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EDITORIAL

GONADAL DYSGENESIS

Gonadal dysgenesis is becoming recognized as by far the commonest cause of primary amenorrhoea. In its classical form (Turner's syndrome) the condition may be divided into 4 clinical parts. First, the patient remains short in stature throughout the whole of her developmental period, ending up at about 4 foot 7 inches. Secondly, she is subject to peculiar and inexplicable oedematous swellings of any part of the body, which may occur from time to time during the early years. Thirdly, she exhibits several of a large number of congenital anomalies. These involve the skin and its appendages, the musculo-skeletal system, the eyes and ears, the heart, the kidneys, the teeth. The best known of these are webbing of the neck or a very short neck, hypoplasia of the mandible with a birdlike facies, asymmetry of the eyes with strabismus, multiple black moles anywhere on the body, a low nuchal hair-line, a rounded, shield-like chest, cubitus valgus and pes cavus, and coarctation of the aorta. Fourthly, the patient fails to develop at puberty. Breasts do not grow, and the nipples remain pin-point, with pale pink areolae; menses do not appear; the vagina and uterus remain infantile; pubic and axillary hair development is variable.

It is plain that the condition in such classical form can be readily diagnosed clinically, even before the usual age of puberty is reached. There are 4 important negative points. (1) The patients are not mentally affected. Although some seem to be a little backward, shy and distinctly puerile in their habits, this may be largely an effect secondary to their disabilities, their upbringing and environment; many have a high intelligence quotient. (2) Their bone development is only a little backward—usually at the retarded end of the normal scale. (3) They are not eunuchoidal in proportions, unlike the prepuberal castrate, and (4) they are in general quite strong and stocky, unlike the much rarer hypopituitary dwarf.

VAN DIE REDAKSIE

GEBREKKIGE ONTWIKKELING VAN DIE GESLAGSKLIERE

Dit word steeds meer besef dat gebrekkige ontwikkeling van die geslagskliere verreweg die algemeenste oorsaak van primêre amenoree is. In sy klassieke vorm (die Turner-sindroom) kan die kondisie klinies in 4 verdeel word. Ten eerste bly die pasiënt gedurende al haar ontwikkelingsjare kort van gestalte, en op omtrent 4 voet 7 duim is sy uitgegroe. Tweedens is sy onderworpe aan eienaardige en onverklaarbare watersugtige swelsels aan enige deel van die liggaam wat gedurende die vroeë jare van tyd tot tyd mag voorkom. Dertens openbaar sy verskeie van 'n groot aantal aangebore afwykings, wat betrekking het op die huid en sy aanhangsels, die spierskelet-stelsel, die oë en ore, die hart, die niere, en die tande. Die bekendste hiervan is 'n 'webvlies' aan die nek, of 'n baie kort nek, onderontwikkeling van die onderkaak met 'n voëlagtige gesig, oneweredige oë met skeelheid, en 'n groot aantal swart moesies oral op die liggaam. Die hare groei agter laag op die nek, die borskas is rond en skildvormig, cubitus valgus, pes cavus, en ook samepersing van die aorta word aangetref. Ten vierde toon die pasiënt geen puberteitsontwikkeling nie. Die borste groei nie en die tepels bly klein, met ligroos tepelhowe; die maandstonde tree nie in nie, en die skede en baarmoeder bly kinderlik, terwyl die ontwikkeling van die skaam- en armholtehare van pasiënt tot pasiënt verskil.

Dit is duidelik dat hierdie toestand in so 'n heel klassieke vorm maklik klinies uitgeken kan word, selfs voordat die gewone puberteitsjare bereik is. Daar is egter 4 belangrike negatiewe punte. (1) Die pasiënt makeer verstandelik niks nie. Party lyk wel 'n bietjie agterlik, skaam en definitief kinderlik in hul gewoontes, maar moontlik is dit grotendeels 'n sekondêre gevolg van hulle abnormaliteite, hul opvoeding en hul omgewing. Baie van hulle het 'n hoë intelligensiekwosiënt. (2) Die ontwikkeling van hulle beenstelsel is slegs ietwat agterlik—gewoonlik sorteer dit onder die agterlikes binne die normale perke. (3) Hulle proporsies is nie eunugagtig nie, en daar verskil hulle van die voor-puberteitgekastreerde, en (4) oor die algemeen is hulle heeltemal

Special investigations into the basic nature of the condition are 3 in number. Laparotomy, which used to be necessary to establish the diagnosis, reveals that all internal feminine organs are normal, but infantile, except the ovaries, which do not develop beyond the stage of the primitive genital ridge. This is seen as a thin white ridge, or streak, of firm tissue lying along the broad ligament on each side. In all cases the appearance has been the same, although microscopical examination in some reveals that early differentiation of sex tissue has occurred. Hence the term 'dysgenesis' has been substituted for 'agenesis'. Secondly, the urinary output of the follicle-stimulating hormone (FSH) of the pituitary is abnormally high. This is because the primitive gonadal tissue produces no oestrogen, so that the normal inhibition of this hormone on pituitary gonadotropin-formation is lacking. This is not found before the age of 12 or 13, since maturation of the pituitary with respect to its gonadotropin production does not occur until then. Unfortunately, the estimation of FSH is a complicated biological procedure undertaken by few laboratories and not always certain in its outcome.

