AN ATYPICAL CASE OF GONADAL DYSGENESIS CLINICAL LABORATORY AND CYTOGENETIC STUDIES

by

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The term "gonadal dysgenesis" was suggested in 1955 by Grumbach *et al.*, to describe patients with undifferentiated gonads characterised by the absence of germ cells. He has catalogued a list of clinical features which predominate in a typical case of gonadal dysgenesis. De La Chapelle (1962), from his exhaustive study on 23 patients concludes that patients having dysgenetic gonads with different sex chromosome complement do not present important clinical differences. In the majority of cases, the sex chromatin pattern is negative (Polani *et al*, 1954) with XO sex chromosome complement (Ford *et al.*, 1959). Though clinically the case presented in this paper can be categorised under gonadal dysgenesis with 45-XO chromosome complement, the special feature noted in karyotyping is only seen in few cases described till now. This rare mosaicism has been confirmed by using different cytological techniques.

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CASE REPORT

MI, age 24 years, came with primary amenorrhoea, stunted growth noticeable since the age of 12 years, absence of breast development and secondary sex characters. Her height was 54.5 cm and weight was 30.0 kgs with a bone age of 12 years. Skeletal-muscular deformities described in typical Turner's syndrome were conspicously absent. Three brothers born after her were apparently normal. She had virginal introitus and a normal sized vagina. Rectal examination revealed a small midline uterine mass. She responded to cyclic therapy with hormones resulting in development of breasts and secondary sex characteristics and is now having cyclic bleeding.

Laboratory and Cytogenetic Studies

Pretreatment serial vaginal smears revealed a maturation index of 69:31:0 suggestive of marked oestrogen deficiency. Urinary gonadotrophins were measured by mouse uterine weight method and these were consistently raised to the levels seen in menopausal women.

Sex chromatin was negative from buccal mucosa cells and 6% positive in vaginal smears. These Barr bodies were smaller than normal. No drumstick was observed in 500 neutrophil cells. Chromosome preparations from the parents' blood could not be done as they were not available.

Chromosome preparations were made from leukocyte culture (Hungerford, 1965). Seventy-five metaphase cells were counted. On analysis, mosaicism, mainly 45 X 0 and few cells hav-

ing total deletion of long arm 46 XX q — (Fig. 1) was observed. Giemsa banding (Drets and Shaw 1971) was used to demonstrate the absence of one of the X chromosomes in the C group which is prevalent in a majority of the cells (Fig. 2). As the buccal smear was sex chromatin negative and 5% of the metaphase cells had a deleted long arm X chromosome which resembles the Y chromosome, it was decided to stain the buccal cells with Quinacrine Mustard (Casperson et al., 1969) in order to visualise any Y body, if present. Results were negative for Y body.

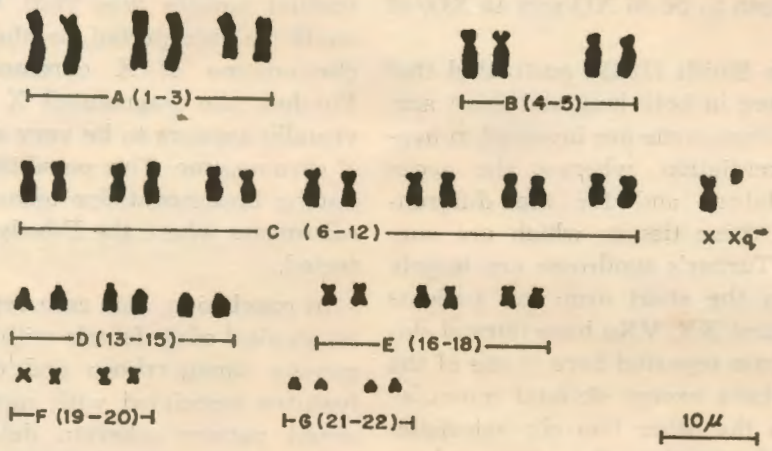

Fig. 1

Fig. 1
Karyotype of a cell showing total deletion of the long arm of one of the X chromosomes. (46 XXq).

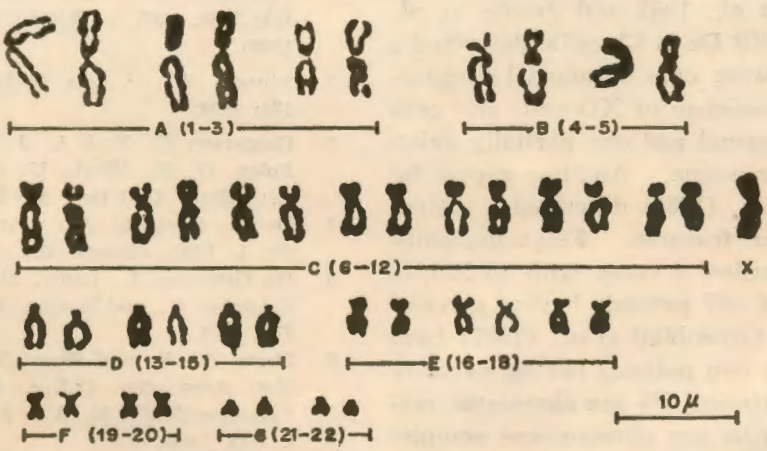

Fig. 2

Fig. 2
Giemsa banding of chromosomes showing absence of one 'X' chromosome (45 X O).

