Correlation between peripheral cytopenias and cytogenetic changes in the bone marrow in a paediatric population. Experience of 22 years.

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1. Introduction

The hemogram is the most requested study and an essential tool in the diagnosis of different pathologies in pediatric age, especially in hematological diseases.

Peripheral cytopenias are the first laboratory finding suggestive of a hematological disease, such as myelodysplastic syndrome, idiopathic thrombocytopenic purpura, among others. Confirmation of these pathologies should include the study of bone marrow, with analysis of this by different methodologies, including conventional cytogenetic karyotype analysis.

2. Objective

In this work, we intend to present and establish a correlation between the results obtained by conventional cytogenetics in bone marrow samples and observation of peripheral cytopenias in a paediatric population over 22 years.

3. Methods

A retrospective 22-year series (1995-2017) of 154 bone marrow samples from a paediatric population was analysed, which at the initial diagnosis presented peripheral cytopenia. The samples were process according to the established protocol for chromosome analysis in bone marrow, including cell culture, for each biological product, followed by a cytogenetic study to identify the karyotype.

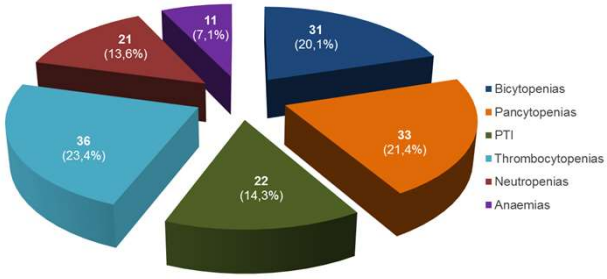

Fig. 1: Distribution of samples according to the different cytopenias diagnosed.

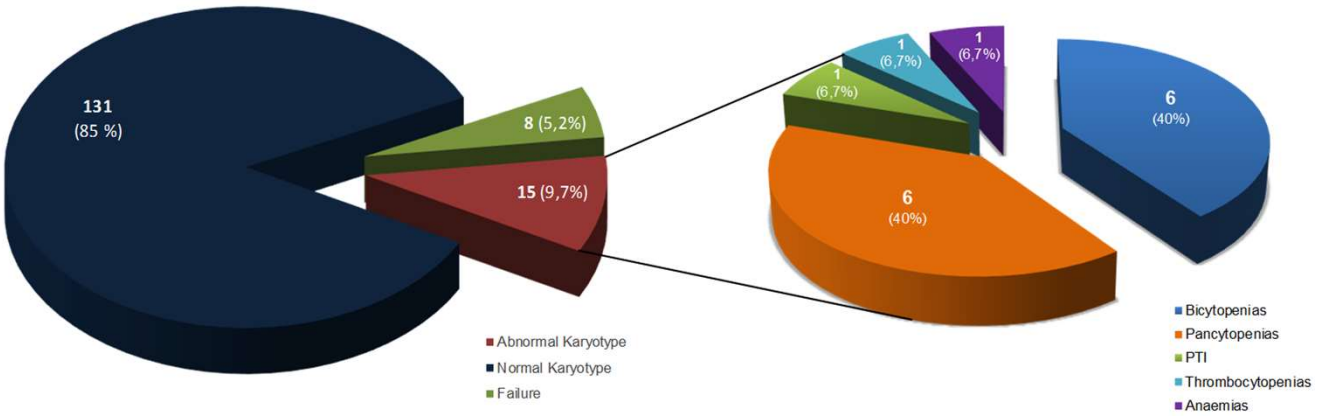

Fig. 2: Number of abnormal karyotypes obtained from 154 analysed bone marrow samples vs peripheral cytopenias.

4. Results

- In the 154 cytopenias analysed, it was verified (**Fig. 1**):
  - ✓ The mean age at diagnosis = 7 years and 6 months
  - ✓ 53% of sex F and 47% of sex M
  - ✓ 33 pancytopenia (21,4%),
  - ✓ 31 bicytopenias (20,1%),
  - ✓ 21 neutropenia (13,6%),
  - ✓ 11 anemias (7,1%) and
  - ✓ 58 thrombocytopenia (37,7%) [22 (14,3%) of idiopathic origin].

- In the 154 samples analysed with peripheral cytopenias, 15 samples with abnormal karyotype were identified (**Fig. 2** and **Table 1**), some of which presented a complex karyotype.

2 and **Table 1**).

5. Conclusion

In this population, most samples with cytopenia/(s) have a normal karyotype, suggesting that they may not result from a malignant haematological disease, but from a transient situation resulting from a viral or bacterial infection, or the genetic alteration responsible for the disease, is not observed by classical cytogenetics.

