RETROSPECTIVE CLINICAL STUDY ON THE INCIDENCE OF ACUTE LEUKEMIA IN HEMATOLOGICAL MALIGNANCIES AND THEIR IMPLICATIONS ON MOUTH TISSUES

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Abstract:

Hematologic disorders in general and hematological malignancies in particular constitute clinical entities with great impact on tissues of the oral cavity.

Objectives: *To distinguish the main general and oral hemorrhagiparous events and their correlation with the results of the laboratory tests.*

Material and method: *The study was conducted on a group of 289 patients with hematological malignancies hospitalized and treated in the Medical Clinic I, Department of Hematology, in the period August 2013 - July 2016.*

Results: *The most frequent bleeding events are met in acute myeloid leukemia, both systemic and oral, the latter presenting the most various forms, from gingival hemorrhage, with a percentage of 32,19% (basically the most frequent events, both systemic and general), to oral purpura (4,79%), petechia on mouth mucosa (5,47%).*

Discussions: *Dentistry and literature data show the role of the dentist in the detection, referral to a hematological consultation and indication of the use of special prophylaxis means. Thus, in patients with gingival bleeding, rigorous oral hygiene is recommended to prevent infections more frequent and severe in patients with leukemia.*

Conclusions: *It is important for the dental practician to know these manifestations because they can modify the steps in the treatment of a pacient.*

Key words: Acute leukemia, mouth, bleeding, lesions.

Introduction

Hematologic disorders in general and hematological malignancies in particular constitute clinical entities with great impact on tissues of the oral cavity, both by the changes caused by the disease itself and by those arising from specific treatments of these diseases, chemotherapy and radiation therapy[1].

The injuries occurred in the oral cavity and cervical facial areas may be reported by the dentist at a thorough clinical examination, and in a medical history properly managed, one may highlight the patient's possible clinical record[2]. Thus, even from this phase, one may shape the premises for an early diagnosis of hematological disease[3], an interdisciplinary collaboration

and a correct treatment in the early stages may be started, on the one hand, and the avoidance of bleeding or infection accidents through inadequate dental treatments, on the other hand.

In the context of this study, the most common local oral - dental injuries and the most serious hemorrhagic and infectious accidents were reported in patients with various forms of acute leukemia.

Objectives:

To distinguish the main general and oral hemorrhagiparous events and their correlation with the results of the laboratory tests.

Material and method

The study was conducted on a group of 289 patients with hematological malignancies hospitalized and treated in the Medical Clinic I, Department of Hematology, in the period August 2013 - July 2016. From this group, we selected the patients with acute myeloid leukemia and acute lymphoblastic leukemia, who, in terms of relative importance within our study, do not represent the largest group but have the highest frequency of hemorrhagiparous lesions, both local and general.

The patients were grouped according to sex, age andorigin.

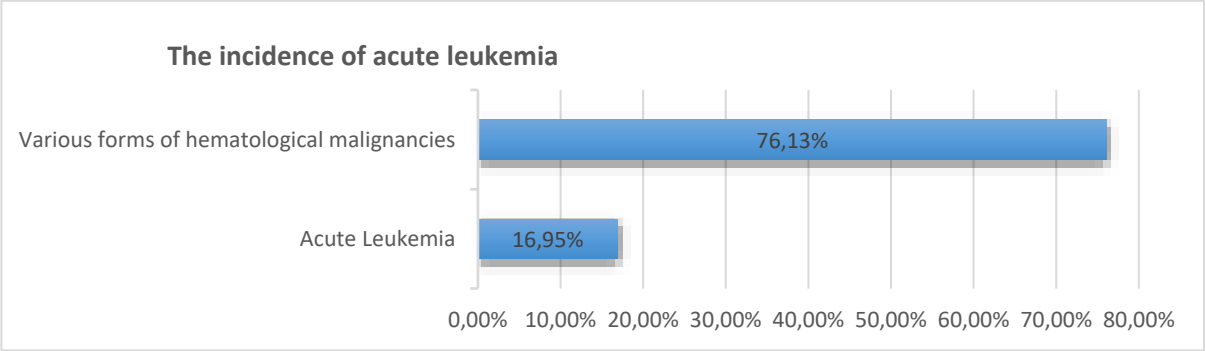
Several parameters were monitored in the clinical observation sheets:

