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Materials and methods

Records were kept of all live births, still births and neonatal deaths occurring at the UCH, Ibadan, during the period of the study. All the neonates were routinely examined by a physician and those with short gestational periods, low birth weights, congenital abnormalities, however trivial, as well as those with birth lengths less than 45 cm were referred to the genetic clinic. Other referrals included cases with suspected congenital anomalies seen at the Paediatric and Infant Welfare Clinics in UCH, and those from government and private health institutions within and outside Ibadan City.

Buccal smear preparations stained with orcein, and examined as outlined by Smith *et al.* (1962) were undertaken in all the cases. Although this method has been found to give reliable results in over 95% of cases with clinical features of the XO syndrome (Lemli & Smith, 1963), chromosome analyses were also carried out in a majority of the cases using our laboratory modification of the short-time lymphocyte culture as described by Moorhead *et al.* (1960). G-banding was carried out using trypsin and in its absence, lipsol as described by Adeyokunnu & Akinkunmi (1981). Other investigations including intravenous urography (IVU) and immunoglobulin studies were also carried out when considered necessary.

Family studies included the age and height of both parents, parity of mothers, multiple pregnancies, history of drug ingestion, exposure to X-rays, and any illnesses during pregnancy. The presence of abnormalities in siblings and close relatives were also ascertained. Autopsies were performed in all cases when death occurred in the hospital.

Results

There were sixteen children with Turner's syndrome during the period of the study. Four of these were delivered in the obstetric unit of UCH while the remaining twelve were referred from other clinics and health institutions in Ibadan because of suspected abnormality.

Incidence

During the period of the study, there were 22 769 consecutive live births (11 789 males and 10 980 females) at UCH. Thus the incidence of the syndrome was 1 in 2745 (4/10 980) among live female births.

Clinical features

The clinical features in the sixteen patients are summarized in Table 1. The most common features were somatic anomalies namely: short stature and short neck in fifteen (94%) of the

TABLE 1. Clinical features in order of frequency

Features	Number	Total (%)
Short stature	15	94
Short neck	15	94
Low posterior hair line	14	87.5
Broad chest with widely spaced nipples	14	87.5
Renal anomalies	14	87.5
Congenital lymphoedema	13	81
Webbed neck/redundant lax neck skin	13	81
Hypoplastic nails	12	75
Odd facies	11	69
Low birth weight	9	56
Cardiovascular anomalies	7	45
Cubitus valgus	6	38
Clinodactyly of fingers	4	25
Pigmented naevi	3	19
Other anomalies	3	19
Arthrogyposis multiplex	1	6
Prune-belly	1	6
Cleft palate		
Accessory nipples	1	6

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THE INCIDENCE OF TURNER'S SYNDROME IN IBADAN, NIGERIA

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Summary

A study of 22 769 consecutive live births in a Nigerian hospital has revealed the incidence of Turner's syndrome to be 1 in 2745 live females. Shortness of stature and neck, low posterior hair line, broad chest with widely spaced rudimentary nipples, congenital lymphoedema, redundant lax neck skin and hypoplastic nails were the most common clinical features. Birth weight was above 2.5 kg in only five of the fourteen cases in which this measurement was taken. Associated renal and cardiovascular anomalies occurred in 87.5 and 45% of the cases respectively. While neither parental age nor the birth rank of the patients were contributory factors in the causation of the syndrome, ingestion of traditional medicinal concoctions during the pregnancy which appeared to have played a role in four out of the sixteen cases requires further studies.

Résumé

Une étude de 22 769 naissances consecutives dans un hôpital nigérien a révélé que la fréquence d'apparition du syndrome de Turner était de 1 pour 2745 enfants de sexe féminin. Petite taille, cou rétréci, les cheveux plantés bas sur la nuque, poitrine large à mamelons rudimentaires largement espacés; lymphoedema congénitale, peau du cou relachée et redondante, ongles hypoplastiques en étaient les principaux symptômes cliniques – le poids moyen à la naissance était moins élevé dans une majorité des cas que pour le reste de la population. Des troubles cardiovasculaires et rénaux associés sont apparus dans 87.5 et 45% des cas respectivement. Alors que ni l'âge des parents, ni le rang de naissance de l'enfant ne sont pas retenus en tant que facteurs causant le syndrome, l'absorption de potions médicinales traditionnelles durant la grossesse semble avoir joué un rôle qui demande une étude plus poussée.

