







CLINICAL REPORT

Mosaic proximal trisomy 13q and regular trisomy 13 in a female patient with long survival: Involvement of an incomplete trisomic rescue and a chromothripsis event

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Abstract

Background: Trisomy 13 or Patau syndrome has a prevalence of 1:10,000–20,000 and is characterized by microcephaly, microphthalmia, polydactyly, as well as other dysmorphic features and malformations, with a patient survival of 13% in the first year. Trisomy 13 presents either as a free chromosome 13 trisomy or associated with a chromosomal Robertsonian translocation, as partial trisomy affecting proximal or distal 13q regions, and also as a mosaic. Mosaic trisomy 13 shows a highly variable phenotype, displaying from mild to severe affectations. We present a 12-year-old Mexican female patient with intellectual disability, dysmorphic features, polymenorrhea, and long survival, whose initial cytogenetic study referred to a small supernumerary marker chromosome.

Methods: GTG banding karyotype, high-resolution chromosomal microarray, and fluorescent in situ hybridization analyses were performed in peripheral blood cells.

Results: Our analyses demonstrated a *de novo* mosaicism in our patient, constituted by proximal trisomy 13q10-q14.3 (82%) and free trisomy 13 (18%) cell lines. Her final chromosomal complement is mos 47,XX,+del(13)(q14.3)[25]/47,XX,+13[7].ish del(13)(RB1+)[17]/13q14(RB1x3)[2].arr[GRCh37] 13q11q14.3(19436286_51726415)x3,13q11q34(19436286_115107733)x2-3 dn.

Conclusions: The wide spectrum of clinical manifestations observed in our patient mainly results from the proximal trisomy 13q, and her phenotype is modified by the presence of a free trisomy 13 cell line. We propose that her mosaicism probably derived from a trisomic zygote that underwent a failed trisomic rescue associated with chromothripsis, originating the cell line with partial 13q proximal trisomy, whose selective advantage could explain the long survival of our patient.

KEYWORDS

chromothripsis, hyperpolymenorrhea, mosaic trisomy 13, proximal trisomy 13q, trisomic rescue

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1 | INTRODUCTION

Trisomy 13 (T13) or Patau syndrome has a prevalence of 1:10,000–20,000 in newborns (Hennekam et al., 2010; Peroos et al., 2012). Its clinical spectrum includes intra-uterine growth restriction, psychomotor, and intellectual delay; sloping forehead, microcephaly, midline defects such as holoprosencephaly, cleft lip with or without cleft palate; small malformed ears; congenital heart disease, including auricular or ventricular septal defects (VSD); limb abnormalities, mainly characterized by postaxial polydactyly, congenital talipes equinovarus or rocker-bottom feet. Eye anomalies reported in T13 are microphthalmia, iris coloboma, and retinal dysplasia. T13 patients also have genitourinary alterations including polycystic kidney disease, hydronephrosis, and horseshoe kidney, as well as cryptorchidism and hypospadias in males, or hypoplasia of labia minora and bicornuate uterus in females. Other clinical data that can be present are aplasia cutis or scalp defects, omphalocele, single umbilical artery, inguinal or umbilical hernia, and hypotonia/hypertonia (Hennekam et al., 2010; Petry et al., 2013; Ribate-Molina et al., 2010; Williams & Brady, 2020; Table 1). T13 patients have a 48% median mortality in the first week of life, which is up to 87% in the first year, and their 5-years survival is 7%; they present intellectual disability (ID), seizures, and failure to thrive (Meyer et al., 2016; Williams & Brady, 2020; Wu et al., 2013). T13 can be observed as a free trisomy (FT13); associated to a Robertsonian translocation; as a partial proximal (PT13q) or partial distal (DT13q) trisomy 13q; and as a mosaic (MT13) with both normal and trisomic cell lines, which may harbor a normal or abnormal chromosome 13 (Alberman et al., 2012; Jinawath et al., 2011; Williams & Brady, 2020). MT13 accounts for 5% of the T13 cases, and shows a widely variable phenotype depending on tissue distribution, type of numerical or structural aberration, or the abnormal to normal cells ratio (Cammarata-Scalisi et al., 2019; Delatycki & Gardner, 1997; Fogu et al., 2008; Griffith et al., 2009; Pachajoa & Meza Escobar, 2013).

