Androgen Insensitivity Syndrome

Absolutely Everything You Need to Know!

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Androgen Insensitivity Syndrome Support Group Australia Inc.

Introduction

> ***The rights of the patient to assign meaning and validity to his or her condition via a diagnosis, and to seek out a support group, must be considered.***

Up to eight weeks gestation, every foetus, whether of typical male or female chromosomal sex, has the capacity to develop either a male or female reproductive system, and in a typical male (XY) foetus the active intervention of male hormones (androgens) is needed to produce a fully male system. A female body type with female external genitalia is the basic underlying human form.

Androgen Insensitivity Syndrome (A.I.S.)

Androgen Insensitivity Syndrome (old name Testicular Feminisation Syndrome) causes an interruption of the foetal development of the reproductive system. In A.I.S. the child is conceived with typical male (XY) sex chromosomes. Embryonic testes develop and start to produce androgens but the body is unable to respond to these androgens to a varying degree. This means that the genitals can vary from completely female if there is no response through to almost completely male if there is a slight insensitivity to androgens or anywhere in between. So the external genital development continues along female lines (the 'backup' route) but the development of female internal organs has already been suppressed by a hormone (Müllerian Inhibitory Factor or M.I.F.) from the foetal testes.

A gene on the X chromosome controls tissue androgen sensitivity, and A.I.S. is an X-linked recessive condition, inherited down the maternal line (or, in an estimated third of all cases, results from a spontaneous mutation). A mother who carries the variant gene has a one in two chance of any XY child having A.I.S. and a one in two chance of any XX child being a carrier of the variant gene like herself, but XX individuals can be tested to see if they are carriers. A.I.S. is a biological intersex condition, in which the reproductive organs/genitalia are partly at variance with the genetic sex.

Forms of A.I.S.

There are two forms; a complete form (Complete Androgen Insensitivity Syndrome or C.A.I.S.) where the tissues are completely insensitive to androgens, and a partial form (Partial Androgen Insensitivity Syndrome or P.A.I.S.) where the tissues are insensitive to varying extents forming a spectrum of outcomes.

At the C.A.I.S. end of the spectrum the external genitalia are completely female (A.I.S. Grades 6 and 7) and the sex of rearing is invariably female. In P.A.I.S., the outward genital appearance can lie anywhere along a continuum from completely female (Grade 6), through mixed male/female, to almost completely male (Grade 1) and can vary somewhat between affected siblings. Some people with P.A.I.S. are males, which supports the A.I.S.S.G.A. position against childhood surgeries. The complete and partial forms may be caused by different variations at the genetic/cellular level and do not usually occur in the same extended family.

Synonyms

Androgen Insensitivity Syndrome, Androgen Resistance Syndrome, Testicular Feminisation Syndrome, Feminising Testes Syndrome, Male Pseudo-hermaphroditism, Goldberg-Maxwell Syndrome (C.A.I.S.), Morris's Syndrome (C.A.I.S.), Lubs Syndrome (P.A.I.S.), Reifenstein Syndrome (P.A.I.S.), Gilbert-Dreyfus Syndrome (P.A.I.S.), Rosewater Syndrome (P.A.I.S.).

Other XY conditions with some A.I.S.-like features: 5 alpha-reductase deficiency, 17 keto-steroid reductase deficiency, XY gonadal dysgenesis (Swyer Syndrome), Leydig cell hypoplasia, Denys-Drash Syndrome, Smith-Lemli-Opitz Syndrome.

XX conditions with some A.I.S.-like features: Mayer Rokitansky Küster Hauser or M.R.K.H. Syndrome, Müllerian dysgenesis.

Incidence

The most accurate figure currently available for C.A.I.S. comes from an analysis (1992) of a Danish patient register, suggesting an incidence of 1 in 20,400 XY births (hospitalised cases only, so true incidence probably higher). P.A.I.S. may be only about one tenth as

common as C.A.I.S..

Effects (C.A.I.S.)

Even in the complete form there will be no ovaries, Fallopian tubes or uterus, and the vagina will be blind ending and possibly short or absent. The undescended testes can result in an inguinal (groin) hernia in infancy and this is when the condition may come to notice in a female child (~50 percent of cases). Otherwise C.A.I.S. may not be discovered until puberty as a result of a girl not commencing her monthly cycle.

Female pubertal development occurs, because the testes produce some oestrogen, but there will be no menstruation and no possibility of conceiving/bearing children. Some girls with A.I.S. may develop some dark, coarse pubic/underarm hair (A.I.S. Grade 6) but this does not develop in true C.A.I.S. (Grade 7) because androgen action is needed for its growth. The nipples usually remain under-developed and pale in colour. The vagina may need to be lengthened before sexual intercourse is possible. The older literature sometimes states that girls with A.I.S. are often tall, that the body form is 'voluptuously female', i.e. with very adequate breast development, and that the skin maintains a good condition, not being prone to acne (which is linked to the action of male hormones).

Gonadectomy (Orchidectomy)

There is a small risk of cancerous changes occurring in the undescended testes after age twenty, and many clinicians recommend their removal in women with A.I.S. before this time. Usually this is deferred until the late-teens to allow a spontaneous feminising puberty to occur, which may have physiological and psychological advantages over one induced by exogenous hormones. Note that girls with C.A.I.S. cannot be masculinised by hormone administration, because of their complete insensitivity to androgens.

