Iran Red Crescent Med J. 2017 July; 19(7):e55573. doi: 10.5812/ircmj.55573.

Published online 2017 July 4. **Case Report**

A Rare Triploidy Case with Long Term Survival: A Case Report Study

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Received 2016 December 12; **Revised** 2017 March 05; **Accepted** 2017 April 09.

Abstract

Triploidy is the most frequent chromosome abnormality in the gestational age. According to the study, survival of more than 2 months in triploid patients is very rare. A 7-year-old girl with mild mental retardation with dysmorphism was referred for genetic counseling and clinical evaluation to Sarem medical genetics department (Tehran, Iran, 2013). Clinical features of the child were mental retardation, prominent upper lip, microgenitalia, prominent forehead, foot fingers syndactyly, and short hypoplastic 5th finger. G banding technique, skin biopsy, and Fluorescence in situ hybridization (FISH) testing were performed. Brain Imaging was evaluated. The karyotype of patient showed triploid (69, XXX) chromosome complement in all the metaphase spreads. However, two cell lines were found in metaphase of cultured cutaneous biopsy. The majority of the cells the body were triploid (69, XXX) and 16% of cells were diploid (46, XX). Findings of the FISH testing using X and Y Satellite enumeration probes in all studied peripheral blood lymphocyte (PBL) cells, included 3 signals and none signal respectively indicating X and Y chromosomes. Also, cultured of cutaneous biopsy finding showed 66% of cells had three signals (triploid) and 34 percent of cells had two signals (diploid) and mosaicism was confirmed. Karyotypes of parents and the brain imaging were normal. This study presents a rare case of triploidy with long survival with normal karyotypes of PBL and mosaicism in skin biopsy and interphase FISH.

Keywords: Triploidy, Mosaicism, Survival, Diploid

1. Introduction

Triploidy cases are the most common cases of chromosomal abnormality in the first trimester of pregnancy1. In 2% of all the conceptuses, spontaneous abortions occurred. A triploid conceptus possesses 69 chromosomes (1, 2). Where some of the different chromosomes in the body's cells such as triploid chromosome and other different chromosomes are either diploid and normal or abnormal is called mosaicism (1-4). Mosaicism of diploid-triploid has been associated with intrauterine growth retardation (IUGR) and postnatal delayed growth, body or facial growth asymmetry, mental retardation (M.R.), low set ears, fingers syndactyly, micrognathia, central obesity, frontal prominent and wide forehead, hypotonic muscular and wide nasal bridge (1-5). Skin pigmentary dysplasia, anomalies in the limb such as syndactyly, clinodactyly and camptodactyl (3), and mental disability (or mental retardation) of variable degree are the main symptoms (2).

The rate of triploidy live birth is one per 10,000 living child (4-6). Less severe cases of mixoploidy (diploid-triploid) and patients with triploidy are more likely to survive. The living patients and cases with long survival are rare and most of them die in the first hours or days (6). Most fetal triploids aborting in first trimester (7 to 17 weeks of gestational age), and few trilploidy who have live birth, in the first hours or days period after childbirth die (7). According to the literature, survival of more than 60 days in triploid patient are very rare and the longest survival time has been 308 days (8).

1.2. Clinical Report

A 7-year-old girl was born to a 30-year-old healthy mother and a 32-year-old father and they were a consanguineous third degree relative. This child was referred for genetic counseling and clinical evaluation to Sarem privet hospital (referral for obstetrics and gynecology along with an equipped genetic center in Tehran). Both her parents

were healthy and had no familial history of mental retardation or chromosomal disease. Moreover, the mother had a history of spontaneous abortion in recent years. The duration of gestation was 39 weeks according to the last menstrual period (LMP). Birth was without complications and was with normal vaginal delivery (NVD) with no abnormalities and her APGAR was 10/10. Birth weight was 2,500 g, length 46.3 centimeter, and head circumference (H.C.) was 30.1 centimeter. Her internal organs were healthy after birth and the patient had hyperbilirubinemia and jaundice with no history of seizure. She was sitting and walking respectively in 14 and 26 months. At the age of 24 months the speaking ability was limited to the vocabulary comprised of about a few words. At the age of 7 years, clinical features of the child were mental retardation, speech development, patchy hyperpigmentation, mandibular hypoplasia and micrognathia, dental decay, shorten philtrum, palmar crease, synductyly, joint laxity, prominent forehead, high nasal bridge, prominent upper lip (Figure 1), short hypoplastic of 5th finger, brachydactyly and syndactyly in all foot fingers, sandal gap deformity and hypo plastic nail in the toes. Review of system and physical examination such as neurologic, internal medicine, cardiology, visual system and ENT were normal. The brain MRI and CT scan showed normal anatomy of the brain, hypophysis gland, ventricles and intracranial condition. Genital system was normal with no ambiguous genitalia. Currently, the patient had a mild mental retardation and was educating in a special school for mentally challenged children. The dysmorphic girl was able to answer the easy questions with brief Phrases and correct and without mistake spelling. The clinical features of this case are presented in Table 1.