- personal information
- histological diagnosis
- clinical examination showing hemorrhagic lesions in the mouth, as well as the general ones

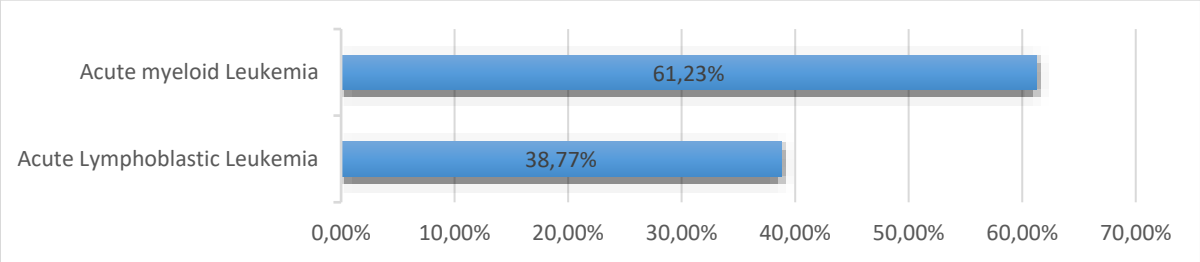
- paraclinical investigations specific to hemostasis disorders:
  - Rumpel Leed test
- laboratory examinations
  - Howell clotting time (N 70-140sec)
  - fibrinogenemia (N 200-400mg / dl)
  - no. of platelets (N 150000-300000 / mm3)
  - prothrombin time (N 11-15sec)
  - thrombin time (N 15-15sec)
  - reptilase time (N 15-15sec)
  - activated partial thromboplastin time (APTT N <40sec)
  - euglobulin clot lysis time (ECLT N men 180 sec, N women 150 sec)
  - immunological dosage (D-dimers N <215 mg / ml)
  - Tr platelet count/μl
  - CE+ C Disruption of coagulation through the involvement of the factors of extrinsic pathway and Involvement common pathway
  - Ci Disruption of clotting through the involvement of the factors of intrinsic pathway
  - Disfbg Dysfibrinogenemia
  - Fbg Fibrinogenemia below <150 mg%
  - Vasc reduced vascular resistance
  - CIDa acute disseminated intravascular clotting
  - CIDc compensated intravascular coagulation

Results

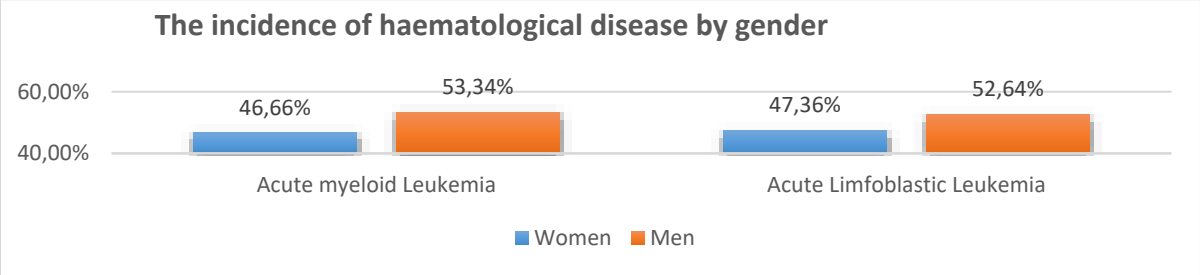
Out of the total of 289 patients with hematological malignancies, 49 cases presented various forms of acute leukemia, representing 16.95%.



