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Constitutional Chromosomal Translocations at the Cytogenetics Laboratory in Cotonou: A Report on 16 Cases

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Abstract

Chromosomal translocations are structural chromosomal abnormalities resulting from the exchange of genetic material between at least two chromosomes. They are associated with various phenotypes depending on the mechanisms of occurrence and the chromosomes involved. We conducted a retrospective study from May 2016 to April 2024 to assess the prevalence and characteristics of chromosomal translocations in the local population. Chromosomal translocations were identified in 1.74% of karyotypes. The phenotypes associated included facial dysmorphisms, recurrent miscarriages, and spermatogenesis disorders. This study highlights the need for early cytogenetic diagnosis to ensure optimal management of patients with these anomalies. However, further studies incorporating high-resolution molecular analyses are necessary to deepen our understanding of the underlying genetic mechanisms and the clinical implications of chromosomal translocations in the Beninese population.

Keywords

Robertsonian Translocations, Reciprocal Translocations, Various Phenotype, Benin

1. Introduction

Chromosomal translocations are structural anomalies of chromosomes that result from the exchange of genetic material between two chromosomes. These translocations can impact differently the individual's phenotype, depending on several

factors, such as the type of translocation, the chromosomes involved, the size of the segments, the genes affected, the presence or absence of genetic material loss (balanced or unbalanced), and the mode of transmission (de novo or hereditary). Reciprocal and Robertsonian translocations are the two most common types and they differ in their mechanisms of occurrence and their significant impact on the carriers' phenotype. Chromosomal breakpoints may disrupt essential genes or interfere with their regulation, potentially leading to development of anomalies or predispositions to certain diseases [1]. These chromosomal rearrangements, whether reciprocal or Robertsonian, balanced or unbalanced, often result from DNA breaks followed by erroneous repair mechanisms, which can lead to genetic imbalances responsible for a wide range of pathologies, including cancers and genetic disorders [2]-[4].

Although these rearrangements can occur between homologous chromosomes, they are most often identified between non-homologous chromosomes [5]. Their prevalence, estimated at 1.67% in hospital cohorts, is significantly higher in specific populations, such as women experiencing recurrent miscarriages or infertile men [6]. Recent studies conducted in the Arab-African world have highlighted chromosomal rearrangements specific to this geographic region and their health consequences [7].

However, these chromosomal anomalies remain poorly documented in Sub-Saharan Africa, particularly in Benin. It is therefore important to better characterize chromosomal translocations in laboratory within the Beninese population and, if possible, establish genotype-phenotype correlations associated with these translocations.

2. Material and Methods

It was a retrospective study including cases of constitutional translocation at the Cytogenetics Laboratory of Cotonou from May 2016 to April 2024. The data were collected in the laboratory's registers. As they were routine patients, written approval was not obtained from the ethical committee of the Faculty of Health Science of Cotonou. The study population includes all the patients admitted to the laboratory during the study period. The karyotype was performed in a G band. The culture tubes were incubated for 72 hours at 37˚C, CO_2 5%. The culture was stopped at the 70th hour by adding 50 µl of colcemide (SigmaR). Hypotonic treatment of the cells with KCl (0.075 M) followed by fixation in ethanol/glacial acetic acid (3:1 vol; vol). A concentrated suspension of cells was placed on slides and dried, for 25 minutes. The chromosomes were obtained by digestion in a trypsin bath and stained using 2% Giemsa solution. They were then dried and examined under the microscope using the programmed image analyzer (Cytovision 7.3.1). The metaphases were captured using a microscope and interpreted in accordance with the international system of Human Cytogenetic Nomenclature (ISCN). The data, collected from a dedicated registry, were subjected to descriptive statistical analysis using Excel and Epi Info version

7.2.6.0. The variables studied included age, sex, the reason for prescription or indication, and the chromosomal formula.