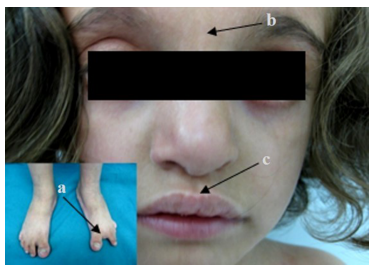

Figure 1. The 7-Year-Old Girl with Dysmorphism and Syndactyly in All Foot Fingers, Sandal Gap, Deformity and Hypoplastic Nail in the A Toes; B, High Nasal Bridge; C, Prominent Upper Lip.

2. Methods

Cytogenetics study was performed in genetic counseling and clinical evaluation of Sarem medical genetics department in Tehran city by using high-resolution G banding techniques, Giemsa staining, karyotyping and Interphase Fluorescence in situ hybridization (FISH). Peripheral blood sample and cutaneous biopsy of the patient were used in this study. In addition, FISH testing was investigated from blood and cutaneous sample, and using chromosomal probes (X and Y). Poseidon probes were from satellite Enumeration with critical regions of SE Y (DYZ3) probe at Yp1101-q11.1 (red) and SE X (DXZ1) probe at Xp11.1q11.1 (green).

3. Results

G banding chromosomal (cytogenetic) analysis was conducted based on cytogenetics protocol G bands from peripheral blood lymphocytes (PBL). Peripheral blood karyotyping indicated triploidy described as 69, XXX in a total of 100 examined metaphases (Figure 2). Chromosome studies on cultured skin biopsy revealed mosaicism for triploid cell line described as 69, XXX[42]/46,XX[8], 84% cells were triploid and 16% were normal female karyotype. The aim of the FISH study was to determine the mosaic level in peripheral blood and skin. All peripheral blood examined cells (50 cells) indicated three green signals for X chromosome consistent with 69, XXX. Interphase Fluorescence in situ hybridization with centromeric chromosomal probes (X and Y) on skin biopsy indicated 33 cells (66%) with 3 green signals of X chromosome and 17 cells (24%) with 2 green signals (Figure 3). FISH result showed a higher level of mosaicism in comparison with classic Cytogenetics result (Tables 2 and 3).

4. Discussion

Complete triploid pregnancies are usually found in spontaneous abortions. According to the study in December 2016, the longest reported survival time has been 308 days (14). Diploid-triploid mixoploidy is rarer and its origin is not well understood (15). The clinical abnormalities are similar to complete triploidy but are milder, and survival is much longer. The genital abnormalities of male patients having diploid-triploid mixoploidy are well documented (16), but no reports concerning the genital and endocrinological findings of female patients are known to us so far. In complete triploidy (69, XXX) hypoplastic external genitalia, unicornuate uterus, and ovarian dysgenesis with few or no oocytes have been described in two fetuses (17-20). Disorders of the CNS in these patients such as abnormalities in the limbic system, hypothalamus, and pituitary gland are not seen.

The mosaicism in patients with triploidy and normal set of haploid chromosomes as we reported are usually

Table 1. Description of clinical features of the present case

Variables	Description	Measuring Equipment's
Mild mental retardation	Mild intellectual disability	Low intellectual impairment
Prominent upper lip	The prominence tubercle of the upper lip was greater	Examination
Microgenitalia	Small external genital	Examination, very small to normal size for his age
Prominent forehead	Heavy brow ridge of frontal	Examination, greater to normal size
Foot fingers syndactyly	Fused the two or more digits together	Examination
Short hypoplastic 5th finger	Incomplete development of organ	Examination

