

SEARCH OF INTRAVASCULAR HEMOLYSIS IN PATIENTS WITH THE CUTANEOUS FORM OF LOXOSCELISM

Pasquale MORENA (1), Kimiyo NONOYAMA (3), João Luiz C. CARDOSO (2) & Orlando C. de O. BARRETTO (3)

SUMMARY

Haptoglobin assay, a highly sensitive method to detect intravascular hemolysis was carried out in the sera of 19 patients referred to Hospital Vital Brazil with the cutaneous form of loxoscelism in order to investigate the occurrence of mild intravascular hemolysis. Data from this series did not show decreased levels haptoglobin, ruling out intravascular hemolysis in these patients with cutaneous form of loxoscelism.

KEYWORDS: Loxoscelism; Hemolysis

INTRODUCTION

The *Loxosceles* sp bite in humans may bring about two distinct clinical patterns: the cutaneous form, characterized by a painful necrotic dermatological lesion, and the viscero-cutaneous form, which in addition to the local lesion, exhibits a severe intravascular hemolytic anemia^{3, 5, 6, 7, 8}.

As few patients catch the spiders and take them to the physician, the diagnosis is made on clinical grounds, based mostly upon the typical dermatological lesion.

Although intravascular hemolysis has not been found in the cutaneous form, as indicated by standard methods like bilirubin assay and reticulocytes counting, we performed this study aiming to detect in this form any presence of intravascular hemolysis using the haptoglobin assay, a potent and sensitive method which detects slight intravascular hemolysis. The haptoglobin forms a complex with free plasmatic hemoglobin which

is cleared by the hepatic tissue, decreasing the plasma haptoglobin levels. Clinical and standard laboratory data were analysed as well.

MATERIAL AND METHODS

Nineteen patients were referred to Hospital Vital Brazil, from 1982 to 1987 with the clinical diagnosis of cutaneous form of loxoscelism. Nine women and ten males, ranging from 13 to 58 years old were studied, up to 4 days after bite. Upper and lower limbs were the preferred sites for the bites, followed by abdomen and back regions. After admission blood samples were taken for hematological and reticulocytes counts. Haptoglobin was assayed by a method described by one of the Authors¹.

RESULTS

The patients presented the classical clinical fea-

(1) Laboratório de Fisiopatologia, Instituto Butantan, São Paulo, Brasil.

(2) Hospital Vital Brazil, Instituto Butantan, São Paulo, Brasil.

(3) Departamento de Psiquiatria, Faculdade de Medicina da USP - Laboratório de Investigação Médica - LIM-23

Address for Correspondence: Pasquale Morena, Instituto Butantan, Av. Vital Brasil, 1500; 05503-000 São Paulo, Brasil.

tures of cutaneous loxoscelism such as pain in the first hours after bite, edema and erythema, with hemorrhagic areas mixed with ischemic ones. These signs occurred in the first 48 hours, and afterwards the pain became more intense, with fever and exanthema. The local lesions exhibited the usual clinical course, with further necrosis, ulcer and difficult cicatrization.

The hematological data disclosed constant neutrophilia and sometimes leucocytosis (5 patients). Reticulocytosis was not observed, and the haptoglobin levels were found to be within the normal range (table 1).

One hundred normal blood donors presented control haptoglobin levels of 210 ± 82 mg % with a range of 103 to 400 mg%¹. The patients studied in this series showed levels of 402 ± 161 mg %, and exhibited values ranging from 156 to 712 mg % which are significantly higher than the control levels ($t = 5.06$; $p < 0.0001$). Regarding the patients with the cutaneous form, the lowest haptoglobin figure of 156 mg% is within one standard deviation below the mean, as well as two other figures of 178 and 199 which are below the normal arithmetical mean; 3 of the values were within one standard deviation above the mean, 6 of them showed values above one standard deviation, and 7 above two standard deviations (see table 1).

DISCUSSION

Although it has been accepted that the cutaneous form of loxoscelism does not present intravascular

hemolysis, we carried out this study in order to confirm this hypothesis, using the haptoglobin assay, a very sensitive method which has been employed to detect sub-clinical and non overt intravascular hemolysis.

In a recent survey⁴ it was observed that 97% of patients with loxoscelism referred to Hospital Vital Brazil exhibited the cutaneous form and only 3% presented the viscerocutaneous form. It has been found that *L. gaucho* is the most frequent *Loxosceles* species in São Paulo³. Although the hemolytic effect of the venom has not been clarified so far, it is known that disseminated intravascular clotting occurs in the patients who present the viscerocutaneous form^{2,9}.

In our series, patients with the cutaneous form of loxoscelism did not present any qualitative or quantitative erythrocyte abnormality, but the leucocytes exhibited a constant neutrophilia, and leucocytosis in some of the cases. As we did not find any case with low eosinophil counts, associated with acute bacterial infections, we suggest that the haematologic response and the inflammatory process are dependent upon the venom action itself rather than to bacterial contamination of the bite lesion.

