

Erysipelas in breast cancer patients after the radical mastectomy

Research article

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Abstract: Erysipelas is a bacterial cellulitis usually associated with Streptococcal infection. It may appear as a complication following mastectomy and radiotherapy for breast cancer. The study involved 17 cases of erysipelas of the upper limbs with a median age of 62 years. Here we described the clinical, therapeutic and evolutionary aspects of erysipelas. Our results indicated that the erysipelas appeared with an average of 9 years after mastectomy and was recurrent in three patients (17.64%). It is associated with obesity in 42% and arterial hypertension in 52.9% of patients with breast cancer after radical mastectomy. Breast cancer patients in advance stages of disease at presentation (T2+ T3) are significantly more subject to erysipelas in comparison to those patients with locoregional stage of disease at presentation (T1), Mann Whitney U-test, ($p < 0.05$). All patients had complete response to antibiotics. The recurrence occurred in 2 patients (11.76%) who underwent radiotherapy with adjuvant tamoxifen and in one patient who underwent chemotherapy and radiotherapy combined. Based on these results it is possible to suggest that patients who received radiotherapy may have an additional risk factor for developing lymphedema and erysipelas

Keywords: Breast cancer • Erysipelas • Lymphedema • Mastectomy • Radiotherapy • Antibiotics

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1. Introduction

Erysipelas (from the Greek: erythros 'red'+ pella, skin) is also known as St. Anthony's Fire. Erysipelas is a bacterial cellulitis usually associated with Streptococcal infection A, C, or G which commonly causes edema [1,2]. It is a sudden illness that presents with painful areas of erythema and can enlarge with well-defined margins [3]. General symptoms and signs such as fever, chills, and malaise together with regional lymphadenopathy, and laboratory findings including leukocytosis, elevated C-reactive protein (CRP), or erythrocyte sedimentation rate (ESR) are usually present. Further bacteriological tests are not necessary to establish the diagnosis and serology is not often performed since most cases are assumed to be caused by *Streptococcus* [3]. Erysipelas is usually diagnosed from the characteristic clinical appearance of the rash. It may appear as a complication

following mastectomy and radiotherapy for breast cancer [4]. Lymphedema is a well known risk factor for developing erysipelas of the upper limbs in women treated for breast cancer.

Mastectomy and radiotherapy can affect the lymphatic circulation favoring the obstruction and progressive destruction of lymphatic communication, that leads to lymphatic stasis which results in lymphedema. Tissue involved in lymphostasis appears susceptible to infection, which in turn can worsen the lymphatic disfunction. Once lymphedema is established, the affected arm is subject to erysipelas developing from minor infections such as paronychia and folliculitis. However, this complication in breast cancer patients are relatively rare and only few cases are reported in literature but it should not be underestimated, because it can be recurrent in some patients and have negative impacts on long term quality of life. [5]

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Since, erysipelas is a highly classical complication of lymphedema usually with recurrent forms the aim of this study was to analyze clinical, therapeutic and evolutionary aspects of erysipelas in our cohort after radical mastectomy.

2. Patients and methods

We conducted a retrospective study of 17 patients with erysipelas of the upper limbs during a three year period, from January 2006 to December 2008 due to previously diagnosed breast cancer. All patients were followed up during the control examinations at the Institute for Oncology and Radiology of Serbia. We have selected our patients consecutively as they had visited the Institute, 3 of the subjects arrived for a planned follow up and 14 patients came due to the erysipelas.

We recorded the age, past medical history, clinical and laboratory findings, treatment and outcome from database at Institute of Oncology and Radiology. The local ethic committee approved the use of clinical and laboratory data for our research. Laboratory parameters such as white blood cell (WBC) count, ASTO (antistreptolysin O) titer and sedimentation rate on admission and discharge day were recorded, when available. Diagnosis was achieved by clinical evaluation. The criteria for the erysipelas were acute fever with a sharply demarcated, warm and indurated painful erythema. Lymphedema was measured by water displacement. All patients were followed up after recorded erysipelas through the check up ambulance of our Institute by both specialist of internal medicine and surgery.