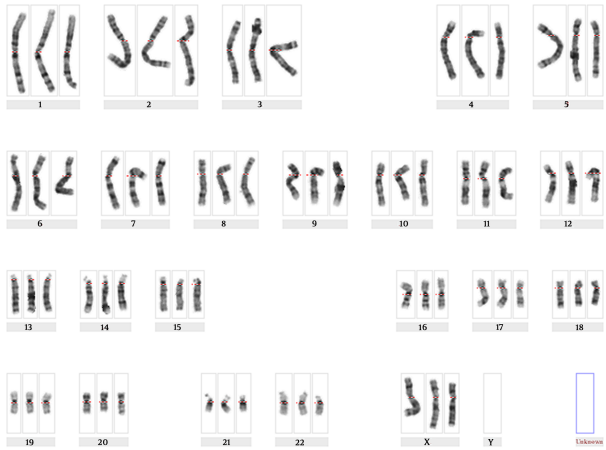

Figure 2. Peripheral Blood Karyotyping Indicated Triploidy Described as 69, XXX in a Total of 100 Examined Metaphases.

Table 2. Twelve Live Cases of Triploidy with Long Survival More Than 45 Days

Clinical Parameters	Present Case (Iran/2013)	Fryns et al. (Belgium/1977) (1)	Schrocksnadel et al. (Austria/1982) (2)	Arvidsson et al. (Sweden/1986) (3)	Sherard et al. (USA/1986) (4)	Tharapel et al. (USA/1983) (5)	Hasegawa et al. (Japan/1999) (6)	Iliopoulos et al. (USA/2005) (7)	Cassidy et al. (1977) (9)	Faix et al. (1984) (10)	Strobel and Brandt (1985) (11)	Niemann-Seyde et al. (1993) (12)	Takabachi et al. (Japan/2008) (13)
Gender	Female	Female	Female	Male	Male	Female	Female	Female	Female	Male	Female	Female	Female
Duration of pregnancy, w	39	39	NA*	31	37	34	31	39	Term	37	32	34	29
Delivery	NVD	Cesarean	NA	Cesarean	Cesarean	NA	Cesarean	Cesarean	Cesarean	Cesarean	Cesarean		Cesarean
Weight, g	2500	1810	NA	700	1417	800	650	1850	1450	1020	890	800	566
Height, cm	46.3	43.5	NA	NA	NA	37	31	42				26.5	28
Survival days	7 y	60 d	210 d	189 d	308 d	74 d	45 d	164 d	160 d	127 d	> 5.5 mo	74 days	221 d
Karyotype	69, XXX	69.XXX	69, XXX	69, XXY	69, XXY	69, XXX	69, XXX	69, XXX	69, XXX	69, XXX	69, XXX	69, XXX	69, XXX

Abbreiation: NA, not available.

considered to be chimerism in origin (21). The fact that the patient had survived to the age of 7 year, prompted us to think that a normal cell line should be present. However, the peripheral blood lymphocyte (PBL) karyotypes showed 100% triploids but the cutaneous cells culture showed the mosaicism. This study showed mosaicism in cutaneous biopsy and interphase Fluorescence in situ hybridization and FISH testing good choice for the evaluation of mosaicism when the peripheral blood karyotype is disputable. Chromosome disorders are suspected in pa-

