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Prevalence of Dacrocytosis in Patients with Chronic Diseases: Splenomegaly is not Mandatory for Teardrop Cells Genesis

Rojas-Maya S[1], Sarias-Cueto LA[1], Perez-Diaz I[2*], Osorio-Landa HK[3], Garcia-Martinez B[4], Fagundo-Sierra R[1], Rivera-Moscoso R[2], Carrillo-Maravilla E[2] and Laguna-Barcenas SC[5]

[1]*Biological and Pharmaceutical Chemistry Central Laboratory, National Institute of Medical Science and Nutrition Salvador Zubiran, Tlalpan, Mexico*

[2]*Medicine Department, National Institute of Medical Science and Nutrition Salvador Zubiran, Tlalpan, Mexico*

[3]*School of Medicine, Monterrey Institute of Technology and Higher Education, Mexico*

[4]*Biological and Pharmaceutical Chemistry, Metropolitan University, Mexico*

[5]*Autonomous University of Queretaro, Queretaro, Mexico*

[*]**Corresponding author:** Perez-Diaz I, PhD, MD, Medicine Department, National Institute of Medical Science and Nutrition Salvador Zubiran, Tlalpan, Mexico, Tel: + +52-54 87 09 00; E-mail: ivan.endocrino@gmail.com

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Abstract

Background: Dacrocytes or "teardrop cells" are elongated red blood cells at one end forming a cell with the appearance of a tear drop and are of varying size. Dacrocytes are frequently observed in complete blood counts of patients with myeloproliferative disease, but can also be found in other systemic diseases in which their prevalence and clinical significance remains unknown.

Objective: To evaluate the prevalence and possible clinical significance of dacrocytes observed in the peripheral blood smear of patients with different systemic diseases.

Methods: This is a descriptive study that analyzed the peripheral blood smears of 35,086 patients in a tertiary care hospital, in search of dacrocytes, and correlating this finding with their clinical and biochemical profiles.

Results: Dacrocytes were intentionally sought in 35,086 peripheral blood smears. The observed prevalence of dacrocytosis was 1.4% (n=492 patients). No statistically significant relationship was established between dacrocytosis and the patients' diagnoses, although there was a tendency to find dacrocytes in patients with cancer (CA) and systemic lupus erythematosus (SLE). Thus the presence of dacrocytes was not associated to the type of anemia or to the degree of renal dysfunction. Our results do not support the theory asserting that dacrocyte formation is a result of splenomegaly since only 28.5% of patients with this erythrocyte anomaly presented associated splenomegaly.

Conclusion: Dacrocytosis may be present, at a very low prevalence, in various systemic diseases. It is independent of the type of anemia and the degree of renal dysfunction. For the first time, splenomegaly is excluded as the only cause of dacrocytosis in peripheral blood smears.

Keywords: Dacrocyte; Systemic disease; Anemia; Renal dysfunction; Splenomegaly

Introduction

Dacrocytes or "teardrop cells" are elongated red blood cells at one end forming a cell with the appearance of a teardrop and are of varying size [1] (Figure 1).

These cells are most frequently observed in peripheral blood smears of patients with primary or secondary myelofibrosis with myeloid metaplasia, different types of anemia including iron deficiency, hemolytic, and megaloblastic anemia, as well as infiltrative disorders of the bone marrow such as leukaemia, lymphoma or metastatic solid neoplasms [2-4]. Furthermore, isolated reports have identified dacrocytes in patients with various systemic diseases associated to chronic renal dysfunction. However, information on the clinical implications of dacrocytosis in these systemic diseases has been practically non-existent and no study has evaluated its relationship with the presence of anemia and renal dysfunction. Whether the dacrocytosis in these patients is a result of concomitant splenomegaly, as it is believed nowadays, also remains unknown. The aim of this study was to determine the relationship between the prevalence of dacrocytosis and systemic diseases, and to correlate the presence of these teardrop cells with different types of anemia, renal dysfunction and splenomegaly in a tertiary care hospital.