3. Results

Of the 918 karyotypes performed during the study period, sixteen (1.74%) translocations were identified, including 14 Robertsonian translocations (87.5%) and 2 reciprocal translocations (12.5%). Table 1 illustrates the socio-epidemiological, clinical, and cytogenetic characteristics of the 16 patients in our study. These translocations were primarily associated with facial dysmorphia suggestive of trisomy 21 (11/16; 68.75%), followed by recurrent miscarriages (2/16; 12.5%), spermatogenesis disorders (2/16; 12.5%), and sexual development anomaly (1/16; 6.25%). Both males and females were affected, with a sex ratio of 1.28, and more than half (9/16; 56.5%) of the patients were under 2 years old. The age distribution of patients with Robertsonian translocations (rob) is represented in Figure 1.

Table 1. Table type styles (table caption is indispensable).

No.	Age	Sexe	Indication	Chromosomal formula
01	20 days	M	Suspicion T21	46, XY, der(14;21)(q11;q10) + 21
02	5 months	F	facial dysmorphism	46, XX, der(14;21)(q10;q10) + 21
03	2 years 7 months	M	Suspicion T21	46, XY, i(21)(q10)
04	2 months	F	Suspicion T21	46, XX, i(21)(q10)
05	3 years	M	facial dysmorphism	46, XY, i(21)(q11.1)
06	26 years	M	Teratozoospermia	46, XY, t(2;15)(p25.3;q22.3q26.3)
07	50 years	M	Teratozoospermia	46, XY, t(2;5)(q37.3;q35.3)
08	3 years	M	Suspicion T21	46, XY, i(21)(q10)
09	9 years	F	Suspicion T21	46, XY, i(21)(q10)
10	37 years	F	Recurrent miscarriages	45, XX, der(13;14)(q11.2;11.2)
11	4 months	F	Suspicion T21	46, XX, i(21)(q11.1)
12	1 months	F	Suspicion T21	46, XX, i(21)(q10)
13	35 years	F	Recurrent miscarriages	45, XX, der(13;13)(q13.2;q11.2)
14	2 months	F	Sexual ambigity	46, XX, der(14;21)(q11.1;q11.1)+21
15	2 months	M	Facial dysmorphism and syndactyly	46, XY, der(14;21)(q11.1;q11.1)+21
16	5 days	M	Suspicion T21	46, XY, i(21)(q11.1)

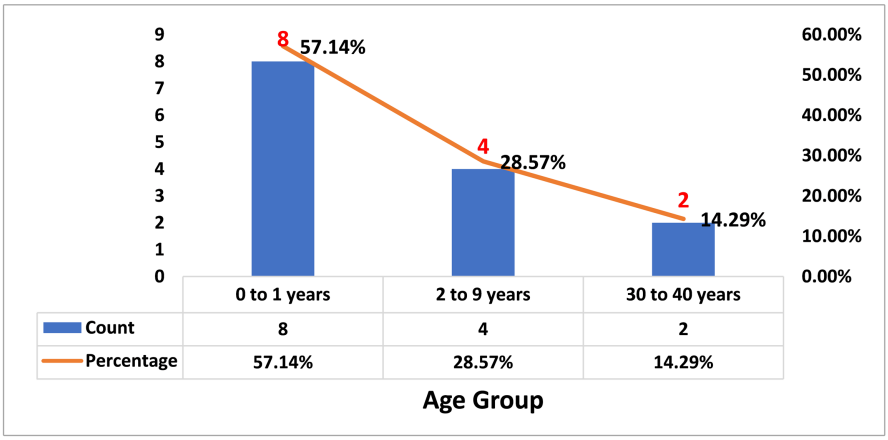

Figure 1. Distribution of patients with Robertsonian translocation according to age group.

Among the 14 patients with Robertsonian translocations, 8 (57.14%) were children aged 5 days to 5 months, while 4 (28.57%) were between 2 and 5 months old. Two carriers (14.3%) of Robertsonian translocations were adults aged 35 and 37 years. The two patients with reciprocal translocations were 26 and 50 years old, respectively. In total, children accounted for 75% of all patients with chromosomal translocations observed in karyotypes, while adults represented 25% of the study population. Figures 2 to Figures 7 display the chromosomal configurations of some patients with these translocations.