The PT13q phenotype is different from the one observed in DT13q, which is more similar to a T13 (Gentile et al., 1999; Rogers, 1984; Tharapel et al., 1986). Growth and psychomotor retardation, microcephaly, epicanthal folds, and micrognathia are common characteristics of both PT13q and DT13q (Tharapel et al., 1986). PT13q affecting the band q14 (PT13q14) is a very rare event, mostly associated with a parental balanced translocation, and its clinical manifestations also include dysmorphic features, the persistence of fetal hemoglobin (HbF), and increased polymorphonuclear projections (Rogers, 1984; Tharapel et al., 1986). Herein, we describe a 12-year-old Mexican female patient with mosaicism for PT13q14 and FT13, and discuss the mechanisms involved in its origin.

2 | CLINICAL REPORT

The proband is a 12-year-old Mexican mestizo female, the only child of a young, healthy, and unrelated couple, who was referred at 2 years of age due to dysmorphic features. The mother's pregnancy length was 38 weeks; a vaginal infection was diagnosed and treated during the last trimester. Delivery was by cesarean section due to cephalopelvic disproportion, and her weight was 2,800gr (P50), height 50 cm (P50), and Apgar score 7/9. Hearing screening at 1 month of age was normal, and by this time she presented a seizure episode associated with a breath-holding spell; thus, she was referred to the pediatric neurology consultation, but did not require further management. The parents also referred that she was diagnosed with probable interventricular communication; however, this congenital cardiopathy did not require further treatment. She could support her head and sit down at 8 months of age, stood up by herself at 1 year 2 months of age; walked unaided, and controlled sphincters at 2 years of age; her menarche was at 11 years of age. A GTG banding karyotype was realized when the patient was 2 years old, and a small supernumerary marker chromosome was identified, while the karyotypes of her parents were normal. The patient lost to follow-up, and at 12 years of age she attended the gynecology consultation due to hyperpolymenorrhea associated with irregular cycles and anemic syndrome; she was then referred to our genetics service. Her current weight is 42.9 kg (P25), height 1.41 m (P25), and head circumference of 53 cm (P50). She has ID, brachycephaly, dysmorphic facial features, right thumb with abnormal folding lines, bilateral clinodactyly, and bilateral brachydactyly of the 3rd, 4th, and 5th toes. Hyperpigmented dermal lesions were observed in her thorax, armpits, and vulva, which in the further clinical dermatological evaluation were diagnosed as eruptive vellus hair cysts (EVHC). Hypopigmented lesions were also observed in her left arm (Figure 1a–f and Table 1). HbF persistence was discarded by electrophoresis analysis and a hysterectomy was carried out in another institution, in order to treat her hyperpolymenorrhea. She says a few monosyllabic words without an appropriate context and attends to a school for children with special needs. The parents declined further clinical or laboratory testing, including renal, heart, and uterine assessments.

3 | METHODS

All the analyses and clinical photographs were carried out in compliance with ethical principles, and written informed consent and institutional approval were obtained. GTG banding karyotype was carried out in blood cells. Genomic copy-number analysis was performed on peripheral blood DNA using CytoScan HD microarrays, according to the

TABLE 1 Clinical characteristics of the different occurrences of chromosome 13 trisomy and our patient