Although the pre-adult risk of cancer is too small to justify it, gonadectomy is sometimes done in infancy or childhood, usually with the intention of avoiding a psychological crisis arising from explaining the need, later on, for such an operation. Obviously, gonadectomies should not be performed on males with P.A.I.S., as they produce the testosterone needed for secondary sexual characteristics, although additional testosterone treatment may be required.

H.R.T./Osteoporosis

When the testes are removed from women with A.I.S. after puberty, immediate long-term female hormone replacement therapy (H.R.T.) is needed to prevent menopausal symptoms and osteoporosis (bone thinning) and protect against cardiovascular disease. In the case of gonadectomy in infancy/childhood, H.R.T. is often started at age eleven, in order to initiate puberty.

Low bone density seems to be more common in A.I.S. women than in XX women. The cause is not clear. Lack of H.R.T. is a risk factor, although some A.I.S. adults have a low bone density in spite of regular H.R.T. Possibly, it is due to that fact that 'XY girls with testes' have lower oestrogen levels than 'XX girls with ovaries' during the time when most bone development occurs. XX girls start producing oestrogen at around age eight (i.e. a year or two before breast development starts) so supplementary low dose oestrogen from this age, with or without gonads in place, may be advisable in A.I.S.. However, the androgen insensitivity itself might contribute to a low bone density in C.A.I.S., irrespective of oestrogenisation.

A.I.S. women should be aware of their increased risk of osteoporosis, especially if they have not used H.R.T. continuously after gonadectomy.

Testosterone treatment in men with A.I.S. will also help prevent osteoporosis.

Vaginal Hypoplasia

Generally the top third of the vagina is missing in A.I.S. but in some cases the vagina may be no more than a centimetre or two in length, or even just a dimple. Clinicians must not overlook vaginal hypoplasia in pubertal A.I.S. patients, because some youngsters discover this by self-examination and can live in fear and isolation with this secret for many years. Vaginal hypoplasia (in both C.A.I.S. and P.A.I.S.) can be treated by the non-surgical method of pressure dilation, performed by the girl herself at home. This is best deferred until she has gone through puberty and is sufficiently motivated. It involves minimal risk and expense, and results in a vagina that closely resembles a typical one. In some cases, the Vecchietti procedure, which is a semi-surgical way of accelerating dilation, has advantages. There are a number of plastic surgery methods of lengthening the vagina using skin grafts, sections of intestine etc. These all have many disadvantages, and should be used only when less invasive treatments have been ruled out. Vaginoplasty in early childhood usually has poor results and should not be done.

Facing the Diagnosis

Some clinicians/parents cling to an old-fashioned, paternalistic attitude and, in a misguided attempt to spare the patient inner conflict, withhold the genetic/gonadal information, but most professional carers now recommend truth disclosure with psychological support/counselling. Otherwise patients will seek diagnostic information via medical libraries or the Internet and bear the burden alone and in silence. Many will wrestle with perplexing half-truths, or reach false conclusions (e.g. that gonadectomy = cancer).

If the parents' emotional needs/anxieties are addressed first (via psychological support/counselling from professionally trained staff) it will be easier for them to provide effective support to their child. Everyone will feel better if there are no taboos about the subject. Talking, like grieving, is therapeutic, enabling feelings to be confronted and resolved. Pushing the matter under the carpet is just storing up psychological trouble for later. It is important that parents encourage discussion with their child, and actively seek out information on their behalf. Unfortunately, keeping the condition a secret can become more important to some parents than acknowledging their child's need for emotional support and appropriate clinical intervention. It wastes mental/emotional energy that is better spent in helping the child come to terms with the truth.

The rights of the patient to assign meaning and validity to his or her condition via a diagnosis, and to seek out a support group, must be considered. Meeting others who are affected is vital and is probably the single most useful therapeutic measure. Doctors may have over-emphasised the extent to which knowledge of their genetic/gonadal status causes lasting distress to A.I.S. women. C.A.I.S. adults tell us that, in the long-term, their XY chromosomes and testes would have been of no material relevance to them – were it not for the isolation, sense of freakishness and stigma which results from an apparent unacceptability of their biological status in the eyes of adults around them since they have a normal feminine gender identity. In C.A.I.S., the person will look like a girl, and problems of psychosexual identity as a biologically determined feature of the condition are unlikely. In C.A.I.S., leanings towards heterosexuality, lesbianism or bisexuality seem no different from females in general.

But over-emphasis on a C.A.I.S. patient's femaleness with an unwillingness to allow exploration of her very real female deficiencies (lack of internal female organs, pubic hair, and menstruation, with possibly a diminished vaginal length) will suggest to her a very considerable anxiety and discomfort on the part of doctors/parents. Preparing the youngster for intimate personal relationships as an adult should be a priority, tempting as it may be to divert attention away from sexuality issues and towards substitute goals.

Many issues with males with A.I.S. centre around the lack of adequate surgical techniques and the reluctance by many to accept that men with A.I.S. exist.

Aims of the Androgen Insensitivity Syndrome Support Group Australia Inc.

To reduce the secrecy, stigma and taboo surrounding A.I.S. and other intersex states, by encouraging doctors, parents and society to be more open.

To put parents and people with A.I.S. and related conditions in touch with each other in a safe and confidential environment and encourage them to seek support and information.

To encourage the provision of psychological support within the medical system, for young people with A.I.S. and their parents.

To increase the availability of information on A.I.S. both verbal (from the health professionals) and written (from the support group and other sources).

To encourage improvements in the treatment for men and women with A.I.S. in both surgical and non-surgical means.

To encourage research into gender identity and sexual identity issues.

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