# Monosomy 22 Mosaicism

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Monosomy 22 is an extremely rare chromosomal anomaly and only six patients have been described in the literature to date since the availability of banding technique(1). A case of monosomy 22 mosaicism is reported here because of its rarity. This is the fourth case reported so far of monosomy 22 mosaicism(2,4,5) and the first one amongst females.

**Case Report**

The proband, a *VA* year old female child, was the first issue of a healthy couple *(Fig.* 1). The second issue which is a male child, is absolutely normal. The age of the mother and father was 30 and 35 years, respectively. The marriage was a non-consanguineous one. A detailed pedigree analysis revealed no chromosomal or genetic abnormality in the family. There was no previous history of miscarriage. The mother was not exposed to any drug or ionizing radiation antenatally. Intrauterine growth retardation was detected at 8 months of pregnancy.

The patient was born at term by breech delivery. Birth weight was 1.6 kg. Poor weight gain and developmental failure were the chief complaints since neonatal period. However, dietary intake was adequate. Her motor and mental milestones were grossly delayed. On examination, she was 61 cm in length, weighed 5.5 kg and had occipito frontal circumference of 37.5 cm; all below the 3rd percentile for that age and sex. She had round facies, hairy forehead, flat occiput, large anterior fontanel, hypertelorism, depressed bridge of nose, low set ears, very short neck, low hair line, high arched palate, widely spaced nipple, bilateral talipes equino varus, squint, myopic right eye, hypotonia and hyperextensible joints. Dermatoglyphic examination revealed bilateral symmetrical palms, faintly developed ridges, and normal palmar creases. There were two arches, one radial loop, and two ulnar loops on each hand. Systemic examination showed marked failure to thrive. Respiratory, cardiovascular and abdominal examinations

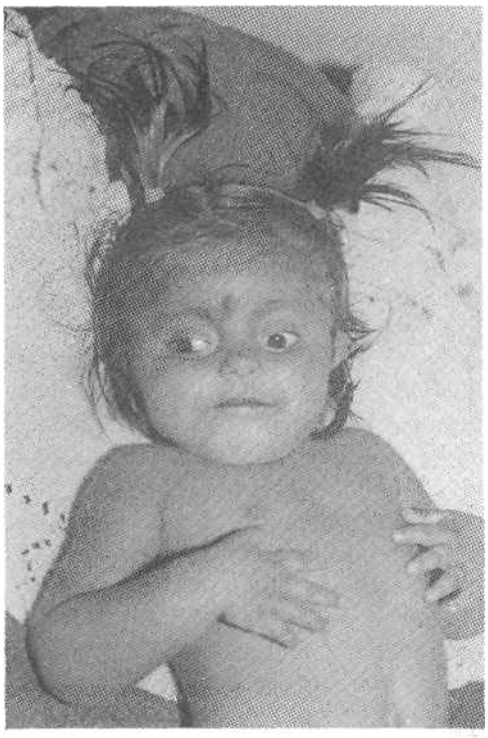

*Fig. 1. General appearance of the patient.*

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were, however, essentially normal. The patient expired at around 2½ yrs of age following an attack of severe upper gastrointestinal hemorrhage. The cause of hemorrhage could not be ascertained. An autopsy could not be performed.

*Laboratory Studies*

Hemogram, urinary studies and thyroid function tests were normal. EEG showed mild dysarrhythmia. Serum IgG, IgA and IgM levels were found to be normal for that age. Fifty metaphases, obtained by standard leucocyte culture techniques, were analyzed(16). G-banded metaphases showed two types of cell line. Thirty five cells (70%) showed monosomy of chromosome number 22 and 15 cells (30%) showed normal 46 xx pattern. So, the Karyotype of the patient is mosaic 46 xx/ 45 xx-22 *(Fig. 2)*. Karyotypes of the parents could not be done.

## Discussion

Autosomal monosomies are lethal and usually not compatible with normal extrauterine life. However, monosomy for the X chromosome is common. Mosaicism is the presence of two or more cell lines with different karyotypes in a patient. A normal diploid line commonly exists with an abnormal cell line. The abnormal line may have a numerical or a structural anomaly. Here, we observed numerical abnormality of the chromosome number 22.

Mosaicism results from nondisjunction, chromosome lag or mitotic instability of a structurally altered chromosome. If the non disjunction and chromosome lag occurs very early in development, such as in the embryo cleavage stage of the inner cell mass of a blastocyst, mosaicism may be detected in multiple tissues in the newborn or adult. If these events take place later in development of the embryo or fetus, they are confined to specific cell lines and unlikely to be detected. Abnormal cell lines that are confined to the chorion are derived from events during cleavage in cells that are destined to become placental tissue only. It

