

Soft tissue infections: risk factors in diabetes mellitus patients

Eduard Lucian CATRINA, Assistant Professor^a;

Sorin ALDOESCU, General Surgeon Specialist^b; Traian PATRASCU, Professor^a

^aGeneral Surgery Department, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

^b"N. Paulescu" National Institute of Diabetes and Metabolic Diseases, Bucharest, Romania

ABSTRACT

Diabetes mellitus patients have a specific immune condition and an increased susceptibility to infections. This paper analyses the presence of the risk factors for soft tissue infections and reveals some statistical correlation between those and the severity of the infection, defined by infection spread and depth of the anatomical structures involved (skin, fascia, muscles).

186 patients with diabetes mellitus, admitted in a surgery department for various soft tissues infections (skin and annexes, subcutaneous tissue, muscles and fasciae) were included in our study. The typical patient was 53.3 years and average duration of diabetes was 10.4 years; sex ratio was almost even (F/M 92/94). Diabetes type distribution in this study was 18.27% type I, 67.7% type II and for the rest of 13.9% diabetes was identified after admission.

Based on the severity of the infections patients were classified in two groups: (A) low severity infections group affecting skin and superficial layer of subcutaneous tissue, 102 patients and (B) severe necrotizing infections group involving deep subcutaneous tissue, fasciae and muscles, 84 patients. Comparative studies of clinical criteria (age, sex, duration of diabetes mellitus, its complications and associated conditions) and biological parameters were performed at admission.

A clear clinical correlation was identified between leucocytosis, neutrophilia, presence of the anemia as well as inflammatory syndrome (CPR,ESR) with severity of soft tissue infection. Age, diabetes duration and the presence of arteriopathy were also associated with the likelihood of severe soft tissue infection.

Key words: soft tissue infection, diabetes mellitus, necrotizing infections.

INTRODUCTION

Diabetes mellitus represents a condition highly susceptible for infections along with old age, anemia, associated neoplasia, immunosupresor and steroid treatments, chemotherapy, IV and urinary cath-

eters held for a long time and even misuse of antibiotherapy.

It seems that the occurrence and unfavorable evolution of infections are stimulated by an immunocompromised status in periods with poor metabolic control with an increased propensity of inflammatory response on diabetes mellitus patient. These lead to soft tissue

Address for correspondence:

Eduard Catrina, Assistant Professor, "Carol Davila" University of Medicine and Pharmacy, 8 Eroilor Sanitari Blvd., Bucharest, Romania
email address: eduardcatrina@yahoo.com

infections having a different severity index, even life threatening depending on level of spreading, depth of affected anatomical structures (skin, subcutaneous tissue, fascia, muscles) and type of pathogens. (1)

Considering that soft tissue infections gravity varies from one patient to another or even from episode to episode in the same patient, it is believed now that infections susceptibility in diabetes mellitus patient is triggered by multiple linked factors.

In this regard, the study tried to identify potential risk factors associated with soft tissue infections in diabetes mellitus patients and to segment them by risk and evolution possibilities. □

METHODS AND MATERIALS

186 patients with type I and II diabetes mellitus and concurrent soft tissue infections admitted in surgery department of Cantacuzino Hospital during January 1st, 2002 to December 31st, 2006 were included in this study. Patients with diabetic foot and complicated infections (primary or secondary, also affecting structures like bones, joints, micro and macro vascular circulation, nerves) were excluded. The cases with infections occurred in relation with surgical interventions were excluded as they can be considered postoperative complications.

Inflammatory syndrome at admission (leucocytosis, CPR, ESR) and diabetic status (age of patients, duration of the disease, long term metabolic control, type of the treatment, associated complications or other conditions) were used to identify the risk factors for infection occurrence and further progression to extensive suppurative or necrotizing processes.

We retrospectively followed the patients grouped in two segments by the severity of the disease:

- group 1 – low severity lesions (simple, localized, non-necrotizing infections interesting skin and its annexes – boils, superficial abscesses, erysipelas, localized cellulitis);
- group 2 – high to extreme severity (necrotizing, disseminated lesions affecting soft deep tissues under superficial fascia – disseminated cellulitis, fasciitis, necrotizing myositis but also deep retroperitoneal infections). □

RESULTS

From 186 patients 94 were males and 92 females. Age ranges from 16 to 82, with an average of 53.34 years. Duration of diabetes varied from 0 to 40 years, with a mean on 10.43. Type I was recorded in 35 patients, type II in 123 patients while for the rest of 26 (13%) metabolic disorder was depicted at the admission for infectious episode. Oral antidiabetic drugs were administered to 69 patients and insulin treatment was used for 117 patients (including pre and postoperative treatment of diabetes patients newly diagnosed.)

Clinical and biological parameters were analysed in the two groups:

- type of diabetes;
- age of diabetes;
- age;
- gender;
- diabetes mellitus complications;
- associated comorbidities (especially chronic renal failure);
- glycosylated haemoglobin (HbA1c) and "a jeune" glicaemia;
- anemia at admission;
- inflammatory syndrome (leucocytosis, neutrophilia, CPR, ESR);
- other biochemical changes.

