GONADAL DYSGENESIS

(A Critical Analysis of Clinical Manifestations in Several Cases)

by

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The term "gondal dysgenesis" has been coined within recent years. The manifestations of this disorder are generally called Bonnivie-Ulrich-Turner's syndrome. This is characterized by short-stature, congenital webbing of the neck with low occipital hair line, wide carrying angle of arms, oedematous build, shield-like chest, high palate, coarctation of aorta and primary amenorrhoea.

Previously it was thought to be caused by non-development of differentiated ovaries (ovarian agenesis). Now-a-days it is presumed to be due to gonadal dysgenesis. This term is used because the gonad is a small ridge of fibrous tissue the character of which is difficult to estimate, as the sex cells are not usually demonstrable in the biopsy material after laparotomy. This abnormality in the gonad is associated with other congenital somatic defects; so gonadal dysgenesis is only one manifestation of the multiple congenital abnormalities. The sex chromatin study has revealed that in the majority of patients it is of negative pattern, though positive sex chromatin smear is not unusual.

In the group who have positive chromatin smear the congenital defects are much less obvious than in the negative group. These patients with positive chromatin smear have a tall build with slight development of breasts. Due to the lack of oestrogen the prepubertal growth of these patients continues for a longer period and the extremities become long. The slight development of the breasts is perhaps due to adrenal oestrogen. These cases are not to be included within the group of Turner's syndrome. They are better designated as Hypo-ovarian symptom complex.

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Material

There were seven cases of Turner's syndrome in this series. They are presented in the following table with characteristic abnormalities. Though it is said that in nearly one-third of the cases coarctation of aorta is present, this was not found in any of the cases of the present series. Lymphoedema which is taken to be a characteristic picture in Bonnivie-Ulrich syndrome was present in two cases only.

Discussion

In 1938 Turner described several female patients who exhibited dwarfism, congenital webbing of the

TABLE I

Shows the Clinical Manifestations of Seven Cases of Bonnivie-Ulrich Turner's Syndrome

Patients	Age	Height	Primary amenorrhoea	Development of Mullerian system	External genitalia	External abnormalities	Other congenital abnormalities	Bones	Sex chromatin	Biopsy of gonad	Mental picture
1. H.C.	17	50″	+	Normal but immature	Normal, no pubic hair	Shield-like chest	Nil	Marked osteoporosis	Negative pattern	Diffuse fibrous tissue	Infantile mental attitude
2. L.K.M.	14	51½″	+	—do—	—do—	Misplaced bilateral fifth toe	Nil	Small 4th & 5th metacarpal bones	,,	—do—	Normal
3. R.B.	16	52″	+	—do—	—do—	Infantile facies, Webbed neck with low occipital hair line	High arched palate	Marked osteoporosis and small 4th & 5th metacarpals	Positive pattern	Diffuse fibrous tissue with (?) two immature follicles	—do—
4. T.D.	15	48″	+	Bicornuate uterus	—do—	Cubitus valgus Lymphoedema	Nil	Osteoporosis	Negative pattern	Diffuse fibrous tissue	Low I.Q.
5. O.J.	19	43″	+	Normal uterus, long infantile tubes	Scanty pubic hair	Short neck infantile facies	Nil	Marked osteoporosis	Positive pattern in the buccal smear & negative pattern in vaginal smear	—do—	Infantile mental make up
6. S.B.	17	52½″	+	Normal but immature	Slightly enlarged clitoris	Shield-like chest; Cubitus valgus, lymphoedema	Nil	Marked osteoporosis	Negative pattern	—do—	Normal
7. S.D.N.	20	53″	+	—do—	Normal, no pubic hair	Webbed neck, misplaced right fifth toe. Shield-like chest	High arched palate	Nil	—do—	—do—	—do—

neck, sexual infantilism and cubitus valgus. Subsequent study of this condition revealed that they are associated with multiple abnormalities; coarctation of aorta and lymph oedema were found to be present in quite a large number of these cases.

Biopsy of the gonad revealed only streaks of fibrous tissue without any sex cells and hence it is difficult to determine the character of the gonads. With the advent of further investigations it is found that 80% of these patients have negative nuclear sex and only in 20% it is of positive pattern.

