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PATAU SYNDROME IN A NEONATE: A CYTOGENETICALLY CONFIRMED CASE REPORT

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ABSTRACT

Background: Patau syndrome is a severe chromosomal disorder caused by trisomy of chromosome 13 and is associated with a characteristic but variable combination of central nervous system, craniofacial, ocular, cardiac, renal, and limb abnormalities. **Case Presentation:** A one-day-old female neonate born at 38 completed weeks to a 46-year-old mother was evaluated for multiple congenital anomalies. Birth weight was 2.37 kg and Apgar scores were 6 and 7 at 1 and 5 minutes. Examination showed cleft lip and palate, low-set ears, left microphthalmia, and polydactyly of the right hand, left hand and left foot. Echocardiography demonstrated a moderate perimembranous ventricular septal defect with left-to-right shunting, a small secundum atrial septal defect, and a patent ductus arteriosus, with preserved biventricular function. Neurosonography was suggestive of semilobar holoprosencephaly. Renal ultrasonography showed bilateral enlarged echogenic kidneys with multiple cortical cysts, consistent with congenital cystic renal dysplasia. Ophthalmological examination confirmed left microphthalmia with iris and chorioretinal coloboma. Conventional GTG-banded chromosome analysis demonstrated 47,XX,+13[20], establishing full, free trisomy 13 without a detectable normal cell line in peripheral blood. **Conclusion:** The coexistence of semilobar holoprosencephaly, orofacial clefting, microphthalmia with coloboma, polydactyly, congenital heart disease, and cystic renal dysplasia is strongly suggestive of trisomy 13. Karyotyping confirms the diagnosis, defines the cytogenetic subtype, and provides the basis for accurate prognostic discussion and reproductive genetic counseling.

INTRODUCTION

Patau syndrome was cytogenetically defined in 1960 and results from the presence of additional chromosome 13 material.[1] The disorder most often occurs as full, free trisomy 13 caused by meiotic nondisjunction, but mosaic trisomy, Robertsonian translocation-associated trisomy, and partial trisomy are recognized. Molecular studies indicate that more than 90% of full trisomy 13 cases are maternal in origin, with both meiosis I and meiosis II errors contributing; advanced maternal age is the principal established epidemiologic risk factor.[2,3]

Patau syndrome is rare. Because a proportion of affected conceptions are lost before or during gestation and because surveillance systems ascertain cases from different gestational thresholds, the true incidence at conception cannot be measured directly and is expected to exceed the observed birth prevalence. In a multi-registry analysis, the total birth prevalence, including live births, stillbirths, and elective terminations for fetal anomaly, was 1.68 per 10,000 births (approximately 1 in 5,950), whereas the mean live-birth prevalence was 0.55 per 10,000 births (approximately 1 in 18,200).[2] A EUROCAT registry analysis reported a comparable total prevalence of 1.9 per 10,000 births and a live-birth prevalence of approximately 0.48 per 10,000 births.[4] Variation among populations reflects differences in maternal-age distribution, prenatal screening and diagnosis, fetal loss, case ascertainment, and pregnancy-management practices.[2,4] The phenotype reflects widespread disturbance of early organogenesis and commonly includes holo-prosencephaly or other cerebral malformations, cleft lip and/or palate, microphthalmia, coloboma, abnormal auricles, polydactyly, congenital heart disease, and renal abnormalities.[4-7]

Because the physical findings overlap with other multiple-malformation syndromes and because prognosis and recurrence counseling depend on the chromosomal mechanism, postnatal cytogenetic confirmation is essential. We report a one-day-old female neonate with a classic multisystem phenotype in whom conventional chromosome analysis demonstrated full, free trisomy 13.

Case Presentation

A one-day-old female neonate was born at 38 completed weeks of gestation to a 46-year-old mother by spontaneous vaginal delivery. The available antenatal record documented four antenatal visits and did not record pregnancy-induced hypertension, gestational diabetes mellitus, significant medication exposure, or radiation exposure. No prenatal cytogenetic diagnosis was available.

The infant cried immediately after birth and did not require active resuscitation. Birth weight was 2.37 kg, length was 45 cm, and head circumference was 33 cm. Apgar scores were 6/10 and 7/10 at 1 and 5 minutes, respectively. Initial examination documented a pink, alert neonate without recorded seizures or clinically significant respiratory distress.