4. Discussion

Chromosomal anomalies involving changes in the number or structure of chromosomes can be either constitutional (present at birth) or acquired. Constitutional anomalies arise during gametogenesis or embryonic development. They are common in human pathology and can cause reproductive disorders (miscarriages, hypo- or infertility), congenital malformations with or without intellectual disabilities, and/or behavioral disorders. Acquired chromosomal anomalies, on the other

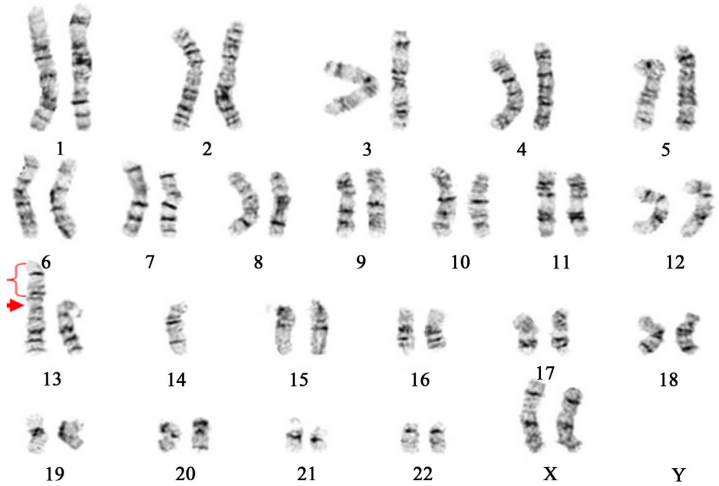

Figure 2. Female karyotype with a structural abnormality: 45, XX, der(13;14)(p13;p13).

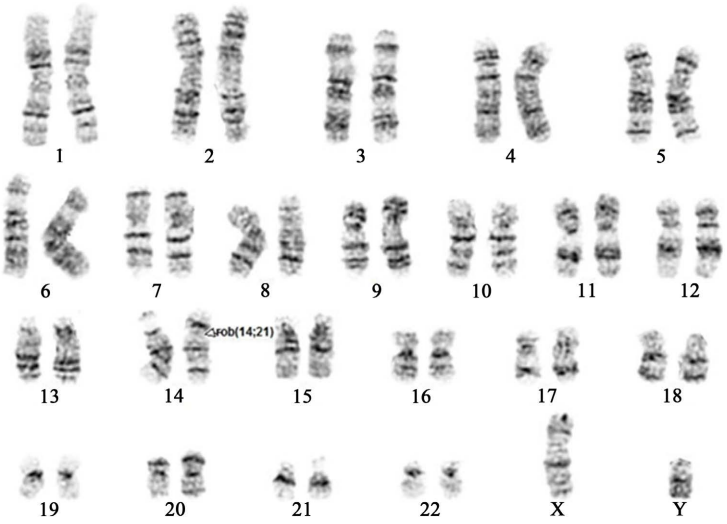

Figure 3. Male karyotype with a Robertsonian translocation, 46, XY, der(14;21)(p11.1;p11.1).

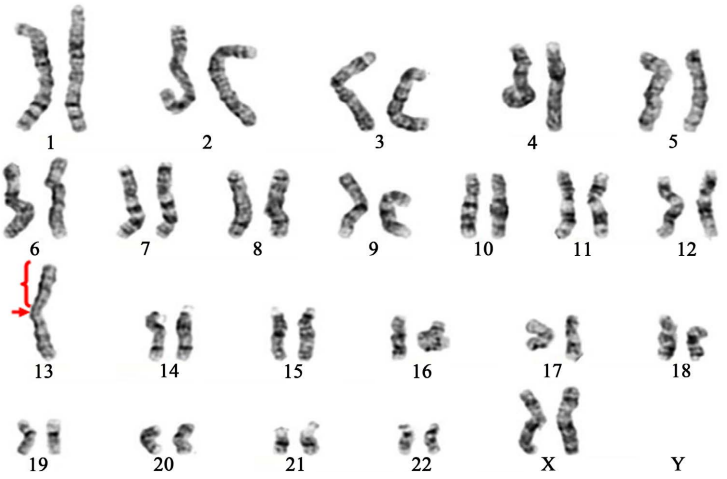

Figure 4. Female karyotype with a Robertsonian translocation 45, XX, der(13;13)(q11.2;q11.2).