Introduction

Turner's syndrome, a clinical condition caused by XO sex chromosome monosomy, has been studied in great detail in different parts of the world (Turner, 1938; Haddad & Wilkins, 1959; Lemli & Smith, 1963; Ferguson-Smith, 1973). In 1959 Haddad & Wilkins noted that this syndrome was rare among Negroes, but there have been, to my knowledge, no studies to validate this observation. In Nigeria, a predominantly negro community, few isolated cases of the syndrome have been reported (Obi & Effiong, 1973; Adeniyi, 1973).

With the establishment of a genetic unit in the Department of Paediatrics, University College Hospital (UCH), Ibadan, in 1972 a systematic study of the pattern of congenital abnormalities began. The present communication reports the incidence, clinical features and possible causative factors in cases of Turner's syndrome seen during an 8-year period, January 1973 through December 1980.

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of the cases had incomplete rotation of one or both kidneys, three each had ureteropelvic obstruction with hydronephrosis and horse-shoe kidneys; duplex ureters occurred in two cases and one case had dysplastic right kidney with aberrant malformed renal artery and left hydronephrosis and hydroureters.

The pattern of somatic and renal anomalies in one of the patients was so rare as to be worth reporting in detail.

Case report

Baby L (Case 16) was a product of normal delivery at term by a multigravida, aged 27 years, with five previous deliveries. The pregnancy was complicated by hydramnios. There was an admission to self-medication with traditional concoction to prevent neonatal death since her three previous consecutive female babies had died from unknown causes on the day of delivery. The heights of both parents were above the average (Table 2).

At birth, the baby weighed 3.95 kg and measured 57 cm crown–heel length. She was phenotypically a female with an unusual facies marked by prominent ears, epicanthic folds and webbing of the neck. There was cleft in the hard palate. The chest was broad and there were three pairs of widely spaced microthelic nipples (Fig. 4). The fingers and toes were small and tapering, and the nails were hypoplastic. The abdomen was distended and renal masses were palpated. Coarctation of the aorta was suspected because the femoral pulses were faint and asynchronous with the radial pulses. The apex beat was located on the right side. There were no heart murmurs.

Buccal smear was chromatin negative. Chromosome analysis of peripheral lymphocytes yielded forty-five X in all the population of cells counted. Intravenous pyelogram revealed features suggestive of gross renal abnormalities. Chest X-ray confirmed the dextrocardia. Estimation of the immunoglobulins revealed marked elevation of IgM, normal IgG and low IgD. IgA could not be detected.

Six hours after birth, the patient became dyspnoeic and extremely mucousy and was admitted into the intensive care unit. There she developed *E. coli* urinary tract infection, *H. influenzae* meningitis, jaundice and severe anaemia. She died at the age of 27 days.

The pertinent autopsy findings were dextrocardia, patent foramen ovale and ductus arteriosus, a dysplastic right kidney supplied by a small aberrant renal artery which arose from the bifurcation of the aorta, left hydronephrosis and hydroureters. The ovaries were small, fibrotic and embedded in the broad ligaments (Fig. 5).

Comments

This infant Turner was unique in having three pairs of microthelic nipples, a finding that had never been reported before. Renal abnormalities are commonly associated with the disorder (Hortling, 1955; Haddad & Wilkins, 1959) but dysplastic kidneys with aberrant renal vessels had not been previously reported. Compared with our other cases this infant was the only one with webbed neck rather than redundant loose skin, and cleft palate rather than a narrow arched palate. She was also one of the three cases without congenital lymphoedema.

Anthropometric data and family studies. Relevant anthropometric measurements and some important obstetric and family data in the sixteen patients were summarized in Table 2.

