Diagnosis of Genetic Defects by Chromosomal Analysis

Pages with reference to book, From 295 To 296

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Abstract

Of 901 karyotypes performed over a period of 4 years, genetic anomalies were detected in 162 cases. Down's syndrome (trisomy 21) was the most common (168.8%) genetic disorder followed by Turner's syndrome, Philadelphia chromosome, Klinefelter\'s syndrome, Edward's syndrome (trisomy 18) and Patau's syndrome (trisomy 13). All the three trisomies were detected very early in life. Mean age at the time of diagnosis for Turner's syndrome was 13.3 years, allowing a timely hormone replacement therapy to improve secondary sexual characters. Patients with Klinefelter\'s syndrome were diagnosed late (mean age 23.6 years), which greatly reduced their chances of an effective therapy to improve the clinical and social outcome (JPMA 45:295,1995).

Introduction

Down's syndrome (trisomy 21) a frequent cause of mental retardation is a common chromosomal disorder[1]. Maternal age has a strong influence on its incidence. The risk is 1 in 1550 live births at 20 years, which increases to 1 in 25 for women aged 45 years. The most common cause of trisomy is meiotic non- disjunction. The increased incidence of non-disjunction with age may be related to cumulative exposure to harmful environmental influences. Sex chromosomal abnormalities, namely Turner's syndrome and Klinefelter\'s syndrome were also identified through karyotyping. Turner's syndrome, characterized by primary hypogonadism in phenotypic females, is due to partial or complete monosomy of the short arm of X-chromosome[2]. Affected girls have short stature and fail to develop secondary sexual characters. Most have primary amenorrhea and their ovaries are transformed into white streaks of fibrous stroma, devoid of follicles. Kline felter's syndrome is male hypogonadism that develops when there are at least two X chroinosomes and one or more Y chromosomes[3]. Advanced maternal age and a history of irradiation of either parent may lead to meiotic error, resulting in Klinefelter's syndrome. Most patients with this disorder have long hands and feet, reduced facial and body hair, gynecomastia and testicular atrophy with low serum testosterone levels. The principle clinical effect of Klinefelter\'s syndrome is sterility. Philadelphia chromosome (translocation between chromosomal 9 and 22) is identified in bone marrow cells in patients suffering from chronic rnyeloid leukemia.

Material and Method

Cytogenetics laboratory of the Pathology Department at AKUH is a referral laboratory for diagnosis of genetic disorders. This study comprises of 901 cases seen over a period off ouryears. Cell culture and chromosome preparation was performed as described4. Five ml peripheral blood was collected in 0.5 ml heparin. 0.5 ml of buffy coat was cultured in growth medium (RPM!, fetal bovine serum, L-glutamine and penicillin-streptomycin solution). Cells were grown in incubator at 37°C with 5% CO2 until confluent. Colcarnid was added to arrest the cells in metaphase. Cells were harvested using trypsin-EDTA solution. Cells were then suspended in hypotonic solution (KCI 0.075 M) and freshly made fixative (methanol and acetic acid) was added to the tube and spun at 800 rpm forS minutes. Supernatant was discarded and fixation was repeated 3 times. Cells were finally suspended in small

volume of fixative and 3 to 4 drops were dropped on a cold wet slide and allowed to thy.. Slides were stained with Giemsa, examined under microscope and a few representative cells were photographed.

Results

From 1991 to 1994, 901 patients were referred for chromosomal analysis. Ninty-seven cases were diagnosed as Down's syndrome. Trisomy 21 was detected in 92 of these cases, whereas, 2 had extra chromosome 21 present as translocation. Three patients demonstrated a mosaic pattern. Down's syndrome was by far, the most common genetic disorder representing 68.6% of all positive cases. Turner's syndrome (10.7%), Philadelphia chromosome(10.0%), Kimefelter's syndrome (5.7%), Edward's syndrome (4.3%) and Patau's syndrome (0.7%) Were other genetic defects detected. Since early detection is important in order to administer appropriate therapy, we looked at the age of detection of these genetic diseases.

