engl JMed 1980;302:198-202.*

5. Viner RM, Teoh Y, Williams OM et al. Androgen Insensitivity Syndrome – A survey of diagnostic procedures and management in the UK. *Arch Dis Child 1997;77:305-9.*

6. Ahmed SF, Chong A, Dorey L et al. Phenotypic features, androgen receptor binding and mutational analysis of 278 clinical cases reported as Androgen Insensitivity Syndrome. *Clin Endocrinol Metab 2000;85:658-65.*

7. Velidedeoglu HV, Coskunfirat *OK,* Bozdogan MN et al. The surgical management of Incomplete testicular feminization in three sisters. *Br JPlast Surg* 1997, 50: 212-6.

8. Wu MH, Hseih MF, Yau MP et al. Bilateral laparoscopic gonadectomy for testicular feminization syndrome *JMed. Sci 1997;13:511-5.*

9. Diaz DC, Chevez-Lopez D. Laparoscopic gonadectomy in women with complete Androgen Insensitivity Syndrome. *J Am Assac Gynecal Laparosc 1996;3:317-9.*

10. Obianwu CW, Patter SF, Bruno AA. Bilateral laparoscopic gonadectomy in a patient with Complete Androgen Insensitivity - A case report. *J Reprod Med 1996,41:270-2.*

11. Ulrich U, Keckstein J, Buck C. Removal of gonads in Y chromosome bearing gonadal dysgenesis and in androgen insensitivity syndrome by laparoscopic surgery. *Surg Endase 1996;10:422-5.*

12. Tangaya M, Mayashi Y, Mogami T et a1. Laparoscopic gonadectomy for testicular feminization syndrome. *Int J Ural* 1995; *2:200-2.*

13. Kallipolitis UK, Milingos SO, Creatsas CK et a1. Laparoscopic gonadectomy in a patient with testicular feminization syndrome. *J Pediatr Adalesc Gynecal 2000;13:23-6.*