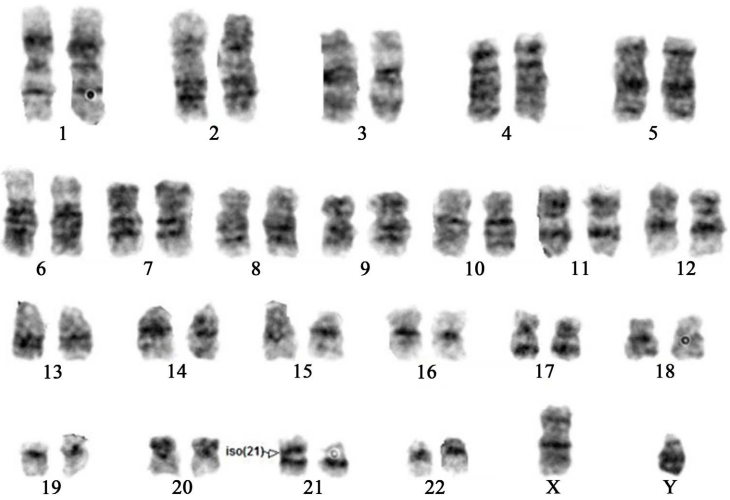

Figure 5. Male karyotype with trisomy 21 involving an isochromosome of chromosome 21:46, XY, i(21)(q11.1).

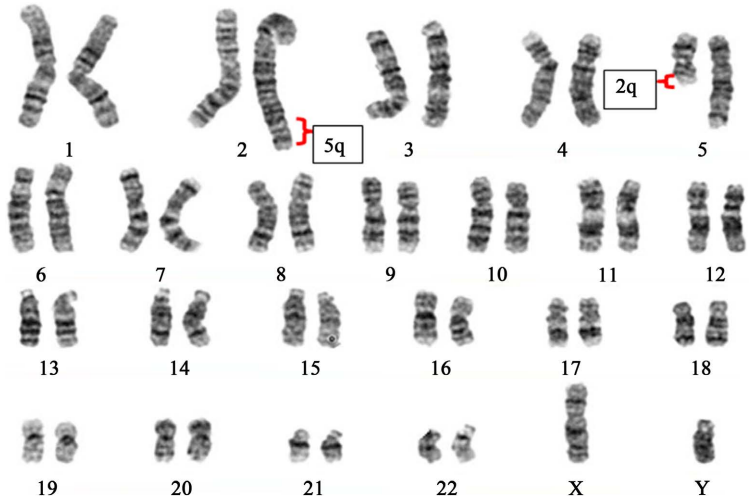

Figure 6. Male karyotype with a reciprocal translocation between chromosomes 2 and 5: 46, XY, t(2;5)(q37.3;q14q35.3).