In the cases presented here it is observed that the clinical manifestations are not essentially the same in all the patients. Dwarfism was present in all the cases and none of the patients exceeded 53" in height. Van Wyk (1952) says that "the dwarfism cannot be ascribed to any recognized hormonal abnormalities and might be considered to be an associated anomaly".

External genitalia were of normal female type except in one where the clitoris was enlarged (Case No. 6). Though it is suggested that in these cases where there is any male feature in the external genitalia one should think of the presence of medullary elements (rete-tubules, Leydig cells) in the gonadal streak, the gonads had only a lump of fibrous tissue as in other cases.

Mullerian development was normal in all the cases but they maintained the infantile characteristics, perhaps due to the absence of ovarian oestrogen. In one case the Mullerian fusion was lacking and this might be taken as an incidental finding as met within otherwise normal females.

Osteoporosis was a constant feature in all these cases. Scanty pubic hair was present in one case only and may be of adrenal origin. It is difficult to find out the cause of the absence of pubic hair in all other cases though 17-ketosteroid excretion was normal in all of them.

Positive nuclear sex was found in one case. Though it is claimed that these cases exhibit fewer of the associated anomalies they were grossly marked in this case (Case No. 3). Both positive and negative nuclear sex were found in the same individual with characteristic anomalies in case No. 5. Grumbach and Barr (1958) have observed XO/XX/XXY mosaicism in a girl with classical Turner's syndrome and positive nuclear sex.

All these patients are phenotypically females who have various congenital defects. The anomalies vary from patient to patient but dwarfism, shield-like chest, rarefaction of bones, amenorrhoea and immature mental make up are constant features. Gonadal dysgenesis is a better term than ovarian agenesis because it cannot be determined histologically whether the rudimentary gonad had been destined to become an ovary or a testis. Complete gonadal aplasia represented by only unidentifiable fibrous streak is the common finding, but medullary elements with rete tubules and Leydig cells or cortical elements with early primordial follicles (Case No. 3) are not rare. Abnormalities in chromosomal number have been noted but patients

Pictures showing different clinical features of Bonnivie-ulrich Turner's syndrome.

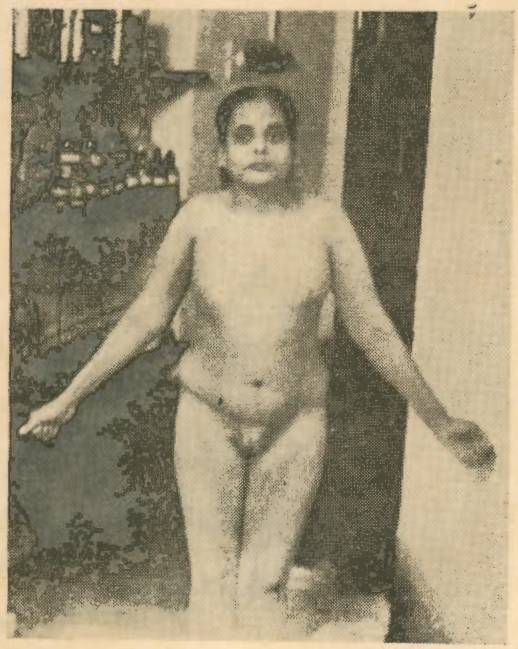

Fig. 1
Shield-like chest, Cubitus valgus. Lymphoedema, Wide nipple line.

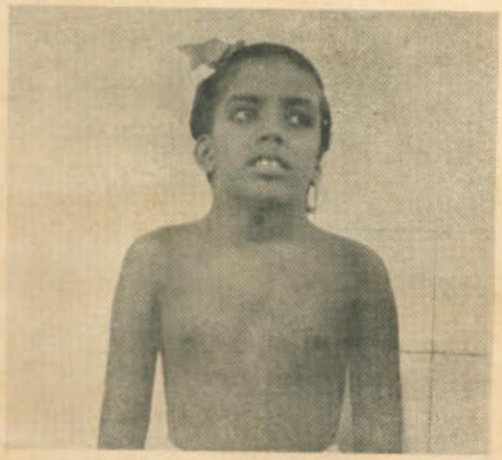

Fig. 2
Webbing of neck, Wide nipple line.