2.1. Therapy

After primary surgery, 6 patients had chemotherapy (all of them received FAC chemotherapy, 5-fluorouracil 500 mg/m², adriamycin 50mg/m², cyclophosphamide 500mg/m² in 6 cycles) followed by postoperative radiotherapy (42,5 Gy in 16 fractions), 7 patients had postoperative radiotherapy with adjuvant tamoxifen and 4 patients had adjuvant tamoxifen only. All patients have completed adjuvant treatment and were considered to be in NED (no evidence disease) stadium.

3. Statistical analyses

The clinical data were collected from medical charts and then analyzed by non-parametric assay (Mann-Whitney U-test).

Table 1. Patients characteristics

| | Number | Percentage |
|--------------------|--------|------------|
| Tumor size | | |
| T1 | 5 | 29.5% |
| T2 | 10 | 58.8% |
| T3 | 2 | 11.7% |
| Nodal status | | |
| N1 | 6 | 35.4% |
| N2 | 9 | 52.9% |
| N3 | 2 | 11.7% |
| WBC increased | 17 | 100% |
| ASTO positive | 6 | 35% |
| Sedimentation rate | 17 | 100% |
| Therapy | | |
| Hemo + Radio | 6 | 35% |
| Tamoxifen +Radio | 7 | 41% |
| Tamoxifen only | 4 | 24% |

Table 2. The patient's co-morbidity

| Diagnosis | No of patients | Percentage |
|-----------------------|----------------|------------|
| Diabetes type II | 5 | 29.2% |
| Obesity | 7 | 41.2% |
| Arterial hypertension | 9 | 52.95% |
| Smoking | 0 | 0.00% |
| Family breast cancer | 0 | 0.00% |

4. Results

The median age of our patients was 62 years, ranged from 48 to 76 years. Other patients characteristics ARE presented at the table (Table 1). Association of other diseases with erysipelas in breast cancer patients is shown at Table 2. No association was found with smoking and family related breast cancer diseases. Median BMI (body mass index) in our patients with erysipelas was 27 kg/m².

All our patients had undergone radical mastectomy according to Madden with lymphadenectomy for breast cancer. The period from surgery intervention to erysipelas appearance was 6 to 12 years with average 9 years. In our cohort the erysipelas was recurrent in three patients. Homolateral lymphedema of superior limb preceded erysipelas in all our patients. Two patients underwent bilateral mastectomy and they both developed bilateral erysipelas. All other patients developed homolateral erysipelas. Axilla involvement was recorded in 9 patients (52.9%).

Figure 1. Acute phase of erysipelas infection of the right arm showing redness and swelling.



Figure 2. Recovery phase of erysipelas after treatments with antibiotics.



The diagnosis of erysipelas was clinical and presented as a warm, indurated, sharply demarcated and painful erythema (Figure 1). The portal of entry in 40% of patients was post traumatic wound and in the rest of patients it couldn't be detected at the moment of diagnosis. All patients had increased white blood cells count (median values of $9.8 \times 10^9/l$ for 17 patients at diagnosis) and elevated sedimentation rate in laboratory findings (median values 45, range from 29 to 98). In 6 patients (35%) ASTO (antistreptolysin O) titer was positive and became negative six weeks after the treatment. The duration of clinically evident erysipelas was 1 to 5 days with an average of 2 days.

Thirteen patients were treated with erythromycin 1500 mg orally, for eight days, with complete response. Four patients received ceftriaxone 2 g intramuscularly, with locally applied 3% boric acid solution, for seven days, also with complete response. Representative figure was shown (Figure 2). None of the patients had physiotherapy as a measure of treatment.

