27

Obtaining A Diagnosis

Investigation, diagnosis and corrective measures for the TG/TS/eunuch population are rarely done in India. These measures are more prevalent in Western countries, where much less stigma is attached to this 'deviant sex' and consequently, remedial procedures are the norm. There, the affected person stands a much greater chance of being able to undertake proper surgical, hormonal and other rehabilitation therapies and lead a life according to the desired gender.

Diagnosis of AIS is usually made at one of these life stages:

As child – following the detection of hernia or 'non-standard' genitalia, i.e. sex organs, such as penis or vagina that are not structured like in the majority of children of the same age.

As an adolescent – with the failure to start menstruating or inability to have an erection.

As an adult – by following his/her medical history and often uncovering lies/half-truths over many years.

Diagnostic Criteria for Gender Identity Disorder

A. A strong and persistent cross-gender identification (not merely a desire for any perceived cultural advantages of being the other sex).

In children, the disturbance is manifested by four (or more) of the following reasons:

1. Repeatedly stated desire to be or insistence that he or she belongs to the other sex,
2. In boys, preference for cross-dressing or simulating female attire; in girls, insistence on wearing only stereotypical masculine clothing,
3. Strong and persistent preferences for cross-sex roles in make-believe play or persistent fantasies of being the other sex,
4. Feeling the intense desire to participate in the stereotypical games and pastimes of the other sex,
5. Strong preference for playmates of the other sex,
6. In adolescents and adults, the disturbance is manifested by symptoms such as a stated desire to be the other sex, desire to live or be treated as the other sex or the conviction that he or she has the typical feelings and reactions of the other sex.

B. Persistent discomfort with his or her sex or sense of inappropriateness in the gender role of that sex.

In children, the disturbance is manifested by any one or more of the following factors:

1. In boys, assertion that his penis or testes are disgusting or will disappear, assertion that it would be better not to have a penis, aversion toward rough-and-tumble play and rejection of male stereotypical toys, games and activities,

2. In girls, rejection of urinating in a sitting position, assertion that she has or will grow a penis, assertion that she does not want to grow breasts or menstruate, marked aversion toward normal feminine clothing,
3. In adolescents and adults, the disturbance is manifested by noticeable symptoms such as preoccupation with getting rid of primary and secondary sex characteristics (e.g. request for hormones, surgery or other procedures to physically alter sexual characteristics to simulate the other gender) or the belief that he or she was born with the wrong gender.

C. The disturbance is not concurrent with a physical intersex condition.

D. The disturbance causes clinically significant distress or impairment in social, occupational or other important areas of functioning.

Investigations

The first test to be carried out in a suspected case will probably be one which examines whether XY sex chromosomes are present. These are often detected either via a chromatin test (cost about Rs 1,500) using a buccal (mouth) smear (a rough indication that looks for a particular colour change in cells under a microscope) or via a blood test (a karyotype test that examines the shape of the actual chromosomes). There is also a new smear test called Fluoro In Situ Hybridisation (FISH), in which the X chromosome shows up as green and the Y as red.

Patients and their parents are often so traumatised by the existence of XY chromosomes that they settle for a diagnosis of 'AIS' and do not pursue further tests to differentiate similar conditions. Nevertheless, it is quite useful to investigate further, particularly in the case of suspected PAIS, which has a presentation similar to several other conditions. However, there are other conditions, apart from AIS, that will produce the same type of genital 'deformity' in a genetic male.

The body's sensitivity to androgens can be tested in infancy by applying testosterone ointment to the pubic region. If no response or only a weak response to the hormone is observed, then the patient has PAIS and a female assignment should be more strongly considered. At puberty, the patient will probably develop breasts and be unable to virilise completely. Also, the phallic enlargement that normally occurs at puberty may not occur. A penis that is marginal in size will remain so.