Reticulocyte counts were normal, and the high levels of haptoglobin rule out the occurrence of intravascular hemolysis. These higher levels of haptoglobin could be explained by the inflammatory reaction around the bite lesion.

TABLE 1
Hematological data and serum haptoglobin levels in patients presenting cutaneous form of Loxoscelism

	mean	± standard deviation	range
Leucocytes	8526	3380	4900-17800
Band neutrophils	2.3	1.1	1-4
Segmented neutrophils	69.9	8.1	55-84
Eosinophils	2.7	1.9	1-7
Basophils	0.2	0.4	0-1
Lymphocytes	21.2	6.8	11-33
Monocytes	3.7	1.6	1-7
Hemoglobin (g Hb/dl)	14.5	1.7	11.7-17.4
Reticulocytes (%)	0.9	0.5	0.1-1.8
Haptoglobin (mg/100 ml of serumbinding capacity to hemoglobin)			
Patients (n:19) **	402	161	156-712
Control (n:100)	210	82	103-410

* BARRETTO et al., 1984¹

** Student's test between patients and controls was $t: -5.06$ $p < 0.0001$

Therefore, the data presented in this study rule out intravascular hemolysis in patients with the cutaneous form of loxoscelism. On the other hand, they reinforce the possibility that the cutaneous form differs sharply from the viscero-cutaneous form, suggesting that they are different diseases sharing *Loxosceles* venom as the common aetiological factor. All individuals who are bitten by *Loxosceles* develop the local and circumscribed necrotic cutaneous form, but only some of them exhibit the prevailing hemolytic manifestations of the viscero cutaneous form. We speculate that an underlying genetic factor could predispose these individuals to the hemolytic venom effects.

RESUMO

Pesquisa de hemólise intravascular na forma cutânea de loxoscelismo.

Dezenove pacientes que apresentaram a forma clínica cutânea do loxoscelismo foram investigados com o propósito de pesquisar hemólise intravascular sub-clínica, lançando mão da dosagem de haptoglobina, um método altamente sensível que permite detectar discreta presença de hemólise intravascular. Não foi encontrada diminuição de haptoglobina, o que descarta uma ação hemolítica do veneno da *Loxosceles* nestes pacientes.

REFERENCES

1. BARRETTO, O. C. de O.; NONOYAMA, K.; MIZUKAMI, S. & MASPES, V. - Método modificado de dosagem de haptoglobina por

eletroforese em acetato de celulose. *Rev. bras. Pat. clin.*, 20: 104-106, 1984.

2. BERGER, R. S.; ADELSTEIN, E. H. & ANDERSON, P. C. - Intravascular coagulation: the cause of necrotic arachnidism. *J. Pediat.*, 80: 1035-1037, 1972.
3. CARDOSO, J. L. C. & BRANDO, R. B. - *Acidentes por animais peçonhentos: clínica e tratamento*. São Paulo, Livraria Editora Santos, 1982.
4. CARDOSO, J. L. C.; FRANÇA, F. O. S.; EICKSTEDT, V. R. D.; BORGES, I. & NOGUEIRA, M. T. - Loxoscelismo: estudo de 242 casos (1980-1990). *Rev. Soc. bras. Toxicol.*, 1: 58-60, 1988.
5. GAJARDO-TOBAR, R. - Mi experiencia sobre loxoscelismo. *Mem. Inst. Butantan*, 33: 689-698, 1966.
6. JORGE, M. T. & RIBEIRO, L. A. - Epidemiologia do acidente por aranhas do gênero *Loxosceles*: estudo prospectivo de 70 casos. In: CONGRESSO DA SOCIEDADE BRASILEIRA DE MEDICINA TROPICAL, 26., Natal, 1990. *Anais*. p. 103.
7. SCHENONE, H.; RUBIO, S.; VILLARROEL, F. & ROJAS, A. - Epidemiologia y curso clínico del loxoscelismo. Estudio de 133 casos causados por la mordedura de la araña de los rincones (*Loxosceles laeta*). *Bol. chil. Parasit.*, 30: 6-17, 1975.
8. SCHENONE, H.; SAAVEDRA, T.; ROJAS, A. & VILLARROEL, F. - Loxoscelismo en Chile. Estudios epidemiológicos, clínicos y experimentales. *Rev. Inst. Med. trop. S. Paulo*, 31: 403-415, 1989.
9. VORSE, H.; SECCARECCIO, P.; WOODRUFF, K. & HUMPHREY, G. B. - Disseminated intravascular coagulopathy following fatal brown spider bite (necrotic arachnidism). *J. Pediat.*, 80: 1035-1037, 1972.

Recebido para publicação em 11/08/1993.

Aceito para publicação em 21/12/1993.