Lot	N = 186 patients
Gender (M/F)	94/92
Mean age	53.34 years (median 54 years)
Diabetes type	
Type I	35 (18.81%)
Type II	125 (67.20%)
Newly discovered	26 (13.97%)
Mean age of diabetes	10.43 years (median 8.5 years)
Treatment type - insulin/OAD	117/69

TABLE 1. Group characteristics

Clinical parameter	Group 1 (N= 102)	Group 2 (N=84)	p (CI 95)
Age	51.51 ± 1.62 years	55.55 ± 1.26 years	0.13
Gender (F/M)	58/44	34/50	0.0282 OR 0.5159
Diabetes type			
Type I	21	14	NS
Type II	72	53	
Newly diagnosed	9	17	
Duration of diabetes mellitus	11.61± 0.91 years (N= 93)	12.84 ±1.08 years (N= 67)	NS
Periferal neuropathy	20	16	NS
Arteriopathy	15	22	0.0648
Chronic renal failure	7	9	NS
Comorbidities - patients (1/2/3/4 conditions)	58 (56.86%) (26/16/12/4)	46 (54.76%) (22/13/8/3)	NS

TABLE 2. Clinical aspects

There are no differences between the two groups concerning type of diabetes ratio, frequency of association between infection and diabetic neuropathy, terminal nephropathy and chronic renal failure. It is also obvious that mean age and diabetes duration are higher in severe infections group than the low severity group.

Gender distribution reveals a higher incidence of severe necrotizing infections in males versus females (almost 1.5/1 male/female in second group). Another finding is the highest percentage of patients with arteriopathy in severe infections group (26.19% of patients with severe infections have a macroangiopathy background), while in low severity group only 14.7% have an arterial involvement. However, Fischer's exact test shows no statistical relevance.

There are no differences between the presence of autonomic neuropathy or other pathological conditions (cardiac, hepatic, cerebral, hematological) and the frequency of their association with low or high severity soft tissue infections. However, it is obvious that this pa-

tients have an immunosuppressed status, in over 50% they have at least another severe condition associated to the diabetes mellitus.

Biological parameters analysed were related to inflammatory syndrome at admission, level of metabolic control and biochemical changes triggered by soft tissue infection progress.

WBC changes represented by leucocytosis and increased PMN as well as inflammatory syndrome (leveled ESR and CPR) are connected with the severity of the lesions. Thus, those variables can be used as criteria for severity detection and/or follow-up for infection evolution in patients with diabetes mellitus.

Though HbA1c is described as a predictive factor for the incidence of soft tissue infections, there is no significant correlation with the severity of those supurations. Anyway, HbA1c is more valuable than "a jeune" glycaemia in predicting a possible more severe infection. (p 0.0112)

A specific comment must be mentioned for hemoglobin levels on these patients. Even

Biological parameters	Group 1 (N= 102)	Group 2 (N=84)	P (CI 95)
WBC (×1000/mm ³)	10.90 ± 0.4	16.79 ± 0.7	<0.0001
PMN (%)	71.46 ± 1.03	80.87 ± 0.96	<0.0001
Hemoglobin (g/dl)	12.80 ± 0.17	11.38 ± 0.24	<0.0001
Anemia (g/dl)	2.31 ± 0.28 (22/102)	2.26 ± 0.21 (59/84)	NS <0.0001
CRP (mg/dl)	59.4 ± 3.26	122.2 ± 8.1	<0.0001
ESR (mm/1h)	55.5 ± 1.9	78.1 ± 2.3	<0.0001
HbA1c (%)	9.6 ± 0.2 (93 cases)	10.4 ± 0.2 (67 cases)	0.0112
Glycemic index (mg%)	241.4 ± 11.8	268.4 ± 13.7	NS
Creatinine (≥1.5mg%)	3.24 mg% (N=11)	2.58mg% (N=20)	NS

TABLE 3. Biological parameters changes in soft tissue infections

though the differences between the hemoglobin levels and the severity of the infections in the two groups seem interdependent, we must underline that normal values of hemoglobin between genders, male/female ratio and minimum/maximum hemoglobin values (Hb <12g/dl in female and Hb <13g/dl in male) can affect the relevance of the finding. We take into account the real value of the anaemia, calculated as the difference between the minimum level of the normal value of haemoglobin level (differentiated for male/female) and the actual haemoglobin value for every patient. The comparison of the determined values does not illustrate a statistical significance between the two groups ($p=0.617$). However, Fischer's exact test for probability of anemia incidence in severe infections group (59 out of 84 patients) compared with anemia incidence in low severity infections group (22 out of 102 patients) indicates a high statistical significant association of anemia with the severity of the infection. ($p < 0.0001$, OR 0.1165, 95 CI 0.059 – 0.226). □

DISCUSSIONS

Epidemiological studies centered on infectious condition topic demonstrate that the incidence of the infections in diabetes patients is higher than in non-diabetic free persons (2, 3). A new concept in recent literature indicates that the high frequency of the infections in diabetic patients can represent, after micro and macroangiopathy, the third complication of the diabetes (3). Also, infectious episodes in these patients are more severe and dragged leading to a high mortality rate among them (3,4,5). Our study shows 40% severe infections from total.