Table 3. Common Features in Patients with Diploid/Triploid Mosaicism

References/Clinical Features	Diploid/Triploid Mosaicism											
	Present Case (Iran/2013)	Tharapel et al (France/1983)(5)	Pettenati et al (USA/1986) (8)	Meinecke et al (Germany/1988) (14)	Donnai et al (UK/1988) (15)	Donnai et al (UK/1988 (15))	Edwards et al (USA/1989) (16)	Wulfsberg et al (USA/1991) (17)	Daubeney et al (UK/1993) (18)	Muller et al (Germany/1993) (19)	Jarvela et al (Finland/1993) (20)	Van de Laar et al (Belgium/1977) (21)
Gender	Female	Female	Male	Female	Female	Female	Female	Female	Female	Female	Female	Male
Mental retardation status	Mod.	NA	Mod.	Mod.	NA	Severe	Mod.	Mod.	Severe	Severe	Mod.	Mod.
central obesity	NA	NA	Mod.	Mod.	Mod.	Mod.	Mod.	NA	NA	NA	Mod.	Mod.
Asymmetry(B	Mod.	Mod.	Mod.	Mod.	Mod.	Mod.	Mod.	NA	Mod.	Mod.	Mod.	NA
Delayed Growth-Mod.	Mod.	Mod.	NA	NA	Mod.	NA	Mod.	Mod.	Mod.	NA	Mod.	
Hypotonia	NA	NA	Mod.	Mod.	NA	Mod.	Mod.	Mod.	Mod.	Mod.	Mod.	Mod.
Micrognathia	Mod.	Mod.	Mod.	NA	NA	Mod.	NA	NA	Mod.	Mod.	Mod.	Mod.
low set ears	Mod.	Mod.	Mod.	NA	Mod.	Mod.	NA	NA	Mod.	Mod.	NA	Mod.
Syndactyly (lower limbs)	Mod.	Mod.	Mod.	NA	NA	Mod.	Mod.	NA	NA	Mod.	Mod.	Mod.
Syndactyly (upper limbs)	Mod.	Mod.	Mod.	Mod.	NA	Mod.	Mod.	NA	Mod.	Mod.	NA	Mod.
small hands	Mod.	NA	Mod.	Mod.	NA	Mod.	NA	NA	NA	NA	NA	NA
Depressed nasal bridge	NA	Mod.	NA	NA	Mod.	Mod.	NA	Mod.	Mod.	Mod.	Mod.	NA
Frontal prominent	Mod.	Mod.	Mod.	NA	NA	NA	NA	Mod.	Mod.	NA	NA	NA
Sandal gap	Mod.	Mod.	Mod.	Mod.	Mod.	NA	NA	NA	NA	NA	Mod.	NA
Short halluces	NA	NA	NA	Mod.	NA	NA	NA	NA	Mod.	NA	Mod.	NA
Seizures	NA	NA	NA	Mod.	Mod.	NA	NA	Mod.	Mod.	Mod.	NA	NA
Respiratory distress	NA	Mod.	Mod.	NA	Mod.	NA	NA	NA	NA	NA	NA	NA
Microstomia	Mod.	NA	NA	NA	NA	Mod.	NA	NA	NA	NA	Mod.	Mod.
Feeding difficulties	NA	NA	NA	NA	NA	NA	NA	NA	NA	Mod.	Mod.	NA
Muscular atrophy, extremities	NA	Mod.	NA	NA	NA	Mod.	Mod.	NA	NA	NA	NA	NA

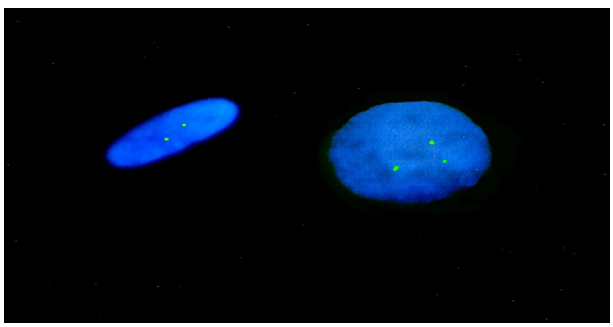

Figure 3. FISH Result Showed Both Two and Three Signals for the Centromere of Chromosome X, Shown As Green Spots.

tients with features characteristic of an established chromosomal syndrome, and in patients with multiple congenital anomalies, mental retardation, without an identifiable etiology. The use of second tissue such as skin in suspected cases of mosaicism is an essential approach to demonstrate the true karyotype of the patients.

In the literature review since 1977 to Dec 2016, twelve live cases of triploidy with long survival (more than 45 days) were found and showed in Table 1. We present the rare case of triploidy with longest surviving age in the Iran and the world, to our knowledge. 10 of 12 cases were girls (Table 2). Also delivery in 5 of 8 cases in Table 1 was cesarean section.

4.1. Limitations

Lack of collaboration of the girl's parents for performing supplementary genetic tests and more clinical examinations was the most important limitation in our study.

Acknowledgments

We would like to thank the parents of the patient for their cooperation. We are thankful to the staff of cytogenetics laboratory at Sarem hospital for their assistance.

