

Prediction Degree Severity of Erysipelas: Risk Index of Hemorrhagic Form of Erysipelas

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Citation: Fokina EG, Gerasimov AN. Prediction Degree Severity of Erysipelas: Risk Index of Hemorrhagic Form of Erysipelas. J Infec Dis Treat. 2016, 2:2.

Abstract

Purpose of the study: The work is devoted to the new method diagnostics of hemorrhagic form of erysipelas as a method of early prediction of severe (hemorrhagic and erythematous-bullous-hemorrhagic) erysipelas forms. The advantage of the method - the ability to carry out the forecast of severe erysipelas in the early stages of the disease (1-2 days). The method allows differentiating patients quickly by severity of the disease to optimize therapeutic measures.

Materials and methods: The patients with focus of inflammation localized on the face (n=24), and the legs (n=36) were studied at various stages of the disease (day 1-3; 4-6; 7-10; and 11-15 from the onset of the disease), undergoing in hospital treatment in Moscow 2nd Clinical Hospital for the Infectious Diseases. Summary in correlation multivariate analysis were examined 60 biochemical and hemostasis factors.

Results: The hemorrhagic form of erysipelas diagnosed in 51.6% of all observations. The erysipelas severity index is calculated as: $3.075 - 0.009 \times \text{«Amylase, serum (IU/l)»} + 0.841 \times \text{«Erysipelas localization (face=1, LL=2)»} + 0.004 \times \text{«CRP, serum (mg/l)»} - 0.071 \times \text{«Albumin, serum (g/l)»} + 0.027 \times \text{«AST, serum (IU/l)»}$; where: 3.075 - non-standardized coefficient; the total amylase in serum (IU/l); the erysipelas localization (face=1, LL=2); the C-reactive protein in serum (mg/l); the albumin in blood serum (g/l); the aspartate aminotransferase in serum (IU/l).

Conclusions: The risk of hemorrhagic erysipelas in that group was in 9.9 times higher-if erysipelas inflammation was on the legs differentiate with the face (Odd Ratio=9.9 [2.8; 34.7]). The proposed risk index of hemorrhagic form of erysipelas is simple to calculate and easy to use.

Keywords: Facial erysipelas; Lower-limb erysipelas; Erythematous-hemorrhagic form; Bullous-hemorrhagic form; Erysipelas recurrence

Received: October 03, 2016; **Accepted:** November 21, 2016; **Published:** November 24, 2016

Introduction

Erysipelas inflammation forms red, swollen and hot to the touch, with clear boundaries inflammatory skin focus (**Figures 1-3**). Local inflammation accompanied by the development of regional lymphadenitis, painful enlarged lymph nodes. Erysipelas inflammation sometimes accompanied by intoxication symptoms, including fever, chills, nausea, vomiting, general weakness, muscle pain and body aches. Erysipelas most frequently occurs on the face and legs [1-5].

In our observation 67% of all clinical cases of erysipelas localized

on the lower limbs (LL). The obesity, diabetes, chronic venous insufficiency and long-time foot and nails fungal infection combined with LL erysipelas often [2,4,6-8]. The risk of erysipelas recurrence was statistically significantly higher - when the inflammation focus was located on the leg - in comparison with the face (Odd Ratio=5.55; [1; 51.2], p=0.009) [2,6,8-11].

The hemorrhagic forms of erysipelas had a prolonged period of tissue repair. Patients with bullous - hemorrhagic form of erysipelas stayed in the hospital longer and required a large amount of medication costs comparing with others forms of

erysipelas. Therefore, it is important to diagnose severe erysipelas in the early stages of the disease-at the first examination of the patient [6,8,10,12-14].

Materials and Methods

The indices of external (prothrombin time, INR) and internal (activated partial thromboplastin time) coagulation pathways, the degree of dysfibrinogenemia (thrombin time, functional fibrinogen activity and D-dimer level), the amount and functional activity of the platelets (aggregation with ADP) and the erythrocytes (aggregation with lanthanoid and protamine sulfate) were studied in 60 patients with erysipelas. Also, we have studied endothelial dysfunction manifested in the decrease of athrombogenicity of vascular wall endothelium (antithrombin III and protein C) and in the increase of adhesive properties of the endothelium (von Willebrand factor).

To describe metabolic changes, we used "biochemical passport", the basis of which amounted to six enzymes (aspartate aminotransferase, alanine aminotransferase, creatine phosphokinase, gamma-glutamyl



Figure 1 Effected erythematous-bullous erysipelas of Patient A's right lower leg.



Figure 2 Pictorial representation of significant edema and lymphostasis of the affected lower limb.