The third special test is that of elucidating the 'genetic' sex of the individual (this fascinating discovery was discussed in a recent editorial¹ in this journal). Examination of the nuclei of stained preparations of skin, leucocytes and other tissues has revealed that about 95% of those apparent females with 'ovarian agenesis' were really genetically destined to have been males. They carry the male (XY) chromosome pattern even in their female organs! We have here the human confirmation of experimental work indicating that when the primitive gonads are removed or destroyed at a very early stage of their intra-uterine development the animal or person concerned develops along usual female lines, irrespective of whether the gonad would have been ovaries or testes. In other words the female is the neutral form; the development of a male requires more than just the male chromosome, it also needs some sort of hormone evocator which is dependent upon the differentiating testes. The name of the disorder had plainly to be changed to 'gonadal dysgenesis'.

Previously we wondered why 'ovarian agenesis' was virtually a female disease. The male counterpart was apparently a rarity and the few described cases seemed to be a hotch-potch of doubtful homology. Now we wonder why the disorder is so predominantly a male disease! There is no clinical difference between gonadal dysgenesis in the 'genetic' male from that in the rarer 'genetic' female.

Armed with this knowledge it is possible to use the

sterk en stewig gebou, in teenstelling met die baie seldsamer hipopituitêre dwerg.

Daar is 3 spesiale metodes van ondersoek om die basiese aard van hierdie kondisie te bepaal. Buik-opening, wat eers nodig was om die diagnose te bepaal, toon dat al die inwendige vroulike geslagsorgane normaal, maar egter kinderlik is, met uitsondering van die eierstokke wat nie verder as die stadium van die primitiewe genitale ruffeltjie ontwikkel nie. Die eierstokke vertoon as 'n dun wit ruffeltjie of strepie stewige weefsel geleë langs die breë ligament aan elke kant. Die voorkoms daarvan is by elke geval dieselfde, hoewel dit by sommige pasiënte deur mikroskopiese ondersoek bewys word dat 'n vroeër onderskeiding van geslagtelike weefsel wel plaasgevind het. Daarom is die benaming 'onontwikkeling van die geslagskliere' vervang deur 'gebreklike ontwikkeling'. Tweedens word abnormaal groot hoeveelhede van die harsingslymklier se follikel-prikkelende hormoon (FSH) in die urine uitgeskei. Die rede hiervoor is dat die primitiewe geslagsweefsel geen estrogeen voortbring nie, met die gevolg dat die normale remmende werking van hierdie hormoon op die vorming van gonadotropien in die harsingslymklier afwesig is. Dit kom nie vóór die ouderdom van 12 of 13 voor nie, want die rypwording van die harsingslymklier wat sy gonadotropien-produksie betref, tree dan eers in. Ongelukkig is die bepaling van FSH 'n ingewikkelde biologiese prosedure wat deur min laboratoria onderneem word, en die resultate van sulke bepalinge is wisselvallig.

Die derde spesiale toets is die bepaling van die 'genetiese geslag' van die individu. (Hierdie boeiende ontdekking is onlangs in 'n hoofartikel in hierdie tydskrif bespreek.¹) Studies van geveerde preparate van die vel, wit bloedliggaampies en ander weefsels het bewys dat ongeveer 95 persent van daardie oënskynlik vroulikes met 'eierstok-onontwikkeling' eintlik geneties bestem was om manlik te wees. Selfs in hulle vroulike organe toon hulle die manlike (XY) chromosoompatroon! Daar het ons dan die menslike bevestiging van navorsings wat daarop dui dat die betrokke dier of persoon in die gewone vroulike rigting ontwikkel as die primitiewe geslagskliere op 'n baie vroeë stadium van hulle baarmoederlike ontwikkeling verwyder of vernietig word, afgesien daarvan of die geslagskliere eierstokke of testes sou gewees het. Die vroulike is m.a.w. die neutrale vorm; die ontwikkeling van die manlike vereis nie alleen die manlike chromosoom nie, maar ook een of ander soort hormoon-evokator wat afhanklik is van die onderskeidende testes. Dit was duidelik dat die naam van die afwyking verander moes word na 'gebreklike ontwikkeling van die geslagskliere'.

Voorheen het ons gewonder waarom 'onontwikkeling van die eierstokke' feitlik uitsluitlik by die vroulike geslag voorkom. Die manlike vorm daarvan was oënskynlik iets seldsaams en die paar beskrewe gevalle het na 'n mengelmoes van betwyfelbare homologie geklink. Nou wonder ons waarom dit grotendeels 'n manlike siekte is! Klinies is daar geen verskil tussen gebrekkige ontwikkeling van die geslagskliere by die 'geneties' manlike en die seldsamer 'geneties' vroulike nie.