The main reasons for high exposure to infections in diabetic patients are related to host and pathologic agents. First risk factor – high glycemia index can be either the reason for high propensity or the effect in developing infectious process (6,7). The medical literature sustain a direct relation between the level of metabolic control and the receptivity to infections (8, 9). Hiperglycaemia represents an independent predictive factor of the complications to the infection, decreasing it below 200 mg% that being a solution for a short term control of the infectious risk in diabetic patients (10) by maintaining normal defense mechanism.

Other authors consider that the high glycemia index is more likely the effect rather than

the cause of the infections and risk can be correlated only with glycosylated hemoglobin levels (8).

Our study results indicate indeed that glycemia index mean is above 200 mg/dl – 241 mg/dl in low severity infections group and 268 mg/dl in the second group. However it is obvious that we can not statistically correlate the severity of infection with the high level glycemia index or even with HbA1c levels which is a retrospective marker of metabolic balance and the last 120 days values of glycemia index (10, 11, 12). HbA1c is considered by others to have at least a high predictive value on chronic complications of diabetes mellitus (12) and even for acute infectious ones (8).

Another infection facilitating factor in diabetes is represented by macroangiopathy, but more important by microangiopathy, with diminished blood flow at tissue level. As a consequence, the immune cell and free oxygen delivery that stimulate the anaerobic/aerobic pathogens development responsible for the frequent necrotizing infections in diabetes are decreased (13). This can explain high incidence of severe infections associated with macroangiopathy (22 out 84 patients with severe infections have arteriopathy compared with only 15 out of 102 from low severity group).

According with immune response in diabetic patients numerous studies reveal that the deficit of PMN function is correlated with hiperglycaemia (14), a reduction in the life of PMN in diabetic serum (15). There is no correlation of PMN deficit with age, gender, chronic complications of metabolic disorder or type of diabetes (16). Our research indicates the possibility of a significant correlation between leucocytes count, free PMN rate and the infections severity in diabetes patients.

Anemia associated with the severe infections has a powerful statistical significance in our study. There are two reasons why anemia is present in many patients in the high severity group: first, a decrease in number of red cells due to sepsis and haemolysis; second, anaerobic germs development is favored by lack of free oxygen at tissue level due also to the decrease in the number of red cells (13).

It is well known that systemic inflammatory response and sepsis reduce the production rate of certain protein fractions (albumin, transferin, fibronectin, retinol binding protein) and accelerate, through inflammatory cytokins (IL-1,

TNF- α , and especially IL-6), the production rate of acute phase protein (CPR, haptoglobin, A type serum amyloid, C3 complement fraction, α 1 antitrypsin).

Prospective studies showed that CPR is significantly increased in sepsis while favorable evolution of infection decreases its level, qualifying it as the most statistical predictive factor (17). High level of CPR at admission along with procalcitonine and C interleukine (18,19) indicate the presence of sepsis and systemic inflammatory syndrome pointing to a follow-up to the discovery of the septic location (20). The same approach but with low sensibility and specificity can be seen for serum fibrinogen and ESR levels. Our study shows in addition a significant correlation of increased levels of CPR and ESR and the severity of infection in diabetic patient and may represent a starting point for establishing a multifactorial correlation and a prognostic score to assess severity of soft tissue infection. This is important as often a clinical aspect is not always correlated with depth and type of involved structures and even less with real spread.

Increased morbidity and mortality associated with infectious diseases is more evident in ICU, in diabetic patients with ketoacidosis, as infections are by far the most frequent cause of metabolic imbalance (6). In these patients acute metabolic complication was induced by infection in 26% to 77% of cases (21) and in deceased (6%) infection was the cause of mortality in 43% of cases (22). In our study we counted 10 deaths in the whole group (5.37%). They were determined mostly by necrositing

infections. From 84 patients in group two (high severity infections group) 8 patients (9.52%) died mainly due to severe sepsis, septic shock and multiple organ failure. \square

CONCLUSION

Our study confirmed the presence of risk factors for soft tissue infections in diabetic patients and highlighting the significant correlation between some of these factors and severity of infections, defined by infection spread and depth of the anatomical structures involved (skin, fascia, muscles).

Male diabetic patients with soft tissue infection and uncertain severity have a higher risk to develop a necrotizing infection with a more severe evolution than a nonnecrotizing infection. The relation between the patient age, diabetes duration, presence of arteriopathy and soft tissue infections is clear but without statistical significance.

Leucocytosis, neutrophilia, inflammatory syndrome markers (CPR, ESR) as well as anemia can be used as diagnostic evaluation tools being strongly correlated with the severity of the soft tissue infections.

As a conclusion, the assessment of some clinical parameters and biochemical indices at admission point can allow the evaluation of the severity of the infection.

The need for operative management in severe infections is absolutely necessary, and the lesions can be successfully treated if the surgeon quickly determines the severity of the infections. \square

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