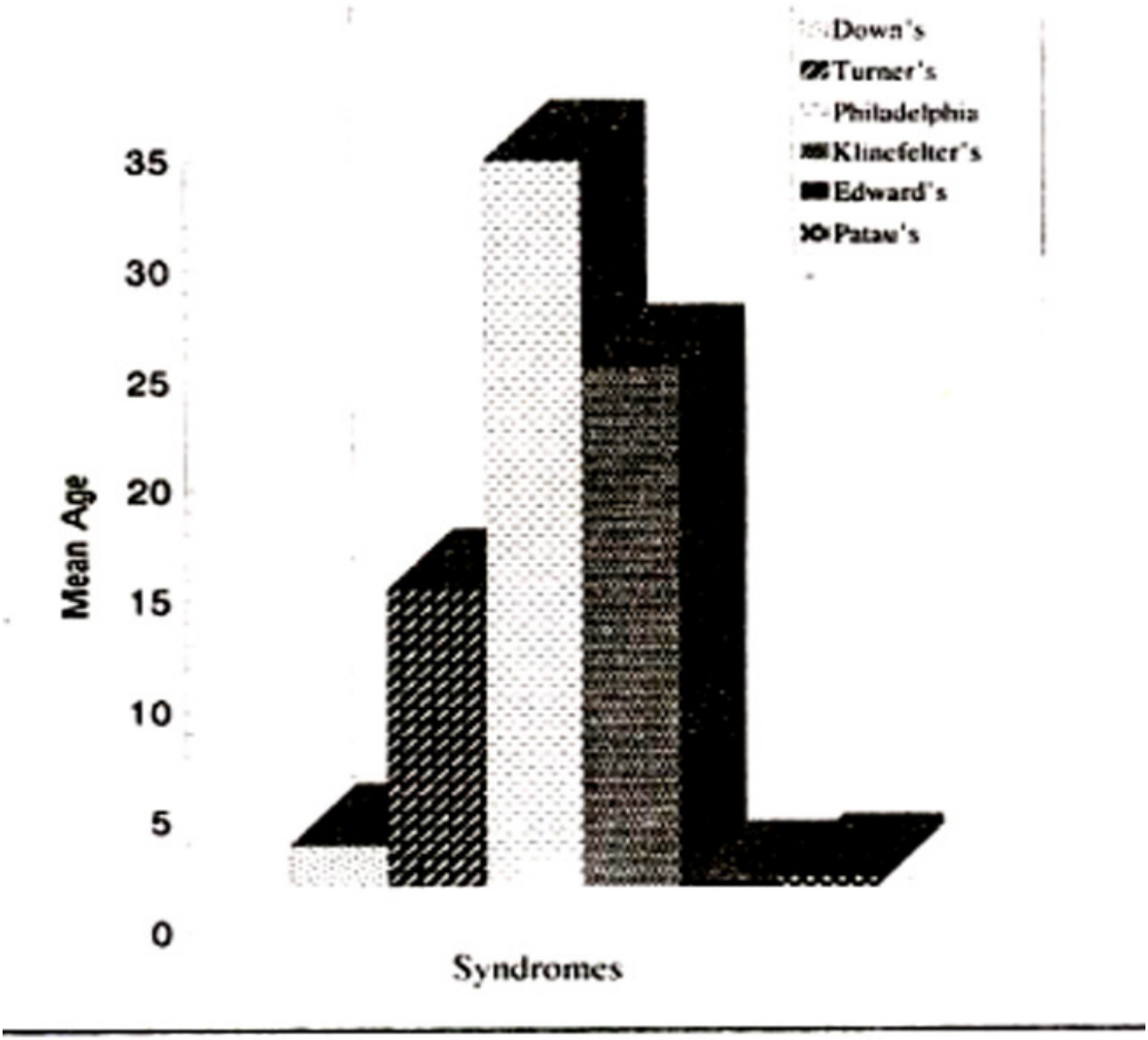

Figure. Mean age at the time of detection.

As shown in figure 1 trisomy 21, 18 and 13 were detected in early childhood. Turner's disease was diagnosed at a mean age of 13.3 years and Klinefelter's syndmme at 23.6 years. A total of 10 cases were diagnosed, out of which 8 had 47 XXY, were mosaics, 47 XX/XXY and 47 XY/XXY. Of 15 cases of Turner's syndrome, 6 had 45 xO kaiyotype, 8 were mosaics and one had 46 X, i (Xq), that is an isochromosome for the long arm of the X.

Discussion

Down's syndrome is a common genetic disease in our population. Prenatal screening for detecting this disorder is now available. Widespread prenatal screening has greatly reduced the incidence of Down's syndrome in Western countries. Although the incidence of Klinefelter\'s syndrome is almost the same as

for Down's syndrome, but the disturbing observation in our study is that Klinefelter\'s comprises only 5.7% of all positive cases. A number of factors might contribute to this finding. These patients might have very subtle phenotypic defect, therefore, their parents do not seek medical help. Secondly and because of the social stigmas attached to features like gynecomastia, absence of facial hair, small penis and testis, such adults hesitate in seeking medical help. Early recognition of Klinefelter\'s syndrome could be achieved by routinely measuring the size of the testes in school boys aged 12 to 15 years and performing a karyotype in boys with a volume of less than 2 ml[5]. Early psychological and educational support and testosterone replacement therapy initiated at onset of puberty may lead to improved social and clincial outcome. Turner's syndrome on the other hand, is picked up at an earlier age (mean age 13.4 years). This allows hormone replacement therapy to be instituted at puberty to develop secondary sexual characters and improve the height of the individual[6,7]. Main presenting complaints that bring these patients to the clinics are primary amenorrhea, short stature and absence of secondary sexual characters.

References

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