Materials and Methods

This is a descriptive research study. Dacrocytes were sought in 35,086 peripheral blood smears of in-patients at a tertiary care hospital. Smears were obtained from the Hematology Laboratory between August and October 2013. The smears with identified dacrocytes were classified according to O'Connor's criteria [5], as normal (0-1 dacrocytes/field), mild (2-5/field), moderate (6-15/field) and severe (>15/field). The following information was obtained from

each patient's clinical chart: gender, age, serum glucose, blood ureic nitrogen (BUN), creatinine, hemoglobin, presence and degree of dacrocytosis, and diagnosis.

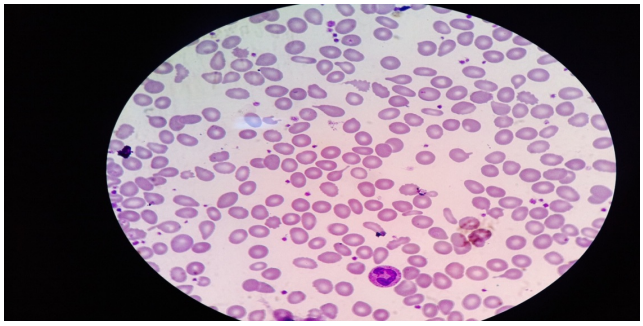

Figure 1: Peripheral blood smear in which true teardrop cells (dacrocytes) are pointed by black arrows.

The presence of anemia was established according to the hemoglobin concentration (<12 g/dL), and the red blood cell indices (mean corpuscular volume [MCV]: normal range 83.5 - 98 fL and mean corpuscular hemoglobin [MCH]: normal range 32.7-34.7 pg) and it was classified in: normocytic normochromic anemia (NNA), microcytic hypochromic anemia (MHA) and macrocytic normochromic anemia (MNA). We had access to the creatinine values of 368 patients, allowing us to calculate the estimated glomerular filtration rate (eGFR) with the MDRD formula (proposed by K/DOQI 2002).

The presence of splenomegaly was determined by reviewing the patients' imaging studies. A diagnosis of splenomegaly was considered only if this finding was clearly documented in the report of any of the following medical imaging of the abdominal area: computed tomography (CT), ultrasound (US), or magnetic nuclear resonance imaging (MRI). Patients with myeloproliferative syndromes were excluded from the present study since dacrocytosis is a frequent finding in this population.

Statistical Analysis

All results are expressed as averages ± SD (standard deviation) or percentages. The comparison among groups was established with the Kruskal-Wallis test. Meanwhile, correlations between variables were determined with the Pearson's or Spearman's correlation tests as appropriate. The statistical analysis was performed with the Stata version 11.1 statistical software program for Windows; p values of <0.05 were considered statistically significant.

Results

Among the 35,086 analyzed smears, dacrocytes were identified in 492 (1.4%), from which 310 (63%) belonged to females and 182 (36.9%) to males. The average patient age was 46.2 ± 17 years (range: 16 to 93 years).

By analyzing the patients' diseases (n=492), we observed that the most frequent diagnoses encompassed all forms of cancer in 103 (20.9%), followed by systemic lupus erythematosus (SLE) in 97 (19.7%), liver cirrhosis in 75 (15.2%) and type 1 and 2 diabetes mellitus (DM) in 37 (7.5%) patients. In terms of dacrocytosis' degree, our findings exposed that 423 (86%) patients had mild dacrocytosis and only a small proportion, 69 (14%), had moderate dacrocytosis. No cases of severe dacrocytosis were detected. As a result, the correlation of the dacrocytosis' degree and the patients' different diagnoses established no statistically significant difference (p=0.06) (Table 1).

Degree of Dacrocytosisϕ			
Diagnosis	Mild (%)	Moderate (%)	Severe (%)
Cancer	88 (17.9%)	15 (3.1%)	-
SLE	85 (17.3%)	12 (2.4%)	-
Liver cirrhosis	67 (13.6%)	8 (1.6%)	-
DM	32 (6.5%)	5 (1.0%)	-
The values are expressed in n (%). Percentages represent the proportion from the total of patients with dacrocytosis (n=492). ϕ There was no significant difference between groups (p= 0.06). SLE: Systemic lupus erythematosus. DM: Type 1 and 2 diabetes mellitus.			