Clinical characteristics	T13	T13 > 5 years (non-mosaic)	MT13	Proband	PT13q13.1	PT13q14
<i>Prenatal complications</i>						
Intrauterine growth delay	87%	Frequent	26%	–	+	NR
Pregnancy complications	Frequent	38%	80%	–	–	NR
<i>Neurological development</i>						
Failure to thrive	87–100%	88–100%	50%	–	–	NR
Intellectual disability/ PMD	100%	100%	83%	+	+	100%
Global delay	100%	100%	76%	+	+	NR
Speech delay	100%	100%	100%	+	+	NR
Seizures	25–50%	62–88%	74%	+*	–	14%
Hypertonia	26–67%	NR	50%	–	–	–
Hypotonia	48%	NR	25%	–	+	14%
<i>Brain/Cranial/Facial defects</i>						
Microcephaly	86%	75%	52%	–	+	29%
Holoprosencephaly	60–70%	–	24%	–	–	–
Brachycephaly	–	–	25%	+	–	57%
Flat occiput	75%	NR	67%	+	–	NS
Sloping forehead	16%	75–100%	78%	–	–	43% (bossing)
Micrognathia	50–84%	NR	62%	–	+	43%
<i>Eyes</i>						
Palpebral fissures	5–27%	+, downslanting	41% upslanting, 29% downslanting	Horizontal	Horizontal	–
Microphthalmia	60–88%	75%	23%	–	–	–
Coloboma/cataracts	63–75%	33%	10–11%	–	–	–
Hypotelorism	83%	–	67%	–	–	–
Hypertelorism	–	+	30%	–	–	–
Epicanthal folds	56%	–	50%	–	–	29%
Strabismus	–	–	45%	+(right)	–	29%
<i>Ear/auditory defects</i>						
Malformed/low set ears	80–92%	63–100%	71–83%	+	+	100%
Hearing loss	50%	38–63%	46%	–	–	NR
<i>Nose</i>						
Broad flat nose/stubby nose	–	75–100%	17%/33%	Stubby	+	71%
Hypoplastic/short nose	NR	NR	58%/40%	–	–	–
Depressed nasal bridge	–	+	69%	–	–	71%
	(100% prominent)					
Broad nasal bridge	23% (root)	75–100%	82%	+	–	–
<i>Mouth</i>						
Cleft lip and/or palate	23–80%	13%	50–73%	–	–	29%
High-arched palate	72%	50%	47%	+	–	11%
Thin upper lip	–	35–53% protruding	50%	+	–	11%
<i>Neck</i>						
Short/thick	79–100%	+	75%	Short	–	43%

(Continues)

TABLE 1 (Continued)

Clinical characteristics	T13	T13 > 5 years (non-mosaic)	MT13	Proband	PT13q13.1	PT13q14
<i>Heart defects</i>	56–94%	50–69% NS, Dextrocardia	+	+	+	NR
Ventricular septal defect	73%	NS	47%	+**	+	NS
Atrial septal defect	91%	NS	41%	–	–	NS
Patent ductus arteriosus	82%	NS	53%	–	–	NS
<i>Genitourinary anomalies</i>						
Uterine abnormalities	50%	25–30%	44%	+***	–	NR
Renal malformations	25–70%	38–63%	33%	–	–	–
<i>Hands/feet anomalies</i>						
Polydactyly of hands/feet	60–78%	38%	33%/22%	–	–	–
Fingers flexion deformity/ clenched hands	68–73%	63–88%	47%	–	–	–
Clinodactyly fingers/toes	–	–	60%/50%	+	–	43%
Brachydactyly fingers/ toes	–	–	36%	3–5th toes	Broad, little toes	NR
Camptodactyly	37–63%	50%	44%	–	–	NR
Prominent calcaneus	28–46%	63–88%	52%	–	–	NR
Nail abnormalities	68%	–	25%	–	–	NR
<i>Skin anomalies</i>						
Scalp defects	44–75%	25–88%	8%	–	–	–
Hemangioma	27–88%	–	60%	–	–	14%
Pigmentary anomalies	NR	NR	82%	+, and EVHC	–	–
Phylloid hypomelanosis	NR	NR	33%	–	–	–
Telangiectatic nevus	NR	NR	33%	–	–	–
Skin redundancy (other than neck)	59% (nape)	–	18.5%	–	–	–
<i>Umbilical hernia</i>	40–83%	–	44%	+	–	14%
<i>Other relevant anomalies</i>						
HbF persistence	Delayed hemoglobin switch and HbF persistence	Low-levels (<1%) reported at older ages	NR	No HbF at 12 years old	NR	67%
Increased PMN projections	25–80%	+	NR	ND	NR	80%

Abbreviations: EVHC, eruptive vellus hair cyst; MT13, mosaic trisomy 13 (Cammarata-Scalisi et al., 2013, 2019; González-del Angel et al., 2014; Griffith et al., 2009; Jinawath et al., 2011; Pachajoa & Meza-Escobar, 2013; Wieser et al., 2015); ND, not determined; NR, not reported; NS, not specified; PMD, psychomotor delay; PMN, polymorphonuclear; PT13q13.1, proximal trisomy 13 to q13.1 (Bertini et al., 2010); PT13q14, proximal trisomy 13 to q14 (Tharapel et al., 1986); T13, full trisomy 13 (Henekam et al., 2010; Peroos et al., 2012; Petri et al., 2013); T13>5 years, non-mosaic trisomy 13 patients with long survival (above 5 years of age) (Fogu et al., 2008; Peroos et al., 2013); +, positive/present; –, negative/absent; *, one occasion, associated with a breath holding spell; **, antecedent of congenital heart disease, probably ventricular septal defect; ***, hyperpolymenorrhea, without structural uterine assessment.

manufacturer's protocol. Analysis of data was carried out in Chromosome Analysis Suite 4.0 (ChAS 4.0) using the human genome reference assembly GRCh37. Microarray materials, instruments, and software were from Thermo-Scientific

Inc. (Waltham, MA, USA). Fluorescent in situ hybridization (FISH) analysis with RB1 probe (Vysis Abbott, Inc. Abbott Park, IL, USA) was carried out in blood lymphocytes metaphases according to fabricant's protocol.