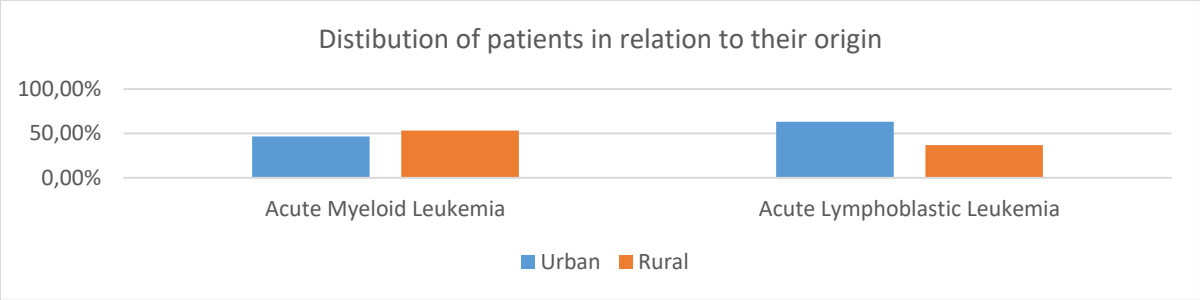
Out of the total of 49 patients with acute leukemia, there were 30 cases of acute myeloid leukemia, representing 61.23% and 19 cases of acute lymphoblastic leukemia, representing 38,77



The distribution by sex is presented as follows: of 30 cases of acute myeloid leukemia, 14 subjects (46.66%) were women and 16 men (53,34%), and of the 19 subjects with acute lymphoblastic leukemia, 9 were women (47,36%) and 10 were men (52,64%), finding an almost equal distribution.



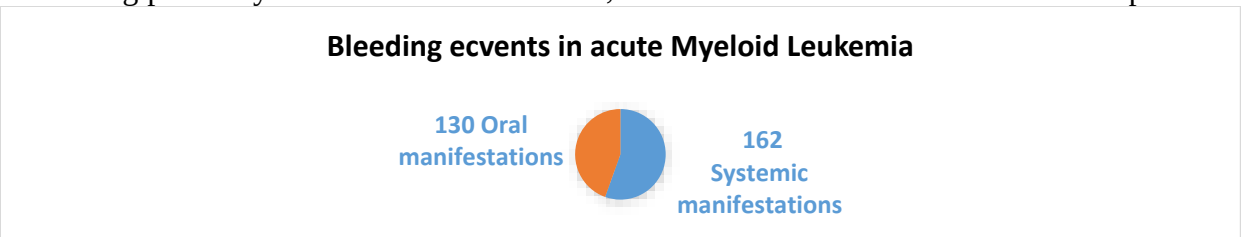
Within the distribution of patients in relation to their origin, there were not great differences in the case of acute myeloid leukemia patients - 14 patients originated in the urban environment (46,66%) and 16 patients from rural areas (53,34%), but in the case of acute lymphoblastic leukemia, the larger share was represented by the patients from urban area, 12, (63,15%), compared to 7 patients from the rural area (36,85%).

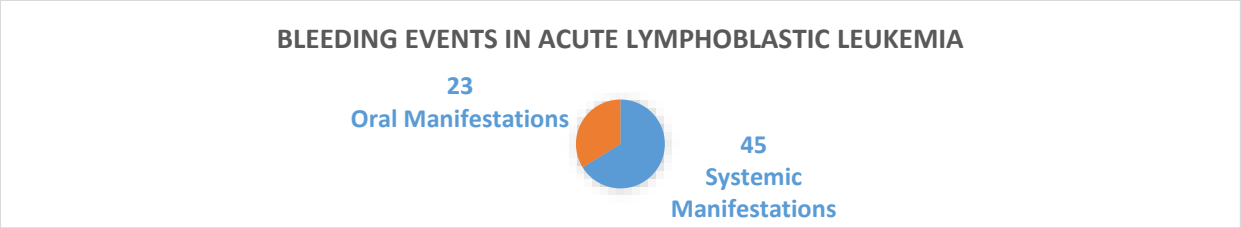


Major bleeding events noticed in patients with acute leukemia.

