



Complicate Course of Severe Erysipelas: Kidney at Risk



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Abstract

Background: Although most cases of Erysipelas have mild course, minority of them can lead to life-threatening conditions, such as acute kidney injury (AKI).

Material and methods: We analyzed the results of treatment of 100 patients diagnosed with erysipelas in the septic surgery department of 5th City Clinical Hospital of Minsk. We evaluated the dynamics of biochemical data presepsin in erysipelas patients in intensive care units paying attention to AKI signs.

Results: In individuals with baseline significantly higher values of urea, creatinine and urine changes, the risks of AKI-like changes are higher. A tendency to more active increase and slower decrease (with clinical improvement) of the level of sepsis marker presepsin in patients with compromised renal function with erysipelas was noted.

Conclusion: The parameters of the kidney function and presepsin level assessment are important prognostic markers in complicated erysipelas.

Keywords: Erysipelas; Acute kidney injury; Presepsin

Introduction

Erysipelas has more than 2000 history. In 1882, Fehleisen proved the invasion of streptococcus lymphatic capillaries, transmitted to other persons [1]. The dermal layer of the skin of the face and lower extremities is involved usually [2], and the beta-hemolytic group A streptococcus is the most typical etiological factor; and group B, C and G streptococci were somewhat less common, with participation of other bacteria [3], among them in 20% the non-streptococcal pathogens are recovered (Staphylococcus aureus, Klebsiella pneumoniae, Hemofilus influenzae, Yersinia enterocolitica and Moraxela spp) [4]. Life threatening in the preantibiotic era, erysipelas currently responds well to treatment with beta-lactam and other antibacterial drugs and resolves without complications in the vast majority of patients [5]. However, relapses and complicated forms, especially in the presence of risk factors, still pose a serious challenge for the medical community [6]. With proper treatment, mortality is not more than 1% [7] and is associated with complications such as pulmonary embolism, sepsis with the development of bacterial toxic shock or acute kidney damage.

Material and Methods

A longitudinal, single-center, prospective study included 100 cases of patients with erysipelas who underwent treatment in the 2nd surgical unit of the 5-city clinical hospital in Minsk in 2016-2017. The diagnosis of erysipelas was established on the basis of clinical and bacteriological data. We registered biochemical parameters of renal function (urea, creatinine, potassium level), and urinalysis (hematuria, proteinuria, cylindruria and leukocyturia). Based on the presence or absence of changes on the part of the kidneys, two comparison groups were created - patients with changes in kidney function and with no changes. In patients hospitalized and / or transferred to the intensive care and intensive care unit (ICU) we also assessed the level of the marker of infectious inflammation and sepsis - soluble sCD14-ST - presepsin (PS) - associated with the activation of macrophages and CD14+ T-lymphocytes by endotoxins. Diagnostically significant PS levels (pg/ml) and the range of values depending on the severity of the condition were specified in the specification for the laboratory analyzer: normal range 294.2 ± 121.4 ; local infection - $721.0 \pm$

611.0; systemic inflammatory response syndrome (SIRS) - 333.5 ± 130.6 ; sepsis - 817.9 ± 572.7 ; severe sepsis - 1992.9 ± 1509.2 [8]. The obtained data were processed in Microsoft Excel.

Results

Of the 100 cases of erysipelas, 53% were women, 47% men. By age, patients were represented by the following ratio: young age 10% (18-44 years old), average age 33% (45-59 years old), old age 29% (60-74 years old), senile age 27% (75-90) centenarians 1% (over 90 years old). Deviations outside the normal ranges were observed in urea in 35% of cases (increased in 35 of 98 examined), creatinine level in 42.2% (increased in 38 of 90 examined patients), and potassium level - in 14.58% (14 out of 96 examined). Protein in urine was found in 25 of 52 cases (48%), squamous epithelium was found in 29 of 53 (54.7%), abnormal level of leukocytes in urine was found in 9 of 31 cases among women (29%) and 5 of 24 cases among men (20.8%), red blood cells in urine were detected in 5 of 13 patients among women (38.46%) and in 2 of 12 among men (16.7%). We have studied the significance of changes in renal parameters as a factor determining the course of the underlying disease. So, patients were divided into a subgroup by average hospital stay of 8 ± 2

days and subgroup with a longer stay (more than 10 days): 42 out of 100 cases (42%), of which 1 patient reported fatal outcome. Among patients with longer periods of treatment, an increase in serum creatinine was noted at 55.6% (in 20 of 36 people), in the "up to 10 days" group - in 33.3% (18 of 54 people), increased urea was observed in 53, 7% (in 22 of 41 people) - in the "over 10 days" group and in 36.84% (21 of 57 people) in the "up to 10 days" group ($p < 0.05$ when comparing between groups according to the Kruskal-Wallis test).