Discussion

De La Chapelle reported that 2-4 cases/ 10000 births are chromatin negative with gonadal dysgenesis. About two-thirds of the cases documented by Ferguson-Smith (1965) is seen to be 45 XO and 45 XO/46 XX.

Ferguson Smith (1965) postulated that genes present in both long and short arm of the X chromosome are involved in ovarian differentiation, whereas the genes for the stature and for the differentiations of these tissues which are anomalous in Turner's syndrome are largely confined to the short arm and patients with XXq and XX/VXq have normal stature. The case reported here is one of the variants where except skeletal muscular deformities the other two characteristics viz. stunted growth and ovarian aplasia are present with XX/XXq sex chromosome complement.

Very few reports are available on partial deletion of one of the 2X chromosome segments in gonadal dysgenesis (De Grouchy *et al.*, 1961 and Jacobs *et al.*, 1961). In 1962 De la Chapelle described a patient showing signs of gonadal dysgenesis with mosaicism of XO cells and cells with one normal and one partially deleted X chromosome. Another report by London *et al.*, (1964) described a patient with similar features. Ferguson-Smith (1965) described 4 cases, with 45 XO/46 XXq out of 287 patients having gonadal dysgenesis. Greenblatt *et al.*, (1967) have reported on two patients having negative sex chromatin and 3% sex chromatin, respectively with sex chromosome complement of XO and X deleted. Goldberg (1968) described a case with short stature, sexual infantilism and primary amenorrhoea having sex chromatin positive cells with total deletion of the long arm of the X chromosome. More recently, Weber *et al.*, (1970) and Stoll *et al.*, (1973) have reported two and one case respectively of gonadal dysgenesis and partial deletion of X chromosome.

As the percentage of sex chromatin in vaginal smears was very low (6%) it could be interpreted as the fragmented chromosome of X chromosome origin. Further, the fragmented X chromosome visually appears to be very similar to the Y chromosome. This possibility was ruled out by flourescent dye technique in buccal smears where the F-body was not detected.

In conclusion, this case report presents an atypical adult female with gonadal dysgenesis, amenorrhoea and other related features associated with mosaic chromosomal pattern wherein deletion of the long arm of the X chromosome is present.

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OBITUARY

It is indeed very sad to pen the obituary of Dr. H. V. Tilak within weeks after his presence on the occasion of the Silver Jubilee celebration of the Federation of Obstetric and Gynaecological Societies ot India. Dr. Tilak died on 24th March, 1975. As a past president of the Federation he was presented a Silver Medal to commemorate the occasion. Over 500 members of the Federation were very happy to see the genial, unassuming senior member so active at the age of 84.

His short life sketch appeared in the Special Silver Jubilee number of the Journal published in February of this year.

All of us who had the privilege to know him pay homage to this godfearing, kind and sincere gentleman. May god rest his soul in peace. Editor.

DR. R. K. K. TAMPAN

B.A., M.B.B.S., F.R.C.S., F.R.C.O.G.

After his early education in Trivandrum, he worked at Madras Medical College as assistant in Physiology and Chemistry departments and later as Tutor in Midwifery. In 1937, he went abroad and took his M.R.C.O.G. and F.R.C.S. (Edin) degrees. In 1945, he became Professor of Obstetrics and Gynaecology at Stanley Medical College and from 1947 he worked at Madras Medical College, as Professor of Obstetrics and Gynaecology and as Obstetrician and Gynaecologist to the Government Hospital for Women and Children, Madras, being appointed to the Office of the Superintendent of the said Hospital in 1948. The Department of Obstetrics and Gynaecology was upgraded in 1952 by the Government of India for training postgraduates and he became its first Director, which post he held till March 1956, when he resigned to take over the post of Professor and later Director of Obstetrics & Gynaecology in Medical College, Trivandrum, where he was serving till the time of his death. During these years, he had endeared himself to his numerous students and patients by his great qualities of kindness, devotion to duty and his unassuming nature. He was a collaborator with Dr. Sir Laxamanswami Mudaliar in his well known book of Clinical Obstetrics. He himself was a very keen student of Obstetrics & Gynaecology and used to take very active part in the Biennial All India Conferences and had contributed various papers and original articles to our Journal. He took a leading part in forming the Federation of Obstetric & Gynaecological Societies of India in 1950 and was an active member of the Journal Committee, where his valuable suggestions and advice were greatly appreciated. In Trivandrum, in the short space of time, he was able to start an Obstetric & Gynaecological Society. He was elected Fellow of the Royal College of Obstetricians and Gynaecologists in 1951. Dr. Tampan was elected President of the Federation for 1959-1960. His Presidential address at the 10th Conference held at Hyderabad in January 1959 was a master piece, bringing out sound ideas on training for our speciality.

Dr. Tampan passed away on 23-9-59 at the age of 60 after a brief illness.

(The Editor deeply regrets on behalf of himself and the Editorial Board this oversight of not including a sketch of late Dr. Tampan in the Silver Jubilee Number published in February 1975).