References

1. Fryns JP, van de Kerckhove A, Goddeeris P, van den Berghe H. Unusually long survival in a case of full triploidy of maternal origin. *Hum Genet.* 1977;**38**(2):147–55. [PubMed: 908561].
2. Schrocksnadel H, Guggenbichler P, Rhomberg K, Berger H. [Complete triploidy (69,XXX) surviving until the age of 7 months]. *Wien Klin Wochenschr.* 1982;**94**(12):309–15. [PubMed: 6289537].
3. Arvidsson CG, Hamberg H, Johnsson H, Myrdal U, Anneren G, Brun A. A boy with complete triploidy and unusually long survival. *Acta Paediatr Scand.* 1986;**75**(3):507–10. [PubMed: 3728010].
4. Sherard J, Bean C, Bove B, DelDuca VJ, Esterly KL, Karcsh HJ, et al. Long survival in a 69,XXY triploid male. *Am J Med Genet.* 1986;**25**(2):307–12. doi: 10.1002/ajmg.1320250216. [PubMed: 3777027].
5. Tharapel AT, Wilroy RS, Martens PR, Holbert JM, Summitt RL. Diploid-triploid mosaicism: delineation of the syndrome. *Ann Genet.* 1983;**26**(4):229–33.
6. Hasegawa T, Harada N, Ikeda K, Ishii T, Hokuto I, Kasai K, et al. Digynic triploid infant surviving for 46 days. *Am J Med Genet.* 1999;**87**(4):306–10. [PubMed: 10588835].
7. Iliopoulos D, Vassiliou G, Sekerli E, Sidiropoulou V, Tsiga A, Dimopoulou D, et al. Long survival in a 69,XXX triploid infant in Greece. *Genet Mol Res.* 2005;**4**(4):755–9. [PubMed: 16475122].
8. Pettenati MJ, Mirkin LD, Goldstein DJ. Diploid-triploid mosaicism: report of necropsy findings. *Am J Med Genet.* 1986;**24**(1):23–8. doi: 10.1002/ajmg.1320240104. [PubMed: 3706409].
9. Cassidy SB, Whitworth T, Sanders D, Lorber CA, Engel E. Five month extrauterine survival in a female triploid (69,XXX) child. *Ann Genet.* 1977;**20**(4):277–9. [PubMed: 305757].
10. Faix R. G. , Barr M. , Waterson J. R. . Triploidy: Case report of a live-born male and an ethical dilemma. *Pediatrics.* 1984;**74**(2):296–9.
11. Strobel SL, Brandt JT. Abnormal hematologic features in a live-born female infant with triploidy. *Arch Pathol Laboratory Med.* 1985;**109**(8):775.
12. Niemann-Seyde SC, Rehder H, Zoll B. A case of full triploidy (69,XXX) of paternal origin with unusually long survival time. *Clin Genet.* 1993;**43**(2):79–82. [PubMed: 8448906].
13. Takabachi N, Nishimaki S, Omae M, Okuda M, Fujita S, Ishida F, et al. Long-term survival in a 69,XXX triploid premature infant. *Am J Med Genet A.* 2008;**146A**(12):1618–21. doi: 10.1002/ajmg.a.32352. [PubMed: 18478596].
14. Meinecke P, Engelbrecht R. [Abnormalities-retardation syndrome caused by incomplete triploidy]. *Monatsschr Kinderheilkd.* 1988;**136**(4):206–9. [PubMed: 3386650].
15. Donnai D, Read AP, McKeown C, Andrews T. Hypomelanosis of Ito: a manifestation of mosaicism or chimerism. *J Med Genet.* 1988;**25**(12):809–18.
16. Edwards MJ, Park J, Wursterhill DH, Graham JM. Clinical-features of diploid polyploid mixoploidy in older individuals. *Pediatr Res.* 1989;**25**(4):A76.
17. Wulfsberg EA, Wassel WC, Polo CA. Monozygotic twin girls with diploid/triploid chromosome mosaicism and cutaneous pigmentary dysplasia. *Clin Genet.* 1991;**39**(5):370–5. [PubMed: 1860253].
18. Daubeney PE, Pal K, Stanhope R. Hypomelanosis of Ito and precocious puberty. *Eur J Pediatr.* 1993;**152**(9):715–6. [PubMed: 8223798].
19. Muller U, Weber JL, Berry P, Kupke KG. Second polar body incorporation into a blastomere results in 46,XX/69,XXX mixoploidy. *J Med Genet.* 1993;**30**(7):597–600. [PubMed: 8411035].
20. Jarvela IE, Salo MK, Santavuori P, Salonen RK. 46,XX/69,XXX diploid-triploid mixoploidy with hypothyroidism and precocious puberty. *J Med Genet.* 1993;**30**(11):966–7. [PubMed: 8301657].
21. van de Laar I, Rabelink G, Hochstenbach R, Tuerlings J, Hoogeboom J, Giltay J. Diploid/triploid mosaicism in dysmorphic patients. *Clin Genet.* 2002;**62**(5):376–82. [PubMed: 12431252].