In the "more than 10 days" patient group, 10 patients were identified with PS profile determined. The inclusion criteria for this subgroup were: more than 1 PS value, data on renal function at baseline, the known outcome of the suspected renal lesion. Within the group, patients were divided into subcategories "with AKI" and "no AKI". It was found that in the "with AKI" subcategory, PS dynamics was characterized by more severe increase (3 people) and / or smoother decrease during treatment (4 people). In the "no AKI" subcategory, no such changes were detected: all five patients showed a rapid decrease from the initial PS level after the start of treatment. The obtained data reflect the known effect of PS accumulation in patients with impaired renal function against the background of a more severe course of erysipelas (Table 1).

Table 1: Time course of presepsin levels in patients with ($n = 10$) changes in renal function.

Subcategory	The increase in PS between two Measurements (Time Interval 3-5 days), Median	PS Reduction between two Measurements (Time Interval 3-5 days), Median	Creatinine Median ($\mu\text{ol} / \text{L}$)
No AKI, $n=5$	10.11% (5 pts)	35.75% (5 pts)	85.17
WITH AKI, $n=5$	30.25% (3 pts)	35.33% (4 pts)	136.18*

*the difference between groups is statistically significant according to the Kruskal-Wallis test.

PS – Presepsin, pts – patients.

Discussion

The acute kidney damage is one of the rare but dangerous complications of erysipelas; it can manifest itself as glomerular or, less commonly, as an interstitial lesion. In most cases, glomerulonephritis is caused by infectious pathogens, and in some cases due to invasion of beta-hemolytic streptococcus. The most typical variant of this course will be post-streptococcal glomerulonephritis. The tropism of streptococcus to the renal structures is currently in no doubt. Many authors described patients with acute renal failure on the background of streptococcal erysipelas, whose renal biopsy specimens revealed acute interstitial nephritis with predominantly mononuclear infiltration. Moreover, after a course of beta-lactam antibiotics (without steroid therapy), renal function recovery was noted. In some cases, it is also impossible to exclude the association of AKI with the toxic effect of antibiotics (antibiotic-induced effect), but the same authors believe that with erysipelas this approach should not be considered quite correct, i.e. the primary cause of AKI is erysipelas, and only secondarily is nephrotoxicity of drugs [9].

Despite the fact that erysipelas-associated sepsis is a rarely described phenomenon, it is clear that only its early diagnosis can reduce mortality, since the development of sepsis threatens kidney function and strengthens the streptococcus tropism to the renal parenchyma, taking into account possible hemodynamic changes, mutually aggravating the threat to life the patient. For the early diagnosis of sepsis, more than 200 markers are currently proposed, among which the determination of levels of C-reactive protein, procalcitonin and PS are of clinical importance. The last marker is the most sensitive and specific and is in certain dependence on the excretory function of the kidneys, similar to procalcitonin. Nakamura et al. [10] proved that in AKI the optimal boundary value of the PS level in the blood is $500\text{pg} / \text{ml}$, whereas in patients with no AKI this level corresponds to $240\text{pg} / \text{ml}$ [10]. Therefore, the presence of AKI additionally increases the level of the marker in the patient's blood, independently determining the outcome. Determining the PS level is critical because the study is technically no different from conventional clinical biochemistry, takes a short time (completion time of about 17 minutes, excluding the collection and transportation of a blood sample) and is highly informative considering correction factors. The findings suggest

that presepsin can be a valuable diagnostic tool that not only plays a role in the diagnosis of erysipelas sepsis, but also indirectly reflects the severity of renal dysfunction.

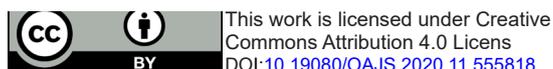
Of course, the gold standard for the diagnosis of AKI, along with the calculation formulas for calculating glomerular filtration rate, is nephrobiopsy. However, this invasive study is not always available in clinical practice, and obtaining the result takes more than 24 hours, and therefore can no longer affect the management of the “acute” patient, providing a remote prognosis and determining management tactics already in the recovery period. In this regard, the assessment of renal function according to the results of routine biochemistry tests and general urinalysis is critical in stratifying the possible risks in patients with RV. According to the literature, among patients with erysipelas, only 47% of laboratory abnormalities in the urinary system are not observed, while 11% have isolated proteinuria, 13% have proteinuria combined with hematuria, and in 23% of cases, hematuria can be an isolated symptom, against the background of registered nephrotic or nephritic syndromes [11,12].

Conclusion

The identification of patients at risk of developing AKI in erysipelas is justified by the increased likelihood of death. In this regard, early diagnosis and active monitoring in intensive care units are important. In erysipelas, due to the affinity of streptococcus to the renal parenchyma, the risk of acute renal damage with a more severe course requiring prolonged hospitalization occurs in a significant number of patients, especially in the presence of initially compromised renal function. Timely identification of such patients through careful monitoring of presepsin levels and parameters of renal dysfunction will improve the prognosis for complicated course of erysipelas.

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