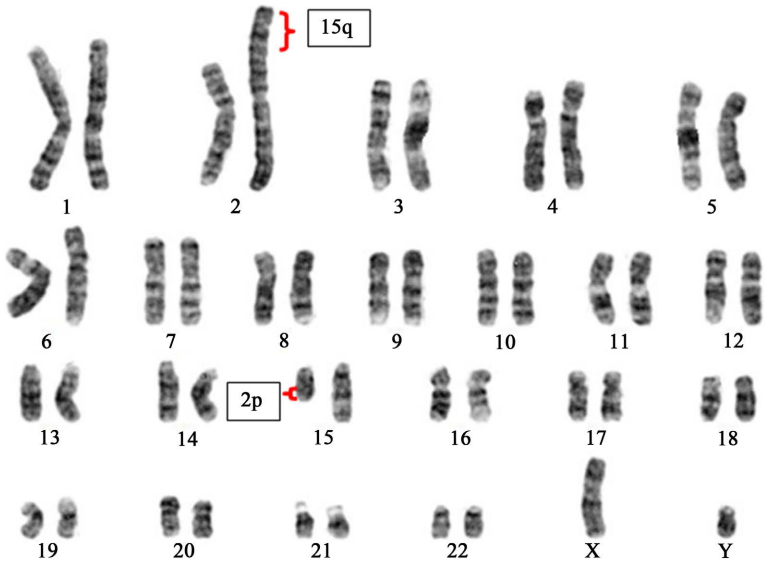

Figure 7. Male karyotype with a reciprocal translocation between chromosomes 2 and 15: 46, XY, t(2;15)(p25.3;q22.3q26.3).

hand, develop within a cell during an individual's lifetime and are primarily implicated in tumorigenesis and the development of cancerous diseases. Acquired chromosomal translocations are not addressed in this study. Chromosomal anomalies can affect any chromosome and are categorized as balanced (no loss or gain of genetic material) or unbalanced (loss or gain of genetic material).

In our study, the prevalence of chromosomal translocations in the laboratory was 1.75%, with Robertsonian translocations (rob) being the most prevalent (87.5%). These findings align with previous studies, emphasizing the significance of these chromosomal rearrangements [6] [8].

The spatial proximity of chromosomes within the nucleus, combined with homologous or pseudo-homologous DNA sequences rich in repetitive elements,

creates a conducive environment for genetic recombination events, leading to the emergence of Robertsonian translocations [9] [10]. Moreover, we observed a high prevalence of unbalanced chromosomal translocations, consistent with existing literature [6]. Both balanced and unbalanced chromosomal anomalies significantly impact fertility and embryonic development, leading to a wide range of severe phenotypes [6]. This observation is particularly evident in the high frequency of trisomy 21 (68.75%) resulting from chromosomal rearrangements in our cohort, especially among individuals under 10 years old. These results align with literature reporting a high frequency of chromosomal derivatives involving chromosomes 21, 13, and 14, often associated with fertility issues and congenital malformations [8] [11]. Chromosomal rearrangements involving the long arm of chromosome 21(21q) are mainly present as isochromosome 21q and, less frequently, Robertsonian translocation 21q;21q [12]. Differentiating between these anomalies requires high-resolution molecular cytogenetic techniques [13].

Additionally, our study identified two cases of balanced reciprocal translocations involving chromosomes 2, 5, and 15 in patients with spermatogenesis disorders. These findings align with reports associating reciprocal translocations with diverse phenotypes depending on the genes involved [7]. Male carriers of translocations produce a significant proportion of spermatozoa with unbalanced translocation combinations, posing varying levels of risk for imbalances in their offspring [14]. Furthermore, the percentage of sperm DNA fragmentation is higher in male translocation carriers.

While notable for its substantial cohort and comprehensive analysis of Robertsonian translocations, this retrospective study has some limitations, including a broad phenotypic spectrum. Retrospective cohort selection could introduce selection biases that could potentially influence the results. Additionally, the absence of detailed molecular analysis is a significant limitation, restricting the scope of conclusions. Despite these caveats, this study contributes to the literature by highlighting the importance of chromosomal translocations in human pathology.

5. Conclusion

This study establishes the central role of chromosomal translocations in the development of various human pathologies, underscoring the critical need for early and accurate cytogenetic diagnosis. Such diagnosis would not only guide patients toward personalized genetic counseling but also facilitate the implementation of tailored therapeutic strategies. However, while these results are promising, further investigations are essential to consolidate these findings and uncover the genetic mechanisms underlying these chromosomal anomalies. Future studies on larger patient cohorts, incorporating high-resolution molecular analyses such as FISH and CGH-array, would significantly advance this field.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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