Table 1: Principal diagnoses of patients and degree of dacrocytosis (n=492).

Interestingly, from all patients with dacrocytosis (n=492), 467 (95%) presented anemia (Hb: 10.3 ± 1.9 g/dL): MHA was the most common form of anemia in 193 (39.2%) patients, followed by NNA in 172 (35%) patients, and MNA was the least prevalent in 102 (20.7%) patients. Only 25 (5.1%) patients did not have anemia. In all the anemia groups, mild dacrocytosis was predominantly observed (87.5% in MHA; 87.2% in NNA, and 79.4% in MNA) (p=0.78) (Table 2).

Degree of Dacrocytosisϕ			
Type of anemia	Mild (%)	Moderate (%)	Severe (%)
MHA	169 (34.4%)	24 (4.9%)	-
NNA	150 (30.5%)	22 (4.5%)	-
MNA	81 (16.5%)	21 (4.3%)	-
N	23 (4.7%)	2 (0.4%)	-
The values are expressed in n (%). Percentages represent the proportion from the total of patients with dacrocytosis (n=492). ϕ There was no significant difference between groups (p=0.78). MHA: microcytic hypochromic anemia. NNA: normocytic normochromic anemia. MNA: macrocytic normochromic anemia. N: No anemia.			

Table 2: Type of anemia and degree of dacrocytosis (n=492)

To evaluate patients' renal function, serum creatinine values were obtained in 80.3% of the cases (n=395), from which 323 (85.4%) values were within the normal range (<1.3 mg/dL) and only 72 (14.6%) patients presented levels above reference values (≥1.3 mg/dL).

Estimation of the glomerular filtration rate (MDRD), revealed that: 51.7% of patients were K/DOQI 1, 24.6% K/DOQI 2, 14.2% K/DOQI3, 4.3% K/DOQI 4 and 5.3% were K/DOQI 5. No statistically significant linear relationship between the degree of dacrocytosis and renal dysfunction was found (rs=0.0136, p=0.2) (Table 3).

According to the imaging charts (n=491), only 140 (28.5%) patients presented splenomegaly, from which 88 (62.5%) had mild dacrocytosis and 52 (37.5%) had moderate dacrocytosis. By comparing of the

degree of dacrocytosis between patients with (n=140) and without splenomegaly (n=351), no statistically significant difference was observed (p=0.45).

Degree of Dacrocytosisϕ			
K/DOQI	Mild (%)	Moderate (%)	Severe (%)
1	175 (44.3%)	29 (7.4%)	-
2	86 (21.8%)	11 (2.8%)	-
3	49 (12.4%)	7 (1.8%)	-
4	14 (3.5%)	3 (0.8%)	-
5	16 (4.1%)	5 (1.3%)	

The values are expressed in n (%). Percentages represent the proportion from the total of patients with renal dysfunction (n=395) ϕThere was no significant difference between groups (p=0.2). K/DOQI: Kidney Disease Outcomes Quality Initiative.

Table 3: Dacrocytosis in patients with renal dysfunction (n=395)

Discussion

The presence of dacrocytes in blood counts is typically observed in patients with myeloproliferative disease, but its prevalence and clinical significance in other systemic diseases such as DM, chronic kidney disease (CKD), SLE and liver cirrhosis remain unknown.

As far as we know, this is the first large scale study addressing the clinical significance of dacrocytes in patients with various chronic diseases. The main pathological entities clearly related to dacrocytosis are myelophthisis and myeloproliferative disorders (polycythemia vera, myelofibrosis and essential thrombocythemia), all associated to splenomegaly.

Very few authors have reported the presence of dacrocytes in patients with different diseases from the mentioned above. After observing dacrocytes in patients with chronic disease, we thought that their presence could be a marker of a particular clinical situation. However, after reviewing those smears, the prevalence of dacrocytes was 1.4%, a much lower percentage than its prevalence in patients with splenomegaly. In consequence, we have posited that dacrocyte formation is not solely a result of splenomegaly.