Gewapen met hierdie kennis is dit moontlik om die ontdekking van 'n manlike 'genetiese' geslag as bevesti-

finding of a male 'genetic' sex as proof of the diagnosis in the apparent female. It is now being found that some cases of this strange condition may have apparently good breast development, some have no evident congenital anomalies, some are even of normal height and to all appearances normal women except for the lack of puberty. We must now suspect that gonadal dysgenesis is the diagnosis in any case of primary amenorrhoea in which there is no obvious causative disease and even in a child whose only abnormal feature is marked smallness of stature, represented by a growth curve below the lower limits of the normal range.

1. Editorial (1955): S. Afr. Med. J., 29, 809 (27 August).

ging van die diagnose by die oënskynlik vroulike te aanvaar. Dit word nou bevind dat die borste by sommige gevalle van hierdie sonderlinge kondisie goed ontwikkel kan wees; sommige toon geen ooglopende aangebore afwykings nie, en sommige is selfs normaal van gestalte en skyn in alle opsigte, behalwe die gebrek aan geslagsrypheid, normale vroue te wees. Ons moet dus vermoed dat ons gebrekkige geslagsklier-ontwikkeling moet diagnoseer by elke geval van primêre amenoree waar daar geen ooglopende veroorsakende siekte is nie. Dit geld selfs ook vir 'n kind wie se enigste afwyking 'n abnormaal kort gestalte is wat verraai dat haar groeikurwe laer is as die laagste binne normale grense.

1. Van die Redaksie (1955): S. Afr. T. Geneesk., 29, 809 (27 Augustus).

EARLY PSYCHIATRY IN NATAL*

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Through the courtesy of Dr. E. Cheze-Brown, then Physician Superintendent of Town Hill Hospital, Pietermaritzburg, I was recently given access to two 'case books' containing the histories of the earliest recorded mental cases treated in an asylum in Natal. These books are bound volumes in hard covers in an excellent state of preservation, evidently specially designed for their purpose, and were manufactured by Shaw and Sons, Printers and Publishers, Fetter Lane, London (Publishers of the Books of the Commissioners in Lunacy). The two books contain the records of 253 cases numbered consecutively in order of admission, the first being dated 23 July 1864 and the last 27 December 1884. Of these 245 are sufficiently complete to serve as a basis for this study. The records used are not all entirely complete, some having been carried over to a 3rd and 4th case book, which are not available. The notes however extend to the year 1889, and all the cases here recorded, except those which died or recovered, extend over a period of at least 2 years.

Historical

Before going into details concerning the contents of these books it is desirable to say something about the historical development of mental institutions in South Africa during the 19th century.

Before accommodation for lunatics became available in Natal the only facilities for housing them were located in Cape Town. The 'Old' Somerset Hospital, which had been founded by Dr. Samuel Bailey in 1818, had some accommodation for mental patients, although the conditions under which they were housed were often unsatisfactory. In 1836 a special ward for lunatics was erected, and in 1837 this held 38 patients.

Robben Island had been used as a convict station by the Dutch East India Company ever since the days of

Van Riebeeck, and at times lunatics were also detained there. This practice was continued by the British when they occupied the Cape in 1806. In 1846 it ceased to be a convict station and became 'a station for lunatics, lepers, and the chronic sick'.¹

Such then was the situation in South Africa when in the early 1860s the increasing population of Natal made accommodation for mental patients there desirable. At first such patients were housed in Grey's Hospital, Pietermaritzburg and in the Pietermaritzburg Gaol.² In 1868 the first asylum was opened as an annexe to the Pietermaritzburg Gaol and housed 24 inmates. By 1875 the 'Temporary Asylum'³ was open on erf 53 in lower Longmarket Street, and this was replaced in February 1880 by the permanent building (Town Hill Hospital) still in use.

The medical man most closely associated with the old asylum was the District Surgeon, Charles Gordon, M.D. In his absence Dr. Charles Ward acted as District Surgeon and also looked after the lunatics. The first full-time Superintendent at Town Hill was Dr. James Hyslop, who assumed duty on 4 July 1882 and was still in charge at the time of Union in 1910.

THE CASE BOOKS

The notes in the two case books are mainly written in two sets of handwritings, with a few notes written in a third hand, and it has not been difficult to identify them. Fortunately all are clear and legible and have not faded with the years—a tribute to the quality of the ink used in Government institutions in those days.

One set of notes, which begin in August 1882, could be readily identified as those of Dr. James Hyslop, because I was familiar with his handwriting from earlier researches in the Natal Archives. It was confirmed by a specimen of a patient's handwriting glued into the case book and initialled 'J.H.' in the identical writing of the other notes, and dated 13.2.83. Incidentally the notes

* A paper presented at the South African Medical Congress, Pretoria, October 1955.