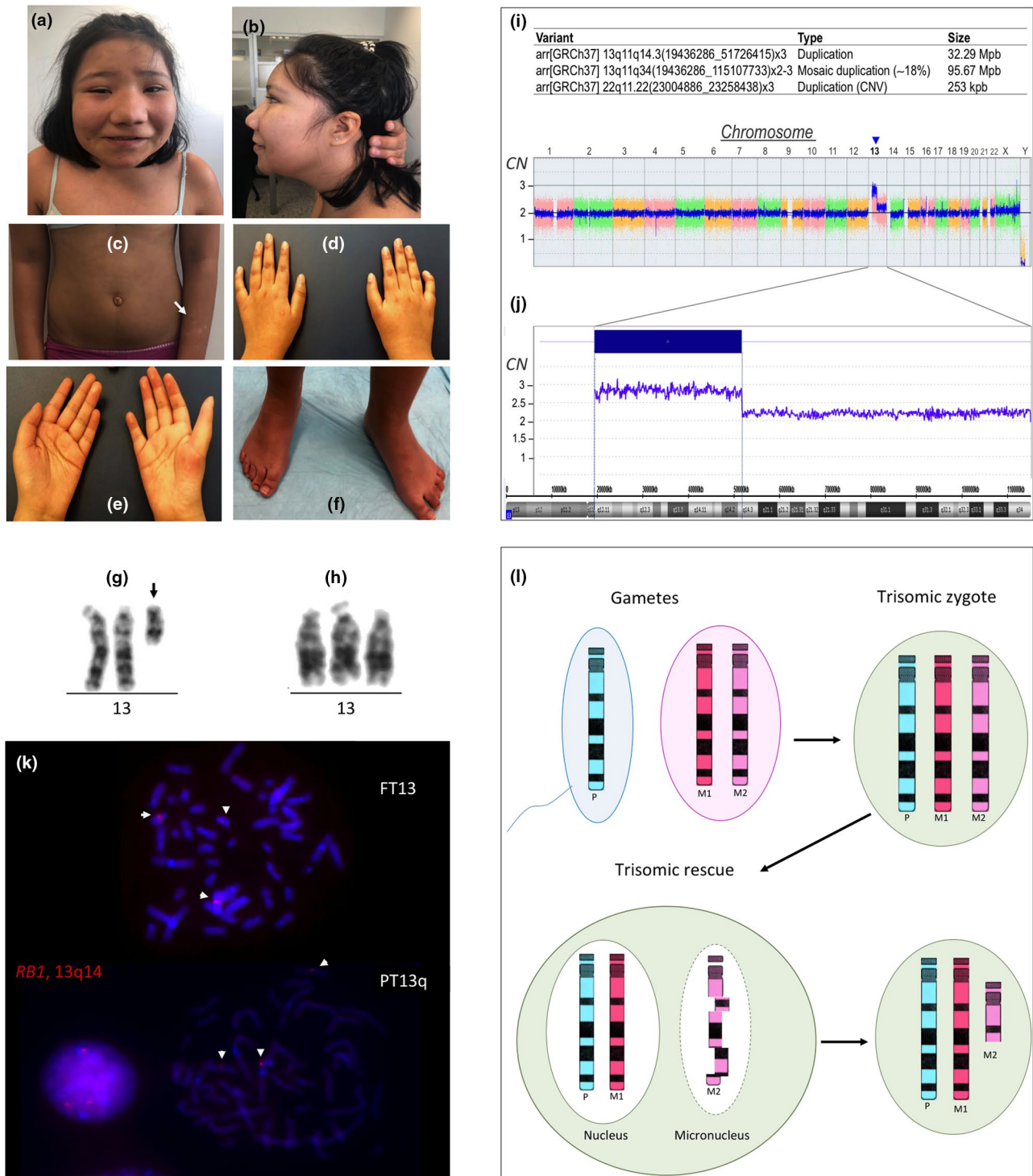


FIGURE 1 Clinical characteristics of the patient. (a, b) Facial dysmorphic features. (c) Hypopigmented spots (white arrow). (d, e) Clinodactyly of the 5th finger and abnormal flexion lines in the right thumbs. (f) Bilateral clinodactyly of the 3rd, 4th, and 5th toes. Partial GTG karyotypes: (g) cell line with a marker chromosome that corresponded to del(13)(q14.3) (black arrow) and two chromosomes 13; (h) FT13 cell line. (i) CytoScan HD microarray analysis results and whole-genome copy-number view, indicating mosaic gains at the chromosome 13 region (blue arrowhead). (j) Close up of the chromosome 13 trisomic region; the X-axis indicates the chromosomal position and the Y-axis corresponds to the copy number scale; cytogenetic bands are indicated. (k) FISH with RB1 probe indicating the presence of 13q14 regions (white arrows) in two metaphases, corresponding to FT13 (top) and PT13q (bottom right), respectively; an interphase FISH is also shown (bottom left). (l) Schematic representation of the proposed mechanism for the mosaic formation: fertilization of a heterodisomic gamete originated a trisomic zygote that underwent an atypical trisomic rescue; shattering of one chromosome 13 that was lagging in a micronucleus, followed by a chromothripsis event, caused loss of most of the 13q distal region. For clarity, only chromosomes 13 are represented. CN: copy number; M1: maternal chromosome 1; M2: maternal chromosome 2; mar: marker chromosome; P: paternal chromosome

4 | RESULTS

The GTG banding karyotype of the patient was 47,XX,+mar[25]/47,XX,+13[7] (Figure 1g,h). Microarray analysis revealed a 32.29 Mb partial duplication of chromosome 13q arr[GRCh37] 13q11q14.3(19436286_51726415) x3, and a 253 kbp duplication at chromosome 22q11.2: arr[GRCh37] 22q11.22(23004886_23258438)x3 (Figure 1i). The latter variant was discarded from further analysis due to overlapping with shorter and highly frequent CNV regions, as well as unrelated gene content, which corresponded to immunoglobulin Lambda joining and variable