Birth weights and heights. Birth weight was above 2.5 kg in only five of the fourteen in which birth weights were recorded. This was low compared with the birth weights of normal Nigerian babies (Effiong *et al.*, 1976). The crown–heel measurements were below the third percentile using Janes' (1970) data, except in four cases (Cases, 2, 10, 12 and 16). In all the cases parental heights were above the mean.

Age of parents. The mothers' ages ranged between 17 and 38 years (mean 25 years) and the fathers' ages varied between 22 and 52 years (mean 32 years).

Parity and birth rank. Four patients were products of the first pregnancy, while the syndrome resulted from the second and third pregnancies in five and two cases respectively. In the remaining five cases there had been five or more pregnancies before the birth of the patient. A history of multiple pregnancies was obtained in only one case, namely Case No. 4 in which the mother's sixth pregnancy resulted

cases respectively; low posterior hair line, broad chest with widely spaced nipples, renal abnormalities in fourteen (87.5%) of the cases respectively; congenital lymphoedema and redundant lax neck skin in thirteen (81%) of the cases respectively and hypoplastic nails in twelve (75%) cases. These features are illustrated in Figs 1–3. Other common features were odd facies with prominent ears, micrognathia and epicanthic folds. Nine (56%) of the cases had low birth weight. Associated cardiovascular anomalies were present in seven (45%) cases and included coarctation of the aorta (two cases) dextrocardia (two cases) and ventricular septal defect (two cases). The cardiac lesion was undiagnosed in one patient before she was lost to follow up. Renal anomalies occurred in fourteen (87.5%) of the sixteen cases and of these twelve were detected through intravenous urographic studies, while the remaining two were found at autopsy. Five

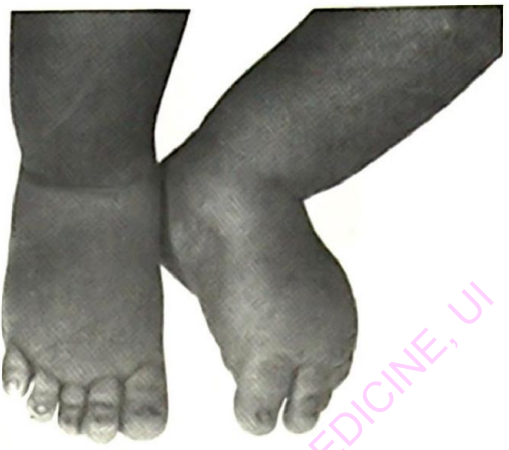

FIG. 2. Same patient as above: note the pedal oedema hypoplastic nails and grooved nail beds.

FIG. 1. Photograph of a 5-month-old XO patient with lymphoedema of both hands and feet and widely spaced rudimentary nipples.

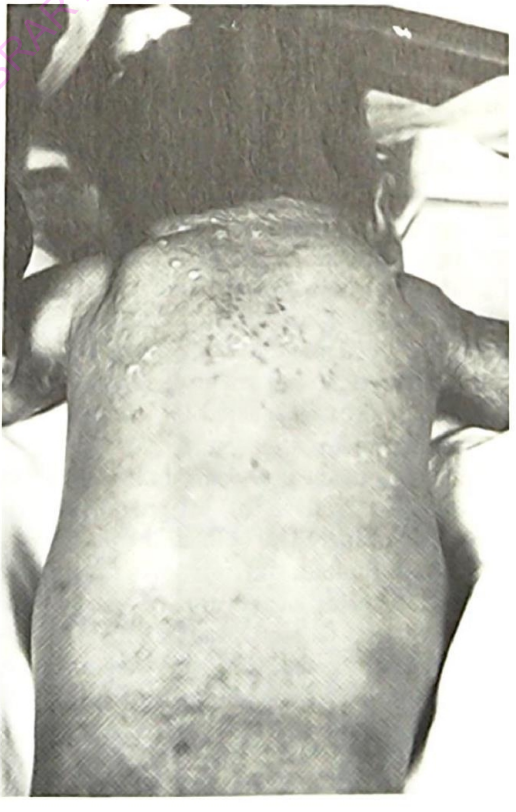

FIG. 3. Photograph of a patient: note the low posterior hair line, prominent ears and pigmented naevi at the back of the upper part of the thorax.