Figure 3 Pictorial representation of Patient A's healthy left limb.

transferase, alkaline phosphatase, lactate dehydrogenase) and six substrates (total protein, albumin, glucose, cholesterol, urea, creatinine) in blood serum [15].

Summary in correlation multivariate analysis were examined 60 biochemical and hemostasis factors, including: creatine phosphokinase-MB fraction, lactate dehydrogenase -1-2 fraction; Magnesium; Calcium; Phosphorus; total amylase; lipoproteins high and low density, triglycerides, haptoglobin, transferrin, ceruloplasmin, C-reactive protein (CRP), some serum protein fractions obtained by electrophoresis on an agarose gel, and the number of leukocytes, erythrocytes and platelets and erythrocyte sedimentation rate in clinical blood test.

The patients with focus of inflammation localized on the face (n=24), and the legs (n=36) were studied at various stages of the disease (day 1-3; 4-6; 7-10; and 11-15 from the onset of the disease), undergoing in hospital treatment in Moscow 2nd Clinical Hospital for the Infectious Diseases.

The average age of the patients was 59 ± 3.2 years (face erysipelas) and 51.7 ± 2.1 years (LL erysipelas, $p=0.053$). The face erysipelas seems to be in the elder age more often. Among 60 patients in the 33% cases was erythematous (Eryth.), 15%-erythematous-bullous (EB), in 23.3%-erythematous-hemorrhagic (EH) and in 28.3% of cases-bullous-hemorrhagic (BH) form of erysipelas.

Erythematous-hemorrhagic (12 cases) and bullous-hemorrhagic (14 cases) forms occur most frequently on the lower limbs comparing with the face (2 and 3 cases, respectively). Erysipelas is usually caused by the group A streptococcus bacteria and treated effectively with antibiotics [4,8,14], so clinical recovery we had in all studied cases. The average time of hospital treatment in patients with the face erysipelas was smaller (8.4 ± 0.4 days) than in patients with the LL erysipelas (11.6 ± 0.7 days; $p_{12} < 0.001$).

Results and Discussion

The hemorrhagic form of erysipelas diagnosed in 51.6% of all observations (Figures 1-3, observations of the author). Patient A., 36 years old, was hospitalized on the 2nd day of illness. Diagnosis: erythematous-bullous erysipelas on right lower leg, 3 degrees of severity; 1st time erysipelas.

Status localis (2nd day from the onset of the disease): on the right lower leg it is erythema with clear irregular contours, hot to the touch, multiple small hemorrhages, multiple flat bullae with serous contents. Significant edema and lymphostasis of the affected lower limb; Patient A., the healthy left limb.

The same patient A., in the period of early recovery (12th day of illness). *Status localis* (11 day from the onset of the disease): on the right lower leg congestive redness, peeling, on the front surface are the crusts in the rejection phase. Edema decreased. The residual effects of the erysipelas.

The risk of hemorrhagic erysipelas in that group was in 9.9 times higher-if erysipelas inflammation was on the legs differentiate with the face (Odd Ratio=9.9 [2.8; 34.7]).

Given that the hemorrhagic form of erysipelas characterized protracted period of recovery and a slow regression of inflammation we proposed special index "The risk of hemorrhagic form of faces", that allows the early stages of the disease to carry out the differentiation of patients with severe hemorrhagic form of erysipelas from another forms. The multivariate analysis obtained the following regression model (Table 1).

The erysipelas severity index is calculated as: $3.075 - 0.009 \times \text{«Amylase, serum (IU/l)} \text{»} + 0.841 \times \text{«Erysipelas localization (face=1, LL=2)} \text{»} + 0.004 \times \text{«CRP, serum (mg/l)} \text{»} - 0.071 \times \text{«Albumin, serum (g/l)} \text{»} + 0.027 \times \text{«AST, serum (IU/l)} \text{»}$; where:

- the level of total amylase blood serum, the value obtained IU/l;
- the erysipelas localization=1-if the erysipelas focus on his face;=2-if the erysipelas focus on the lower limbs;
- CRP levels in the blood serum, the value in mg/l;
- albumin blood serum obtained value in g/l;
- AST enzyme activity level in the blood serum, obtained the value in IU/l.

The following table was calculated for the translation of severity of the index to the probability of hemorrhagic (EH and BH) forms of erysipelas (Table 2).

For example, if the virtual patient on admission: the total amylase serum=36 IU/l, the erysipelas focus on the lower limbs (=2), CRP=140 IU/l, the albumin serum=28 IU/l, AST=32 IU/l, the

Table 1 Index "The risk of hemorrhagic form of erysipelas".