Dysmorphological and Systemic Examination

Craniofacial examination showed cleft lip with cleft palate, low-set dysplastic ears, and marked reduction in the size of

the right globe. Limb examination demonstrated polydactyly involving both the hands and the left foot. The combination of midline craniofacial, ocular, and limb anomalies raised strong clinical suspicion of an underlying chromosomal disorder.

Cardiovascular Evaluation

Two-dimensional echocardiography demonstrated a moderate-sized perimembranous ventricular septal defect with left-to-right shunting, a small secundum atrial septal defect, and a patent ductus arteriosus. Biventricular systolic function was preserved, with no evidence of significant pulmonary hypertension.

Abdominal and Renal Evaluation

Abdominal and renal ultrasonography showed bilaterally enlarged echogenic kidneys containing multiple small cortical cysts, consistent with congenital cystic renal dysplasia. The liver, spleen, gallbladder, and urinary bladder were otherwise unremarkable, and no major intra-abdominal structural anomaly was identified.

Neurological Evaluation

Neurosonography revealed abnormal fusion of the frontal horns with incomplete anterior separation of the cerebral hemispheres, suggestive of semilobar holoprosencephaly. No intraventricular hemorrhage or hydrocephalus was observed.

Ophthalmological Evaluation

Ophthalmological examination demonstrated left-sided microphthalmia with iris and chorioretinal coloboma. The right eye was structurally normal on bedside examination.

Cytogenetic Methodology

Peripheral-blood lymphocytes were cultured for 72 hours in RPMI-1640 medium supplemented with 20% fetal calf serum, L-glutamine, penicillin, streptomycin, and phytohaemagglutinin. Cultures were incubated at 37 degrees C in a humidified atmosphere containing 5% CO_2. Colcemid was added during the final 60 minutes to achieve metaphase arrest. Cells were treated with 0.075 mol/L potassium chloride hypotonic solution and fixed in methanol:acetic acid (3:1). Chromosome preparations were subjected to conventional G-banding by trypsin using Giemsa staining.

Metaphases were evaluated at an approximate resolution of 450-550 bands per haploid genome with the help of Olympus BX-63 microscope using ASI software . Twenty metaphases were fully analyzed and karyotyped, and additional metaphases were counted and screened for a second cell line. Chromosomal nomenclature was assigned according to ISCN 2024.[8]

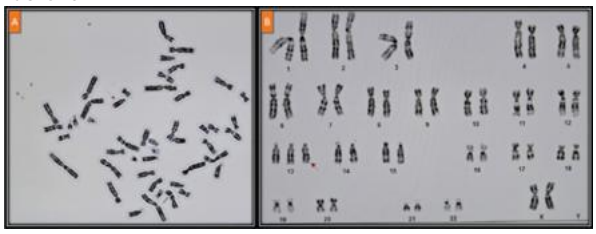

Figure 1. Representative GTG-banded Karyogram Demonstrating a Female Chromosome Complement with an Additional Free Chromosome 13: 47,XX,+13[20].

Cytogenetic Findings

All 20 fully analyzed metaphases contained 47 chromosomes, comprising two X chromosomes and three copies of chromosome 13. The final karyotype was 47,XX,+13[20]. No disomic cell line was identified among the additional metaphases screened, and no visible structural rearrangement involving chromosome 13 was detected at the achieved banding resolution. These findings established full, free trisomy 13, with no mosaicism detected in peripheral blood. Low-level mosaicism below the analytical sensitivity of conventional chromosome analysis and tissue-restricted mosaicism cannot be excluded by examination of a single tissue.

Management and Follow-up

Supportive neonatal care was initiated, including cardiorespiratory monitoring, intravenous glucose-containing fluids during establishment of enteral nutrition, and expressed breast milk through an orogastric tube. A specialized feeding bottle was planned because of the cleft lip and palate. Multidisciplinary assessment involved neonatology, cardiology, ophthalmology, radiology, and cytogenetics/clinical genetics. The subsequent hospital course, discharge status, survival outcome, and details of any later intervention were not available in the supplied clinical records and were not inferred.