constituents. According to the microarray data, the partial chromosome 13q11-q14.3 duplication was nested in a mosaic duplication region spanning the complete chromosome 13q arm arr[GRCh37] 13q11q34(19436286_115107733)x2-3 (Figure 1j). The proportion of the complete duplication in the mosaic was approximately 18%. Therefore, the partial proximal 13q duplication was expected to appear in ~82% of the cells. These data were consistently confirmed by FISH assay (Figure 1k). Her final karyotype was: mos 47,XX,+del(13)(q14.3)[25]/47,XX,+13[7].ish del(13)(RB1+)[17]/13q14(RB1x3)[2].arr[GRCh37] 13q11q14.3(19436286_51726415) x3,13q11q34(19436286_115107733)x2-3 dn.

5 | DISCUSSION

MT13 patients without a euploid cell line have been rarely reported (Fogu et al., 2008; Gentile et al., 1999; Jinawath et al., 2011; Reardon et al., 1981), and to the best of our knowledge, no patients with a chromosomal composition similar to that of our patient have been described. Furthermore, patients with PT13q without other chromosomal imbalances are very rare. For instance, only one female patient with PT13q secondary to a t(13;21)(q13.2;p13) with a der(13)-like ring has been reported (Bertini et al., 2010). Comparative genomic hybridization analysis in this patient revealed a duplication of 16.6 Mb from 13q11 to 13q13.2 in all her cells, which probably derived from a trisomic zygote with an isodicentric chromosome 13q. This 3-year-old patient showed the main clinical data reported for PT13q (Rogers, 1984; Tharapel et al., 1986) including reduced head circumference, mild facial dysmorphic features (micrognathia, prominent nose with a broad base, short philtrum, and thin lips), large anteverted ears, broad little toes, and diffuse hypotonia; additionally, she presented a severe cardiac defect (tetralogy of Fallot) and ID, with the absence of language and autistic-like behavior (Bertini et al., 2010). The authors explained the autistic behavior by the effect of the 13q breakpoint (FRA13A) on the *NBEA* gene (MIM 604889), which has been reported as deleted in patients with autism.