Peripheral cytopenias are extremely important for the suspicion of pediatric hematological diseases, especially in the myelodysplastic syndrome.

The analysis of the bone marrow by conventional cytogenetics plays a fundamental role in the diagnosis and confirmation of these pathologies, in the clinical and prognostic evolution of the same, allowing the establishment of risk groups, which allows the choice of an appropriate therapy.

However, micro-arrays should be performed with the aim of identifying micro-deletions / duplications or loss of heterozygosity that are characteristic in this group of pathologies.

Tab. 1: Abnormal karyotypes obtained from the 154 bone marrow samples analysed.

Cytop.	Sample	Abnormal Karyotype	Diagnostic Hypothesis
Pancytopenia	I	46,XY,t(15;17)(q22;q21)[29]/46,XY[1]	Acute Promyelocytic Leukemia (PML/RARA)[1,2]
	II	43~45,XX,der(5;17)(p10;q10),-6, der(7)t(2;7)(q13;p22)[cp30]	Myeloid Neoplasms [(MDS (?) vs AML (?)][3]
	III	46,XY,del(4)(q21)[2]/46,XY,del(7)(q22)[2]/46,XY,del(7)(q11.2)[2]/46,XY,der(7)(del(p15)del(7)(q22)[2]/46,XY,del(2)(p11),del(7)(q11.2)[3]/46,XY[19]	MDS(?)[2,8] and AML (?)[2,8] ou decifit of B12 vitamin and folic acid(?)[4]
	IV	47,XX,+8[20]/46,XX[10]	MDS(?) vs AML (?)[2,5]
	V	46,XX,del(5)(q15q31),t(15;17)(q22;q21)[21]/46,XX[9]	Acute Promyelocytic Leukemia (PML/RARA)[1,2]
	VI	47,XXY[15]/46,XY[35]	↑risk of systemic lupus erythematosus (?)[6,7]
	VII	[illegible]5]/50,i[illegible],XY[2]	MDS(?) vs AML (?)[9,10,11]
Bicytopenias	VIII	46,XX/tetraploidy/octoploidy	Megakaryocytic Leukemia(?)[12]
	IX	47,XY,+21c[30]	Down Syndrome→ autoimmune diseases (immunodeficiency)[13]
	X	47,XY,i(18)(p10)c[30]	Infection (?)
	XI	46,XY,del(10)(p11.1p11.2)[7]/46,XY[23]	Congenital Monoblastic Leukemia (?)[14]
	XII	47,XY,+mar[19].ish der(22)(wcp22+,D14Z1/D22Z1+)/46,XY[11]	MDS(?)
PTI	XIII	47,XY,+21c[30]	Down Syndrome→ autoimmune diseases (immunodeficiency)[13]
Tromb.	XIV	Hipodiploidia	ALL(?) [15]
Anemia	XV	47,XY,+21c[30]	Down Syndrome→medullar insufficiency or anemia after infectious intercurrence.[13]

6. Bibliography
1.Swerdlow S. *et al.*, (2008).IARC Lyon.
2.Creutzig, U. *et al.*, (2016) "Cancer: 1-10.
3.Hong M. *et al.*, (2016) Cancer Genet 209(5):205-14.
4.Wollman MR1, Penchansky L, Shekhter-Levin S J Pediatr Hematol Oncol. 1996 May;18(2):162-5.
5.Huret, JL. Atlas Genet Cytogenet Oncol Haematol. 1999;3(1):28-29.
6.Alvarez, A. et al., (1994) Acta Médica Portuguesa, 7:35-38.
7.https://ghr.nlm.nih.gov/condition/klinefelter-syndrome
8.Desangles, F., Atlas Genet Cytogenet Oncol Haematol. 1999;3(3):141-143.
9.Ma, ESK ; Wan, TSK., Atlas Genet Cytogenet Oncol Haematol. 2003;7(3):185-185.
10.Viguié, F, Atlas Genet Cytogenet Oncol Haematol. 2001;5(4):294-295.
11.Huret, JL, Atlas Genet Cytogenet Oncol Haematol. 2000;4(1):19-19.
12.Renner D. Queisser W.Q. (1988) "Acta Haematol 1988;80:74–78.
13. Hingh, Y. C. M The Journal of Pediatrics 147 (6): 744–747.
14. Seo, IS (1986) American Journal of Pediatric Hematology/Oncology 8(2):158-62.
15. Farias M. Et al., J. Bras. Patol. Med. Lab. 2004, 40(2): 91-98