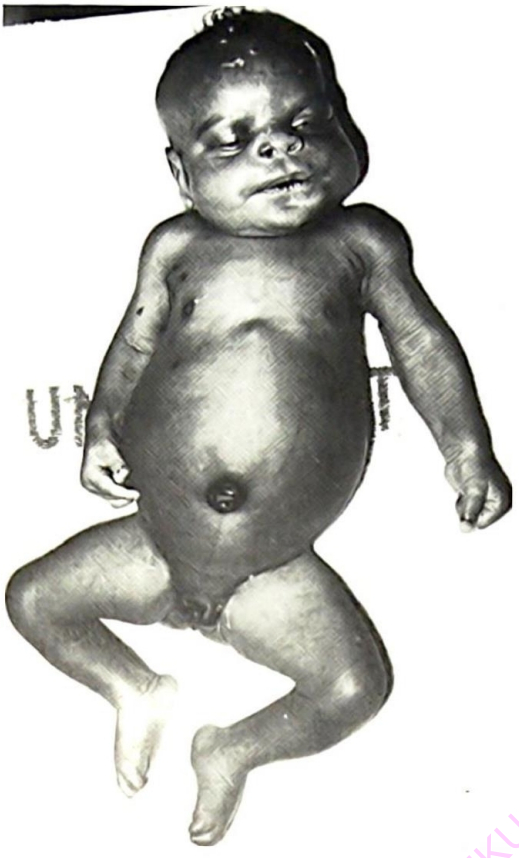

FIG. 4. Photograph of an infant with odd facies, three pairs of widely spaced microthelic nipples and abdominal swelling.

in a set of dizygotic twins one of which was the patient.

Environmental factors. Drug ingestion during pregnancy was admitted by four mothers. The mother of Case 2 (Table 2) was on a traditional concoction for fertility. The couple had been married for 12 years before the birth of their child when the mother was 31 years old and the father 36 years. Four years later the same concoction was ingested by this mother during the second pregnancy which resulted in the birth of the patient. The mother of Case 12 (Table 2) took an abortifacient unsuccessfully; while that of Case 14 took some traditional medication in hope of a male child, five previous pregnancies having resulted in females. In Case 16 the mother took some traditional drugs in a bid to prevent obstetric disaster, three previous children having died on the days of delivery from unknown causes. Three of the mothers were exposed to X-rays after the sixteenth week of pregnancy because of suspected twin pregnancy in one mother (Case No. 4) and gross hydramnios in the other two (Cases 14 and 16). All the sixteen pregnancies except three were carried to term.

Abnormalities in parents and siblings. Thirty out of the thirty-two parents were examined and found to be phenotypically normal. Forty-nine siblings were clinically and cytogenetically evaluated and forty-six of these were normal. The sibling abnormalities included myelomeningocele (sibling of Case 4) cleft palate (sibling of Case 8) and prunebelly syndrome (sibling of Case 14).

Discussion

The incidence of Turner's syndrome has been reported to be between 1 in 2500 and 1 in 5000 among live female births (Geneva Conference, 1966; Carr, 1967; Sorsby, 1973). The present study which has revealed an incidence of 1 in 2745 among female live births suggests that the anomaly is not rare among negroes. Lack of previous reports from predominantly negro communities, including Nigeria, might have been due to under ascertainment at birth, high mortality of cases in infancy and early childhood and lack of centre equipped for minimal cytogenetic studies of suspected cases.