Crt. No.	Systemic Hemorrhagiparous Syndrome	Patients*			
		Acute Myeloid Leukemia		Acute Lymphoblastic Leukemia	
		Number	Percentage %	Number	Percentage %
Systemic Manifestations					
1	Cutaneous Purpura	20	6,84%	2	2,94%
2	Superficial hematoma bruising	56	19,17%	9	13,23%
3	Deep hematoma	8	2,73%	7	10,29%
4	Epistaxis	28	9,58%	9	13,23%
5	Hematuria	20	6,84%	11	16,17%
6	Hemoptysis	12	4,1%	5	7,35%
7	Digestive hemorrhage	10	3,42%	-	-
8	Brain hemorrhage	8	2,73%	2	2,94%
Oral manifestations					
9	Gingival hemorrhage	94	32,19%	14	20,58%
10	Purpura on mouth mucosa	14	4,79%	-	-
11	Oozing hemorrhage	4	1,36%	-	-
12	Oral Hematoma	2	0,68%	-	-
13	Petechia on mouth mucosa	16	5,47%	9	13,23%
	Total	**292**		**68**	

* Please note that due to the prolonged evolution of the disease and repeated hospitalizations for treatment or intercurrent disorders of the same patient, polymorphic aspects of the hemorrhagiparous syndrome have been noticed, in simultaneous and / or successive relapses.

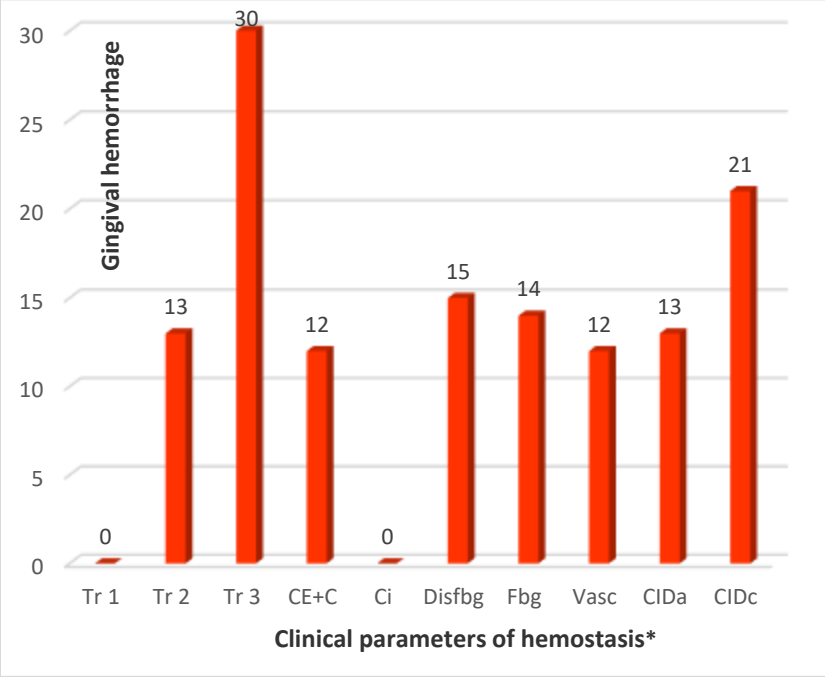




The analysis of the data presented above shows that the most frequent bleeding events are met in acute myeloid leukemia, both systemic and oral, the latter presenting the most various forms, from gingival hemorrhage, with a percentage of 32,19% (basically the most frequent events, both systemic and general), to oral purpura (4,79%), petechia on mouth mucosa (5,47%).

The correlation between the various oral hemorrhagiparous events and the changes in the clinical parameters of hemostasis in patients with acute leukemia.

In gingival hemorrhage, the correlation between these parameters and the clinical manifestation is represented in the chart below