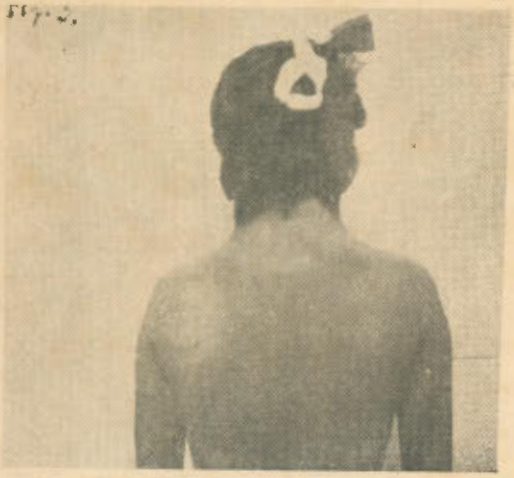

Fig. 3
Webbing of neck with low occipital hair line.

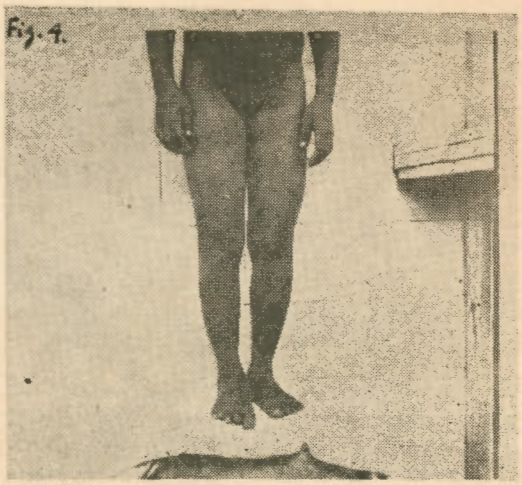

Fig. 4
Misplaced toes.

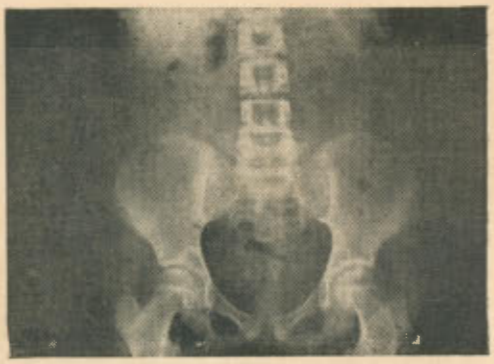

Fig. 5
Marked Osteoporosis of pelvic bones and spines.

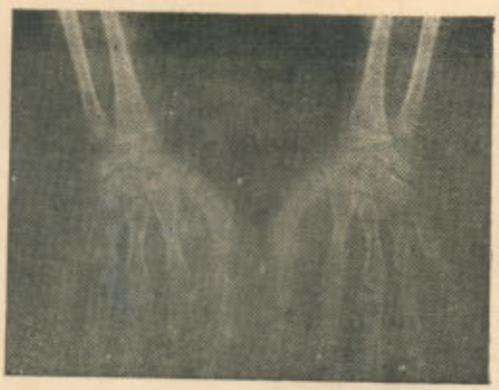

Fig. 6
Marked osteoporosis of the bones of the upper extremity. Small 4th and 5th metacarpals.

with normal chromosomal pattern have been found to have similar gonadal and somatic defects. The cause of the abnormalities in gonadal differentiation is difficult to postulate. The following theories have been forwarded:

(a) "Inheritance of an abnormal complement of sex chromosomes due to non-disjunction of parental germ cells during meiosis or mitotic non-disjunction during early cell cleavages of the furtilized ovum.

(b) "Inheritance of abnormal or mutant sex determining germs without morphologic evidence of an abnormal karyotype.

(c) "Noxious environmental influences which inhibit normal development of the foetal gonad."

Whatever may be the ultimate mechanism it may be presumed that abnormality in gonadal differentiation is not the only feature in this condition; a basic lesion in an unknown manner might be causing the syndrome both at the gonadal and somatic level.

Summary

(1) Clinical manifestations of Turner's syndrome have been presented at the onset.

(2) Seven cases have been presented with their clinical findings and investigations and few typical pictures have been inserted.

(3) Dwarfism, shield-like chest. osteoporosis, amenorrhoea are noted as constant features in these cases. Coarctation of aorta was not found in any of the cases in the present series.

(4) Variations in the nuclear sex and chromosomal pattern and diverse histological picture in the gonadal biopsy have been discussed.

(5) Possible causative mechanisms have been quoted. An unidentified lesion causing both gonadal and somatic abnormality is suggested.

Acknowledgement

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