The prevalence of teardrop cells in healthy people is not well known. In exploratory way, we studied 20 blood smears from healthy blood donors (data not shown), 12 men and 8 women between 18 and 60 years old. In these samples any morphological red blood cell change or anemia were found. Nevertheless this is a small sample and more studies should be performed in order to compare the prevalence in healthy patients.

Among our patients' diseases, the group with the highest prevalence of dacrocytes was the one of patients with non-hematological malignancies (20.9%). This could be related to the use of some chemotherapeutic drugs that may potentially injure erythrocytes by several mechanisms such as hemolysis induction, decreased Epo production or the proliferation of hematopoietic precursors [6].

SLE was the second most common disease associated to dacrocytosis (19.7%). Tesser-Poloni et al. reported a clinical case in which dacrocytes were observed in the peripheral blood smear and in the urinary sediment of a 34 year-old female with SLE and normal renal function. The patient had MHA (Hb 9.8 g/dL, VCM 70.4 fL) and no other associated hematological abnormalities. The author attributed the urinary dacrocytes to mechanical causes resulting from trauma to the urinary tract after vesical catheter placement [7].

Dacrocytosis was present in 15.2% of our patients with liver cirrhosis. Alcoholic liver cirrhosis has been associated to hemolytic anemia and abnormally shaped erythrocytes such as acanthocytes (burr cells), being hemolytic anemia a result of erythrocyte destruction in the spleen [8]. Hypersplenism secondary to portal hypertension results from splenomegaly, a condition that many authors relate to erythrocyte deformities, but only the splenomegaly associated to myeloproliferative disease leads to dacrocytosis.

Seven percent (7.5%) of our patients with dacrocytosis had DM. Epo deficiency has been postulated as a contributor to the anemia observed in DM patients with or without associated kidney disease [9,10]. This mechanism does not explain red blood cell deformity, so DM could directly lead to erythrocyte deformity through the effects or accumulation of advanced glycation products [11].

We cannot attribute dacrocyte formation to CKD in our study, since the majority of our patients presented normal renal function, even in patients with end-stage kidney failure we did not observe a higher degree of dacrocytosis. Erythrocytes in patients with CKD undergo rheological changes that make them more liable to disintegration since they are also more prone to oxidative stress. This may contribute to decreased red blood cell survival, [12] and increased deformity due to intracellular calcium accumulation leading to erythrocyte cell membrane abnormalities [13].

Anemia was present in 95% of our patients, although no association was established with the dacrocytosis' degree. These cells have been reported in great numbers in a form of iron deficiency anemia characterized by its microcytic and hypochromic phenotype. Nevertheless, the mechanism through which erythrocytes adopt this pear shape remain unexplained. We must emphasize that 39.2% of our study population displayed this form of anemia but with a mild degree of dacrocytosis.

Although most authors agree that splenomegaly is one of the main mechanisms leading to these abnormally shaped erythrocytes, only 28.5% of patients in our study had splenomegaly. There was no significant difference when comparing the degree of dacrocytosis between patients with and without splenomegaly, thus suggesting that other factors could possibly be participating in the genesis of deformed erythrocytes.

Since no direct correlation was observed between dacrocyte formation and splenomegaly, we suggest that the genesis of these cells may anatomically take place elsewhere in the body, and result from different factors to those previously proposed by other authors. Drugs, membrane glycation, or autoimmune states, among others may directly affect the integrity of erythrocyte membranes, increasing their tendency to deformity and decreasing their elasticity. Considering this property is a pivotal characteristic for their passage through narrow conduits such as blood vessels, the half-life of erythrocytes diminishes.

Conclusion

Dacrocytosis is a morphological erythrocyte abnormality which is not pathognomonic of any specific disease, as it could be found in different types of pathological entities. We observed that they do not correlate with different degrees of renal dysfunction and/or anemia.

Furthermore, splenomegaly is not a clinical characteristic directly responsible for the formation of dacrocytes.

Conflict of Interest

The authors do not have any conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Ethical Approval andInformed Consent

The Institutional Review Board approved the study (approval number 1267). All procedures in human participants were performed according to the ethical standards of the institutional and/or national research committee, with the 1964 Helsinki declaration, and its later amendments or comparable ethical standards.

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