Cytogenetic characterization of Philadelphia chromosome variants identified in a mexican mestizo population

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Introduction

Philadelphia (Ph) chromosome is the derivative chromosome 22 of the translocation t(9;22)(q34.1;q11.2). Its presence is **pathognomonic** for chronic myeloid leukemia (**CML**). Ph translocation variant (vPh) **involves ≥1 chromosome** in addition to chromosomes 9 and 22.

Aim

Characterize the chromosome **breakpoints** of Ph translocation variant identified in a Mexican mestizo CML population.

Objectives

Because our main objective is to describe a situation or phenomenon, rather than to test causal relationships then it **do not require explicit or specific** hypotheses.

Summary

On this analysis, the distribution of the breakpoints exhibited a clearly **nonrandom pattern** in all chromosomes involved, several studies suggest that these regions may be particularly prone to breakage. Two different mechanisms are known to generate vPh: a **one-step mechanism** in which chromosomal breaks **occur simultaneously** and a **two-step mechanism** involving **two sequential translocations**. The effect of vPh on prognosis is unclear, but may further classify CML in specific subsets requiring different therapeutic approaches.

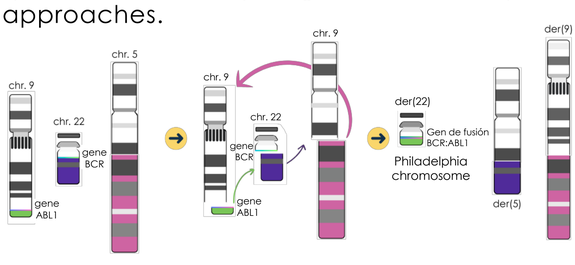


Figure 1. Schema of one-step mechanism. An example proposed for the t(5;9;22)(q15;q34;q11.2)

Methods

Descriptive and retrospective study. A total of 29 cases were selected based on karyotype analysis that showed vPh associated with CML clinical diagnosis. The samples were collected from peripheral blood and/or bone marrow. Karyotypes were obtained from cell cultures without mitotic stimulant and analyzed through GTG banding technique. All the samples were referred to Mendel Laboratories from institutions all over Mexico between 2018 and 2024.

Results

Data indicated that 18 (**62%**) cases showed the vPh as the **sole abnormality**. Furthermore, five cases (**17%**) were classified as **complex karyotypes**, including two or more abnormalities in addition to the vPh **(figure 1).** Otherwise, it was observed that the most frequently implicated **breakpoint** in vPh was **11q13** (three cases) followed by **1p36.2** and **5p15.1**, both present in two cases. Based on karyotypes, we found nine cases with clonal evolution and eleven with divergence.

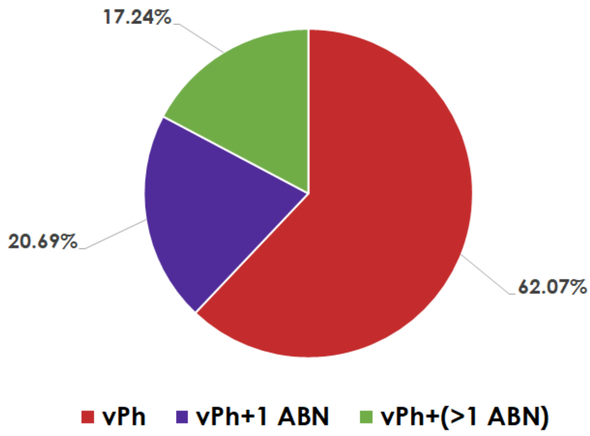
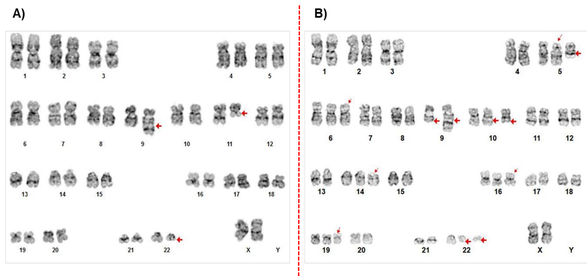


Figure 2. Distribution of Ph translocation variant and additional cytogenetic abnormalities in cases with chronic myeloid leukemia



46,XX,t(9;22;11)(q34.1;q11.2;q12)[15]/47,XX,t(9;22;11)(q34.1;q11.2;q12),+der(22)t(9;22)(q34.1;q11.2)[5]

53,XX,+5,t(5;9;22)(q15;q34.1;q11.2),+6,add(9)(q34.1),add(10)(q22),+del(10)(q23),+14,+16,+19,+der(22)t(9;22)(q34.1;q11.2)[10]/46,XX[8]

Figure 3. Karyotype with Ph translocation variant **A)** as a single abnormality and **B)** with complex karytype

Discussion

Additional cytogenetic abnormalities (ACAs) represent **38%** of the vPh cases distributed in all age groups. Among the complex karyotype, three cases were found with ACAs associated with the **major pathway**: **double Ph** (+der(22)t(9;22))and **trisomy 8** associated with poor prognosis. A wide range of studies will need to be performed to establish a **meaningful correlation** between vPh and their timing of onset, as well as, their effect on the course of the disease.

References

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3. A Unique Three-Way Variant Philadelphia Chromosome t(6;9;22)(p21.3;q34;q11.2) in a Newly Diagnosed Patient with Chronic Myeloid Leukemia Responded to Flumatinib, *OncoTargets and Ther*

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