Indicator	B	Statistical error "B"	β
Constant	3.075	1.6031	
The total amylase, serum (IU/l)	-0.009	0.0102	-0.128
The erysipelas localization (face=1, LL=2)	0.841	0.3436	0.3179
C-reactive protein (CRP), serum (mg/l)	0.004	0.003	0.1634
The Albumin, serum (g/l)	-0.071	0.0359	-0.231
The Aspartate aminotransferase (AST), serum (IU/l)	0.027	0.013	0.2258

Note: The Erysipelas study group, all forms (N=60); **B**-non-standardized coefficient; **Statistical error "B"**-the statistical error coefficient "B"; **β** (Beta)-standardized coefficient.

severity of the index will be equal to: $3.075 - 0.009 \times 36 + 0.841 \times 2 + 0.004 \times 140 - 0.071 \times 28 + 0.027 \times 32 = 3.869$. By comparing the obtained value with the table values (from 3.5) of 3.869, we find that the virtual patient has a high risk of the most severe-bullous-hemorrhagic form of the erysipelas.

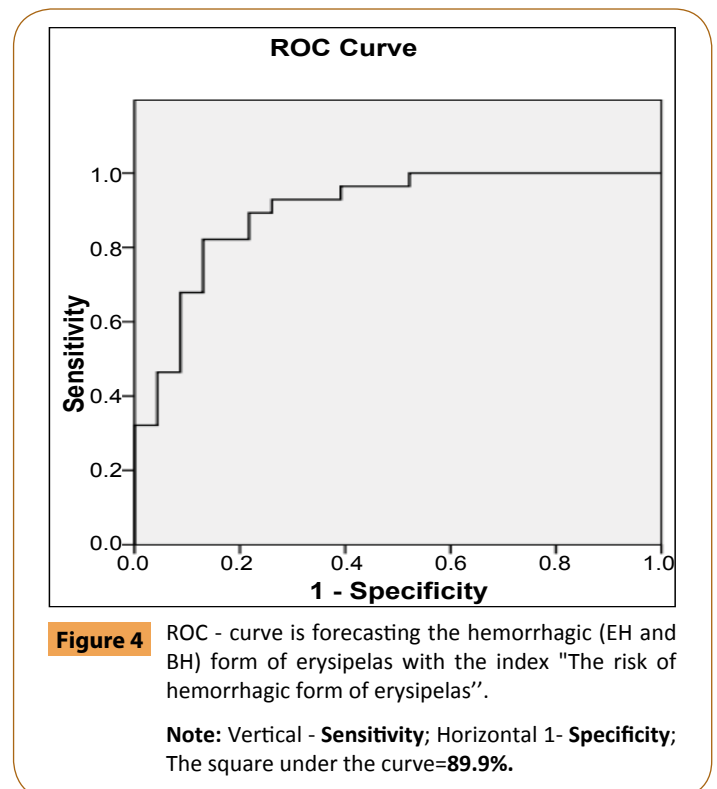
To evaluate the clinical significance of the index "The risk of

Table 2 The joint distribution of the index of severity and form of erysipelas in the patients examined.

Index forecast for the form of erysipelas	All forms of erysipelas (Eryth., EB, EH, BH)				
	Eryth.	EB	EH	BH	Total
up to 1.5	8	1	0	0	9
1.5-2	2	2	1	0	5
2-2.5	4	1	1	1	7
2.5-3	2	1	6	5	14
3-3.5	1	1	3	4	9
from 3.5	0	0	2	5	7
Total	17	6	13	15	51

Table 3 The table of conversion our prognostic index in the form of erysipelas.

Index forecast for the form of erysipelas	All forms of erysipelas			
	Eryth.	EB	EH	BH
up to 1.5	88.89%	11.1%	0%	0%
1.5-2	40.00%	40.00%	20.0%	0%
2-2.5	57.14%	14.29%	14.29%	14.29%
2.5-3	14.29%	7.14%	42.86%	35.71%
3-3.5	11.1%	11.1%	33.33%	44.44%
from 3.5	0%	0%	28.57%	71.43%
Total	33.33%	11.76%	25.49%	29.41%



hemorrhagic form of erysipelas" it applied to examine all our patients retrospectively (**Table 3**). The pattern of connection of the proposed index of severity and the hemorrhagic form of erysipelas further illustrated by the ROC - curve (**Figure 4**).

Conclusions

1. The risk of hemorrhagic complications in lower-limb erysipelas was in 9.9 times higher than in facial erysipelas, (Odd Ratio=9.9 [2.8; 34.7]).

2. The proposed index has practical importance for the optimal hospital management of patients with erysipelas according principles of personalized medicine.
3. The proposed index is easy to use (in Russian). Find on: http://1mgmu.com/progi1/roga_forma.aspx

Acknowledgements

This study designed and conducted without funding or sponsorship. No reported conflict of interest by the authors.

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