Our patient was initially referred due to dysmorphic features; as she grew up, other clinical characteristics developed, such as ID and hyperpolymenorrhea. She was diagnosed with a PT13q14 and FT13 chromosomal mosaicism, and her clinical features are in accordance with those reported to diverse extents in PT13q14, MT13, and T13 patients (Table 1 and Figure 1a–f). She presented ID and speech disabilities, which are traits observed in the majority of individuals affected by any of the three mentioned entities. She has several facial dysmorphic features, including a stubby nose, high palate, and thin upper lip, which are frequent in PT13q14 patients (Tharapel et al., 1986, Table 1). Interestingly, our patient presented an uncomplicated VSD, and despite heart anomalies have not been described in PT13q14 patients, this trait affects a high percentage of T13 and MT13 patients (Table 1). Our patient has clinodactyly and abnormal flexion lines in both hands and feet, as reported in MT13 and PT13q14 patients (Table 1). Despite the presence of an FT13 cell line, she does not exhibit clinical manifestations of holoprosencephaly, although it was not possible to carry out further neurological assessment. Cleft lip/palate, polydactyly, or other severe anomalies, which have also been associated with DT13q, were absent in our patient. The most relevant differences between the clinical traits observed in our patient and the typical T13 presentation include the presence of horizontal palpebral fissures and strabismus, the type of malformations observed in fingers and toes, and the type of skin abnormalities (Table 1).

Different skin abnormalities have been described in patients affected by the distinct cytogenetic trisomy 13 forms, including scalp defects, hemangiomas or pigmentary anomalies, such as the lines of Blaschko, among others (Table 1). MT13 patients present hypomelanosis of Ito, the lines of Blaschko, and a peculiar phylloid pattern characterized by hypo- and hyperpigmented areas (Griffith et al., 2009; Salas Labadía et al., 2019; Taibejee et al., 2004; Wieser et al., 2015). These characteristics are also present in patients with mosaicism for distal trisomy or tetrasomy 13q, and in a patient with distal monosomy 13q, suggesting that the genes involved in this phenotype might be located at the 13q distal region (Dhar et al., 2009; Faletra et al., 2012; Myers et al., 2015). The presence of hypopigmented lesions in our patient, albeit not corresponding to the typical phylloid presentation commonly associated with MT13, may constitute a manifestation of the underlying chromosomal mosaicism for FT13. Three candidate pigmentary genes identified in the human genome are located within the 13q distal region: *EDNRB* (endothelin receptor type B; MIM 131244) in 13q22, and *EFNB2* (ephrin-B2, MIM 600527) in 13q33.3, both of which function as growth factor receptors involved in melanoblast migration; *DCT* (dopa-chrome tautomerase, MIM 191275) is located at 13q32.1, and functions as a melanosomal enzyme (Dhar et al., 2009;

Faletra et al., 2012; Taibjee et al., 2004). The role of these genes in human disease is not yet known, however, it has been suggested that duplications or triplications may cause their overexpression, thus producing the pigmentary phenotype. Alternatively, mosaic expression of these genes may impair melanoblast migration and melanocyte formation leading to the depigmentation phenotype (Dhar et al., 2009; Faletra et al., 2012). Our patient also had clinically diagnosed EVHC, which are usually sporadic, although an autosomal dominant inheritance pattern has also been proposed (Anand et al., 2018). However, these lesions could be originated by the MT13, as hidradenitis suppurativa has been reported in an MT13 patient (González del Ángel et al., 2014), and also in a patient with mosaicism for trisomy 13q distal (Faletra et al., 2012). EVHC is considered a variant of steatocystomas multiplex (SCM), and several hypothesis have suggested that these are different evolutionary stages of the same entity known as multiple pilosebaceous cysts. They share the same clinical characteristics and management, and differential diagnosis can only be achieved by histopathological analysis (Marrugo Lara et al., 2018; Waldemer-Streyer & Jacobsen, 2017).