The clinical presentation of the syndrome was clear-cut in a majority of the present series. Seven characteristic somatic abnormalities namely: shortness of stature; shortness of the neck; low posterior hair line; broad chest with widely spaced tiny nipples; congenital lymphoedema; redundant lax neck skin and hypoplastic nails were prominent and occurred in 75% or more of the patients. Buccal mucosal cell examination for negative chromatin bodies were therefore useful mainly for confirming the clinical diagnosis, while chromosome analysis was only important in suspected XO mosaics, for example, XO/XY persons with partially masculinized external genitalia. The above seven somatic features are thus of sufficient diagnostic value in most cases and therefore particularly useful in situations where well-equipped cytogenetic laboratories do not exist. Congenital lymphoedema and cutis laxity of the neck occurred more fre-

TABLE 2. Summary of anthropometric measurements and family studies in 16 XO patients

	Case No.																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Mean
Birth weight (kg)	2.13	2.9	?	?	2.3	2.6	2.4	2.0	2.3	2.1	2.9	2.7	2.05	2.4	2.2	3.95	2.50
Birth crown–heel length (cm)	40	50	65*	64†	44	48	45	47	49	50	44	54	40.5	44	42	57	46.75
Maternal age at birth (yr)	23	35	32	38	22	18	22	29	24	26	20	17	25	23	19	27	25.0
Maternal height (in)	62	64	63	61	64	65	59	61	63	64	61	65	58	59	64	64	62.31
Paternal age at birth (yr)	26	40	44	52	29	22	35	41	27	31	24	22	29	42	24	34	32.63
Paternal height (in)	?	66	64	65	70	68	67	62	68	69	64	68	63	?	69	69	66.57
Parity (birth order)	1	2	5	8	3	1	2	4	2	3	1	1	2	6	2	6	3
Pregnancy carried to term	+	+	+	+	–	+	+	–	+	+	+	+	–	+	+	+	
Multiple pregnancies	–	–	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–
Drugs	–	+	–	–	–	–	–	–	–	–	–	+	–	+	–	+	
X-ray exposure	–	–	–	+	–	–	–	–	–	–	–	–	–	+	–	+	
Siblings with abnormalities	–	–	–	+	–	–	–	+	–	–	–	–	–	+	–	+	
UCH delivered	+	+	–	–	–	–	–	–	–	–	–	–	+	–	–	+	

* Height at 8/12 not included in the mean.
† Height at 6/12 not included in the mean.

+, Positive response; –, negative response; ?, unknown.

the difference in the phenotypic appearances observed in many cases. In this regard, the probable contribution of traditional medicinal herbs, which were used by 25% of pregnant mothers in the present series, in giving phenotypic expression to Turner's syndrome in their offsprings require further study.

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FIG. 5. Autopsy specimen of patient (Fig. 4) showing dysplastic right kidney supplied by a small aberrant renal artery which arises from the bifurcation of the aorta and left hydronephrosis and hydroureter.

quently in the present series than in the series by Lemli & Smith (1963).

An unusually high incidence (87.5%) of associated renal abnormalities was found in the present study. This compares with the incidence of 60–70% reported by previous workers (Hortling, 1965; Levin, 1962; Lemli & Smith, 1963). It was not possible to link the presence of renal abnormalities with any particular clinical features. Prominent ears singled out by Hilson (1957), odd facies and micrognathia by Warkany, Passarge & Smith (1966) and Jolleys (1966) as pointers to prompt search for renal abnormalities were present in only 50% of the cases in the present series. It is noteworthy that in the present series four of the patients with renal abnormalities also had abnormal immunoglobulin levels and developed urinary tract infections with gram-negative organisms.

In the present series analysis of possible contributory factors to the disease has confirmed the findings of Boyer, Ferguson-Smith & Grumbach (1960) and Jacobs *et al.* (1963) that neither parental age nor the birth rank of the patients was a contributory causative factor of the syndrome.

Trisomies of the autosomes in the D groups of chromosomes (Therman *et al.*, 1963) and in the G groups (Johnston *et al.*, 1963) have been recently associated with Turner's syndrome, but these associations were not evident in the present series. Twinning has also been reported to be common among XO sibships (Valentine, 1965). Nigeria has the highest twinning rate in the world with one in twenty-two deliveries being twins (Nylander, 1969). Yet, in the present study only one out of forty-nine sibships was a set of twins.

The rare case reported in detail in the present series had features which had not been reported previously. This leads one to conclude that the missing X chromosome might be responsible for the primary defect in Turner's, but subtle differences in intra-uterine and environmental factors might be responsible for