DISCUSSION

This neonate showed a highly concordant clinical-cytogenetic phenotype of Patau syndrome. Population-based data indicate that congenital heart defects, nervous system anomalies, ocular abnormalities, polydactyly, and orofacial clefts are among the most frequent structural abnormalities in live-born infants with trisomy 13.[4,5] The simultaneous presence of microphthalmia, oral clefting, and polydactyly is particularly recognizable, although no single feature is pathognomonic and laboratory confirmation remains necessary.[6]

Full trisomy 13 introduces an additional copy of the entire chromosome into every cytogenetically detectable peripheral-blood cell. The resulting genome-wide dosage imbalance alters the stoichiometry of many transcripts, proteins, and regulatory networks during early embryogenesis. The phenotype is therefore best understood as a multigenic developmental disorder rather than the consequence of a single abnormal gene. Molecular studies show that most cases arise from maternal meiotic nondisjunction, frequently in association with abnormal recombination and advanced maternal age.[3]

Holoprosencephaly results from failed or incomplete cleavage and patterning of the embryonic forebrain. Ventral forebrain development and midline craniofacial morphogenesis depend on coordinated *SHH, NODAL, WNT, FGF*, and related signaling networks.[9] Chromosome 13 contains *ZIC2* at 13q32, a dosage-sensitive transcriptional regulator important in neurulation and forebrain development. Nevertheless, chromosome 13 rearrangement studies indicate that holoprosencephaly associated with chromosome 13 imbalance cannot be explained by duplication or deficiency of a single locus alone; interaction among multiple dosage-sensitive regions and wider developmental pathways is more plausible.[10]

In semilobar holoprosencephaly, posterior portions of the cerebral hemispheres show greater separation than the frontal regions. The observed fusion of the frontal horns and incomplete anterior hemispheric separation therefore fit the expected anatomical pattern. The close embryological relationship between the ventral forebrain and the frontonasal process also explains the association of cerebral midline defects with cleft lip and palate. Ocular malformations reflect disturbed optic vesicle development and, in the case of coloboma, incomplete closure of the embryonic optic fissure.

The cardiac, renal, and limb abnormalities likewise reflect disruption of early tissue patterning, proliferation, and cell migration. Septal cardiac defects and persistent ductal patency are well recognized in trisomy 13.[4,5] Fetal pathological studies have documented enlarged cystic kidneys with abnormal cortical differentiation and persistent

blastemic tissue, providing a biological correlate for the echogenic enlarged kidneys with cortical cysts in the present neonate.[7] Polydactyly is consistent with disturbed anterior-posterior limb patterning, a process that is also dependent on tightly regulated morphogen signaling. These organ-specific manifestations must not be interpreted as independent defects; they represent different expressions of a common early developmental dosage disturbance.

The karyotype 47,XX,+13[20] establishes full, free trisomy 13 rather than a Robertsonian translocation, partial trisomy, or cytogenetically demonstrable mosaicism. This distinction is clinically important. Full trisomy generally produces the classic multisystem phenotype and is associated with a higher mortality burden than mosaic or partial forms. Contemporary population-based data confirm that long-term survival is substantially better in mosaic or partial trisomy than in full trisomy, although occasional long-term survival also occurs in full trisomy.[11]

The classic phenotype in this case is therefore concordant with the full-trisomy cell line. However, prognosis cannot be predicted solely from the chromosome count. The type and severity of cerebral malformation, respiratory instability, feeding ability, renal function, cardiac physiology, infections, and the level of medical support all influence outcome.

Prognosis and Clinical Decision-making

Trisomy 13 remains associated with high fetal, neonatal, and infant mortality. In an international multi-registry study, approximately 48% of live-born infants died within the first week and 87% died within the first year.[2] These population estimates are important for counseling but are not to be presented as deterministic predictions for an individual child. More recent outcome studies demonstrate that a minority of affected children, including some with full trisomy, survive for years.[11]

Current pediatric guidance advises against automatically withholding potentially beneficial treatment solely because of a diagnosis of trisomy 13. Comfort-focused care remains an ethically acceptable option, but medical and surgical interventions should be discussed through individualized, family-centered shared decision-making that considers the severity of each anomaly, physiological feasibility, likely burdens and benefits, and parental goals.[12] For congenital heart disease, expert consensus similarly recommends case-by-case assessment rather than diagnosis-based exclusion from cardiac intervention.[13]

In the present neonate, the perimembranous VSD, small ASD, and PDA were accompanied by preserved biventricular function and no significant pulmonary hypertension at the initial study. This finding supports careful longitudinal physiological assessment. The major neurological abnormality, renal dysplasia, feeding difficulty associated with cleft lip and palate, and ocular anomaly would also need to be incorporated into treatment plan.