Apart from the above, the following tests can be done to confirm the presence of AIS:

1) Blood Tests

- Karyotype (done on people suspected of having AIS),
- 17-hydroxy-progesterone (if Congenital Adrenal Hyperplasia, an XX intersex condition, is suspected),
- Testosterone,
- Dihydro-testosterone (DHT),
- Androstenedione,

- Gonadotropins (i.e. FSH – Follicle Stimulating Hormone and LH - Luteinizing Hormone).
- HCG (human chorionic gonadotropin) stimulation test (3-day or 3-week test). By administering human chorionic gonadotropins (similar to pituitary hormones) and checking for resulting androgen production, it is possible to check whether a patient suspected of having AIS might instead have a deficiency in androgen production rather than response to androgens.

2) Urine Tests

Urinary steroids may be measured, though this is not always very useful. They may help with 5-alpha-reductase, also known as 3-oxo-5-alpha-steroid 4-dehydrogenase. It is an enzyme involved in steroid metabolism. It participates in three metabolic pathways: bile acid biosynthesis, androgen and oestrogen metabolism and prostate cancer.

3) Imaging

- Ultrasound of pelvis for uterus and ovaries. These tests check for the presence or absence of internal Mullerian (female) structures and differentiate AIS from conditions such as Swyer's Syndrome, Gonadal Dysgenesis, MRKHS (Mayer Rokitansky Kuster Hauser Syndrome),
- Ultrasound of groins for testes,
- Patient may also have an MRI scan if the above procedures are not found useful,
- X-ray studies involving a radio-opaque dye injected into the urogenital sinus can be used to determine the extent of development of the

vagina.The vagina and labia minora may be fairly well developed but not evident on external examination, due to labial fusion.

4) Examination under Anaesthetic

This may be done when planning for surgery, if imaging is inconclusive. It may occasionally include a laparoscopy (examination of abdominal contents via telescopic device through small incision).

5) Genital Skin Biopsy

This is generally done to look for DNA (although this can also be done using blood).

6) Gonadal Biopsy and Histology

A histological tissue analysis of the testes or gonads being removed can be done. In cases of AIS, these tissues are supposed to look normal and be functioning (although they do not produce mature sperm cells). In other cases, the gonads may be present as streaks, under-developed or even as ovo-testes. This test is rarely done now, unless looking to confirm the presence of an ovo-testis.

7) DNA Studies

This is usually done on blood. The clinical suspicion has to be very high to make it worthwhile. In some conditions, e.g. CAIS, the faulty gene can be identified in about two thirds of people with this condition.

This means that if identified, other members of the family could be screened as a precautionary

measure, to see if they carry it too. They are very expensive and time consuming 'needle in a haystack' tests.

8) Familial Analysis

While about a third to a half of cases of AIS occur due to spontaneous mutations, the other cases follow a specific line of inheritance, viz. through maternal lines. In cases where a relative with a similar condition is known in a non-maternal line or when there is consanguinity (close blood relationship) between parents, one may suspect that the girl does not have AIS but another condition with an autosomal inheritance that does not involve either of the sex chromosomes but one of the 46 other chromosomes.

9) Tissue-Level Defect

The exact nature of the defect at the tissue level in AIS has been the subject of considerable research. A recent study on the molecular basis of the phenotypic variation in AIS puts forward evidence that most, if not all, cases of complete AIS can be explained by androgen receptor defects. However, the majority of Partial or Incomplete AIS subjects exhibit no defect in androgen-receptor binding, suggesting that other genetic defects are involved. It is also possible to have the same genetic defect and different genital appearances. CAIS and PAIS may thus be caused by different defects at the genetic/ cellular level and are thought not to occur in the same family.

Some More Factors

In the absence of biochemical testing, the following clues to ascertain presence of carrier status in a family can be used:

- maternal relatives affected by AIS,
- delayed puberty in an XX female,
- reduced pubic/axillary hair in an XX female,
- asymmetric pubic/axillary hair in an XX female,
- reduced bone density in an XX female.

There are various commercial testing laboratories in the US and continental Europe. The number of families requiring this service is small, since AIS is a rare phenomenon. However, the demand has increased in recent years and will probably continue to grow, as intersex becomes less of a secret issue within families and society, due to the integration offered by globalisation. Indian society is just starting to become more open and accepting like western cultures.