The persistence of HbF has been reported in T13, including patients with long survival (Redheendran et al., 1981), and in up to 28% of PT13q14 patients (Tharapel et al., 1986). It has been demonstrated that the overexpression of miRNA genes localized in 13q14.2, *MIR16-1* (MIM 609704), and *MIR15A* (MIM 609703), results in elevated HbF levels in human erythroid progenitor cells (Sankaran et al., 2011). This could be partly mediated through downregulation of the *MYB* transcription factor gene (MIM 189990), which is a direct target of these microRNAs, and constitutes a potent negative regulator of HbF expression; this could explain the delayed fetal-to-adult hemoglobin switch and persistence of fetal hemoglobin observed in patients with T13 or PT13q (Sankaran et al., 2011). However, despite that our patient has three copies of this miRNA cluster, she does not display persistence of HbF. This is probably due to her older age, as the reported levels of HbF in T13 patients of 5 and 11 years of age is <1% (Redheendran et al., 1981).

The long survival in our patient may be associated with her chromosomal mosaicism, probably due to a selective advantage of the PT13q14 over the FT13 cell line and also due to lack of severe anomalies such as holoprosencephaly or detrimental cardiac defects (Fogu et al., 2008; Meyer et al., 2016; Pachajoa & Meza Escobar, 2013; Peeros et al., 2012; Wu et al., 2013). With the onset of puberty, our patient developed menstrual cycles, as described in several older T13 and MT13 female patients (Fogu et al., 2008; González del Ángel et al., 2014; Redheendran et al., 1981); however, these were irregular and she presented severe hyperpolymenorrhea.

The events that originate chromosomal mosaicism for a free trisomy are complex and may include a trisomic rescue or

a postzygotic non-disjunction. For a mosaic with a complete trisomy and a structurally abnormal chromosome 13, other processes such as chromoanagenesis, a term that comprises mechanisms such as chromothripsis, chromoanasythesis, and chromoplexy, might be involved. Chromothripsis refers to the localized shattering and reshuffling of one or a few chromosome segments during a one-step catastrophic event, with the incomplete repair of double-strand breaks through non-homologous end-joining; the implicated chromosomes can be confined into a micronucleus, hence the constrained nature of these alterations. Micronuclei formation can result from chromosome segregation failure, but can also be caused by a wide variety of stresses occurring during any stage of the cell cycle. These events can take place in germinal cells or preimplantation embryos, and occur more frequently than previously considered (Koltsova et al., 2019; Pellestor & Gatinous, 2020; Zepeda-Mendoza & Morton, 2019). In a free trisomy, a trisomic rescue can take place in order to obtain a balanced karyotype; a possible complication that may arise from this process is uniparental disomy, which may be particularly relevant if imprinted genes are located within the implicated regions (Jinawath et al., 2011). We propose that the mosaic in our patient originated from an FT13 zygote that underwent an atypical and failed trisomic rescue (Figure 1-I). It is possible that one chromosome 13 lagged in a micronucleus due to anaphasic delay, and following chromosome shattering, a chromothripsis event might have originated the loss of most of the chromosome 13q distal region, giving rise to the PT13q14 cell line. These cells prevailed over the FT13 cell line due to selective advantage, and this could ultimately explain the long survival of our patient, as well as her main clinical characteristics. Similar mechanisms have been described for several patients with T13 and different chromosomal rearrangements, such as translocations, rob(13;14), i(13q) and r(13), among others (Bertini et al., 2010; Chen et al., 2004; Fogu et al., 2008; Gentile et al., 1999; Jinawath et al., 2011; Reardon et al., 1981). Most of the FT13 are originated from maternal meiosis, in which reduced recombination and age effects increase non-disjunction events (Bugge et al., 2007; Hall et al., 2007); also, women with a previously affected pregnancy, may have a higher risk of aneuploidy, even under 35 years old (De Souza et al., 2009; Warburton et al., 2004). Genetic counseling was provided to our patient and her family, taking into account these considerations and the *de novo* nature of her chromosomal imbalance.

In conclusion, we present a 12-year-old Mexican female patient with a PT13q14 (82%) and T13 (18%) mosaic, displaying ID, dysmorphic features, pigmentary abnormalities, and hyperpolymenorrhea. We propose that her mosaicism derived from an FT13 zygote that underwent a failed trisomic rescue in which a chromothripsis event caused the loss of most of the 13q distal region, and that selective advantage of the PT13q14 cell line might explain her long survival.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

V.F.M.B. wrote the manuscript. V.F.M.B., A.C., and F.F.R. discussed the results and critically revised and edited the manuscript. V.F.M.B., M.R.R.V., and A.M.C. contributed to the acquisition and analysis of clinical data. A.C.M., A.C., and E.M.C. performed karyotyping and FISH analyses. L.E.C.O. and F.F.R. performed the microarray experiments and data analysis.


DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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