Genetic Counseling

Genetic counseling must be offered in a staged, non-directive manner and should address the diagnosis, cytogenetic mechanism, expected clinical spectrum, uncertainty of individual prognosis, reproductive risk, prenatal testing options, and psychosocial needs of the family.

Explanation of the result. The finding 47,XX,+13[20] means that the infant has three separate copies of chromosome 13 in all 20 fully analyzed peripheral-blood metaphases. No visible Robertsonian translocation or other structural rearrangement was detected. The result therefore represents full, free trisomy 13. The phrase "no mosaicism detected" is used because low-level or tissue-restricted mosaicism can remain undetected in a peripheral-blood study. Full, free trisomy 13 is usually a sporadic event caused by nondisjunction during gameto-genesis. More than 90% of informative cases are maternal in origin, and both maternal meiosis I and meiosis II errors occur. The maternal age of 46 years in this case materially increases the baseline risk of meiotic aneuploidy. Nothing in the available history suggests that the condition resulted from parental behavior, diet, routine medication, or an avoidable antenatal exposure.[3]

Parental karyotyping. When the affected child has a clearly demonstrated free trisomy without a visible structural rearrangement, parental karyotyping is not routinely required to explain the result because a balanced parental translocation is not the mechanism. If a Robertsonian translocation had been identified, karyotyping of both parents would be essential and testing of other relatives might be indicated.

Recurrence risk & Maternal-age effect. The recurrence risk after a pregnancy or child with free trisomy 13 is low but is higher than the age-specific population risk alone. Population-based data demonstrate an increased relative risk of the same trisomy in a subsequent pregnancy.[14] For this mother, any future-pregnancy estimate must incorporate the high age-related risk of aneuploid conception at the time of the next pregnancy. A single universal percentage should not be quoted without considering the mother's age at conception and the gestational age at which risk is being expressed. Counseling commonly uses the greater of the empiric recurrence estimate and the maternal-age-related risk; a fetal-medicine or clinical-genetics service should provide the individualized figure.

Testing in a future pregnancy. Preconception review should be followed by an early dating scan and discussion of both screening and diagnostic testing. Cell-free DNA screening can assess risk for trisomy 13 from early pregnancy and is the most sensitive screening approach for common autosomal trisomies, but it is not diagnostic. A high-risk screening result requires genetic counseling, detailed ultrasound evaluation, and confirmatory testing by chorionic villus sampling or amniocentesis. Definitive cytogenetic analysis should include a method that can establish whether any detected chromosome 13 gain is free or translocation-associated. A detailed fetal anatomical survey remains necessary because screening does not assess all structural or genetic disorders.[15]

Interpretation of prenatal tests. Chorionic villus sampling evaluates placental tissue and can occasionally be complicated by confined placental mosaicism; discordant results may require amniocentesis. Amniocentesis evaluates fetal-derived cells and is generally performed later. Rapid aneuploidy testing may provide an early result, but conventional karyotyping remains valuable for defining the chromosomal structure. Chromosomal microarray can detect copy-number imbalance but does not replace parental karyotyping when a balanced Robertsonian rearrangement is suspected.

Reproductive and psychosocial support. Counseling should acknowledge grief, uncertainty, cultural and religious values, family resources, and differing goals of care. Parents should receive balanced information about both the high risk of early death and the documented possibility of longer survival. Bereavement support, neonatal palliative-care consultation, and condition-specific family support groups may be offered irrespective of whether the family chooses comfort-focused care or selected life-prolonging interventions.[12]

Limitations

Limitations include the absence of prenatal imaging records, molecular testing, post-discharge follow-up, and a documented long-term clinical outcome. Conventional karyotyping at 450-550 band resolution cannot exclude

submicroscopic copy-number changes, low-level mosaicism, or mosaicism confined to tissues other than blood; however, these limitations do not alter the primary diagnosis of full, free trisomy 13 in the analyzed peripheral-blood cells.

CONCLUSION

Patau syndrome should be suspected in neonates with characteristic multisystem congenital anomalies. Accurate specification of the cytogenetic subtype is essential for diagnosis, prognosis, individualized care planning, and reproductive genetic counseling. Counseling should be balanced, non-directive, and based on contemporary evidence rather than describing trisomy 13 as uniformly incompatible with life.

Declarations

Competing Interests: The authors declare no competing interests.

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