***Legend**

Tr = platelet count/μl
Tr 1= Tr > 100.000/μl
Tr 2= Tr between 50.000 - 100.000/μl
Tr 3 = Tr < 50.000 /μl
CE+ C = Disruption of coagulation through the involvement of the extrinsic pathway and common pathway factors
Ci = Disruption of clotting through the involvement of the factors of intrinsic pathway
Disfbg = Dysfibrinogenemia
Fbg = Fibrinogenemia below <150 mg%
Vasc = reduced vascular resistance
CIDa = acute disseminated intravascular clotting
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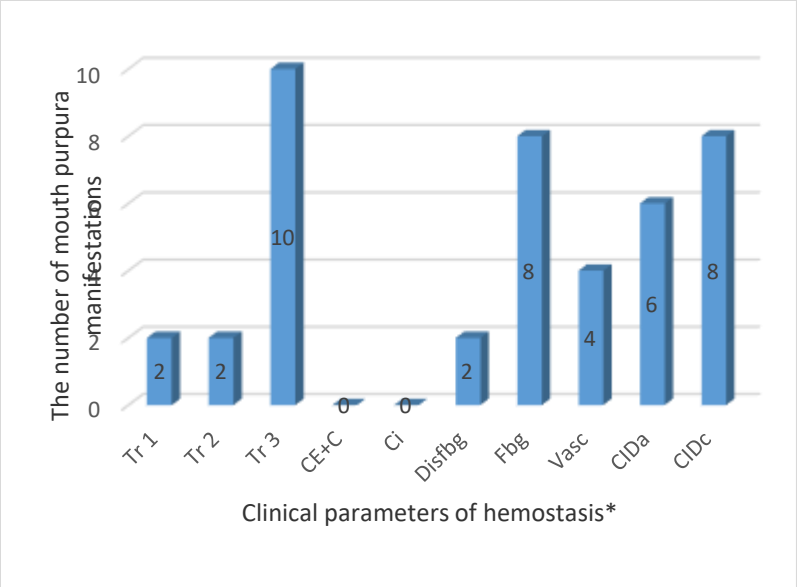
In patients with purpura in the mouth, the major paraclinical changes are as follows:



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Local hemorrhagiparous events like gingival bleeding and mouth purpura were correlated most frequently with the following paraclinical parameters:

- thrombocytopenia platelet count below 50,000
- fibrinogenemia
- dysfibrinogenemia
- disseminated intravascular clotting

Discussions

Knowing the hemorrhagiparous manifestations of the oral cavity present in acute myeloid or lymphoblastic leukemia is important having several aspects, of which, the management of these lesions applied by the dentist is particularly important.

Dentistry and literature data show the role of the dentist in the detection, referral to a hematological consultation and indication of the use of special prophylaxis means[5]. Thus, in patients with gingival bleeding, rigorous oral hygiene is recommended to prevent infections more frequent and severe in patients with leukemia. It is also recommended to use a soft toothbrush, mouthwashes with anti-fibrinolytic and antiseptic substances (chlorhexidine 0.12%)[5]. In more serious forms, in patients with ulcers caused by gum infections, it is recommended the coating with antibiotic solutions or even general administration of antibiotics[5].

Conclusions

Acute lymphoblastic and myeloid leukemia represent a low percentage of hematological malignancies but with a significant echo related to event at the level of oral - maxillary - facial area, which motivates the dentist to know these thoroughly, both for early diagnosis and to adapt the treatment of these patients[4].

References

1.Presant CA, Safdar SH, Cherrick H (1973). Gingival leukemic infiltration in chronic lymphocytic leukemia. *Oral Surgery, Oral Med, Oral Pathol*, **36**, 672-4.
2. Reenesh M, Munishwar S, Rath SK (2012). Generalised leukaemic gingival enlargement: a case report. *J Oral Maxillofac Res*,
3.Sepúlveda E, Brethauer U, Fernández E, et al (2012). Oral manifestations as first clinical sign of acute myeloid leukemia: report of a case. *Pediatric Dentistry*, **34**, 418-21.
4.Carolina F, Rogerio J, Lazara J, Cassia M, Paulo S, Leukemic Oral Manifestations and their Manifestations. *Asian Pacific Journal of Cancer Prevention, Vol 17, 2016*
5. Silva BA, Siqueira CR, Castro PH, et al (2012). Oral manifestations leading to the diagnosis of acute lymphoblastic leukemia in a young girl. *J Indian Soc Pedod Prev Dent*, **30**, 166-8.
6. Caroline Zimmermann, Maria Inês Meurer, Liliane Janete Grando, Joanita Ângela Gonzaga Del Moral, Inês Beatriz da Silva Rath, Silvia Schaefer Tavares, Dental Treatment in Patients with Leukemia, J Oncol. 2015; 2015: 571739