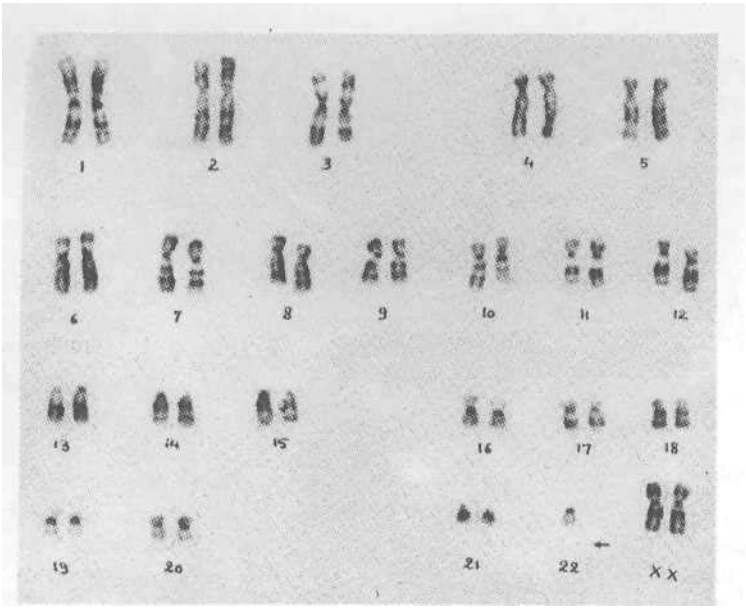


*Fig. 2. Karyotype of the patient showing monosomy 22.*

**TABLE *I*—*Important Observed Features of Monosomy 22 with Mosaicism***

| Feature | Lewinsky (5) | Moghe (2) | Verleos (4) | Garcia (3) | De Cicco (1) | Present |
|---|---|---|---|---|---|---|
| 1. Father's age (yr) | - | 33 | | | 22 | 35 |
| 2. Mother's age (yr) | 17 | 30 | - | | 22 | 30. |
| 3. Gestational age (wks) | - | | | | 32 | Term |
| 4. Birth weight (kg) | 1.76 | | | | 2.2 | 1.6 |
| 5. Epicanthal folds | - | + | - | | _ | - |
| 6. Abnormal palpebral fissures slant | - | Upward | - | - | - | - |
| 7. Hypertelorism | - | - | | - | - | + |
| 8. Large anterior fontanelle | - | _ | _ | - | - | + |
| 9. Low set ears | - | + | — | - | - | + |
| 10. Flat nasal bridge | _ | Prominent bridge | — | _ | _ | |
| 11. Narrow hairy forehead | - | + | | - | - | + |
| 12. Face | - | Flat | | Adenoid | Round | Round |
| 13. Short Neck | - | - | - | - | + | + |
| 14. Low hair line | - | - | - | — | + | + |
| 15. Squint | - | - | - | | - | + Myopic |
| 16. Cutaneous syndactyly | — | + | - | - | - | - |
| 17. Simian Creases | - | - | - | - | — | - |
| 18. Widely spaced nipples | - | | | - | - | + |
| 19. Musculo-skeletal & other anomalies | Gastro jejunal atresia; absent cerebral diastolic flow | - | - | Genus Valgus splay foot | Malopp-osed thumb; dysplasia of hip; mutiple cardiac anomalies | Club foot |
| 20. Hypotonia & hyperextensible joints | - | + | - | - | | + |
| 21. Growh percentile | - | - | | | <3rd | <3rd |
| 22. Genitalia | - | Small penis | — | - | | - |
| 23. Delayed motor & mental development | - | + | + | ++ | — | ++ |

*(Contd.)*

TABLE I *(Contd.) —Important Observed Features of Monosomy 22 with Mosaicism*

| Feature | Lewinsky (5) | Moghe (2) | Verleos (4) | Garcia (3) | De Cicco (1) | Present case |
|---|---|---|---|---|---|---|
| 24. Other anomaly | | - | - | flatocciput; dolichocephalic head | - | - |
| 25. Type | Mosaic | Mosaic | Mosaic | Complete | Complete | Mosaic |

[—] = Not available or not reported. [+] = Reported

seems, therefore, that the abnormal development process here started very early.

Monosomy 22 mosaicism is a rare chromosomal abnormality and only three cases are reported before. All three were males and the first two were diagnosed in early childhood(2,4). The third case was diagnosed antenatally. He had no dysmorphic feature and was anatomically normal except the gastroschisis and absent cerebral diastolic flow(5). The present one was female and diagnosis at $1^{1/2}$ year of age.

The first case of monosomy 22 was reported in 1973 and prior to this, in three instances monosomy for a 'G' group chromosomes had been described(l). However, definite identification of the 'G' group chromosomes in those three instances was not possible for non-availability of banding technique. Since the availability of banding technique, six cases of monosomy 22 have been reported(l-5). Out of these six reports, three were monosmy 22 with mosaicism(2,4,5) and the present case is the fourth of this kind and first amongst females. The important observed features of monosomy 22 with mosaicism are summarized in *Table I.* Various facial abnormalities observed by us, were not observed by others. The two abnormalities, which were observed both by Moghe *et al.(2)* and us, were narrow hairy forehead and low set ears. Lewinsky *et al.(5)* did not observe any facial dysmorphic features. The detailed clinical abnormalities of the third case(4) are not available. The variation in observation of facial abnormalities is evident from *Table I* (items 5 to 15). Similarly, there was wide variation in manifestations of musculo-skeletal abnormalities. A significant delay in motor and mental development was observed by almost all. External genitalia abnormality is not common. There is no definitive clinical feature available at present, by which the disease can be diagnosed immediately, nor is there any combination of features by which it can, at least, be suspected. However, monosomy 22 may present with humoral immnodeficiency(3). We did not observe any humoral immunodeficiency.

Recurrence risks for offspring with mosaicism are low and are equivalent to the population at risk. In this context, it may be noted that the second child of the couple is absolutely normal.

In conclusion, there is tremendous heterogenity in phenotypic expressions. More cases will have to be documented in detail, however, before a specific monosomy 22 mosaicism syndrome can be delineated.

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