During the period of three years, the recurrence occurred in 2 patients (11.76%) who underwent

radiotherapy with adjuvant tamoxifen and in one patient (5,89%) who underwent chemotherapy and radiotherapy combined. The recurrence of erysipelas at one patient had occurred after one year and at two patients after two years.

5. Discussion

Recurrent erysipelas has been described in literature and can occur not only in breast cancer patients [1]. The large number of studies were done to identify the potential risk factors and to establish the prophylactic measures [1]. Previous study indicated that erysipelas is more prevalent among young and the elderly people with most frequently located on the lower extremities [3] in comparison to healthy controls.

We have analyzed 17 patients with erysipelas of the upper extremity after breast cancer therapy with an average age of about 62 years. All examined patients in our study, underwent radical mastectomy with homolateral lymphadenectomy.

Erysipelas is a well-known complication of surgical and radiotherapy for breast cancer [4]. From investigated patients in our study erysipelas was evident in 4 (24%) received only tamoxifen and 13 (76%) of them had postoperative radiotherapy and hemiotherapy.

Both radiotherapy and hemiotherapy can affect lymphatic circulation that may result in lymphedema which is the main risk factor for developing erysipelas. Despite the relative frequency, there are few recent data on the epidemiological and clinical characteristics of erysipelas in breast cancer contrary to erysipelas in general populations [3]. Previous studies show that lymphedema appeared several years after mastectomy and postoperative radiotherapy with prevalence up to 32.5% in several study [4,5]. Only one study based on 7 cases showed that erysipelas can appear between 10 months and 6 years after completion of loco-regional therapy for breast cancer. Also, these authors postulated that lymphedema in addition can precede development of the other secondary complications, such as erysipelas infection of the upper limb [8]. Only one study performed in Brazil, with the mean follow-up time about 1 year showed rate of 4.5% of complications of breast cancer patients.

Developing lymphedema in our group of patients was recorded approximately 9 years after primary oncology treatment. The majority of patients in our study with late erysipelas had obesity (41.2%) and arterial hypertension (52.95%). We postulated that these diseases can be additional risk factor for developing late erysipelas in our breast cancer patients. Previous study indicated that

no association was observed with diabetes, alcohol, or smoking in patients with erysipelas of the leg [1]. Similar to previous reported data we also didn't show association with smoking and family associated breast cancer in our study. Results from many studies indicate that prevention of risk factors is very important to avoid lymphedema formation [6] that agree with our findings.

The development of late lymphedema in breast cancer patients can be significantly associated with the number of lymph nodes removed and type of postoperative radiotherapy [7]. Also, it has been shown that sentinel biopsy of axillary lymph nodes decreases the incidence of lymphedema and erysipelas [8].

Here we report that erysipelas was associated with breast cancer patients in advanced stages of disease at presentation (T2 + T3) in 70.5% cases, that is significantly different (Mann-Whitney U-test) in comparison to T1 stage at presentation (29.5%).

Regarding the treatment of patients with erysipelas, diverse results were reported in literature [3,4,9,10]. Treatment with erythromycin is not usual but efficient. The treatment for our patients during acute phase was an antibiotic. All patients had complete clinical responses to macrolide antibiotics and cephalosporines (that were given in order to avoid adverse reactions of penicillin) in contrast to Penicillin G— which was the treatment of choice in some other studies [3]. In comparison to Penicillin treatment, in our study we have complete responses in all patients (100 %). Based on our experience, we obtained regression of signs and symptoms of erysipelas approximately 2 days after initiating antibiotic treatment. The application of penicillin has been recommended in patients with erysipelas, but

one study showed regression of symptoms only in one patient after penicillin application [9].

Prevention of erysipelas requires avoidance of trauma and treatment of venous and lymphatic stasis in patients with or without breast cancer. In this sense, trauma, excessive heat, constrictive clothing, and exaggerated exercise should be avoided and weight gain should be discouraged. Previous study indicated that sentinel lymph node biopsy can also reduce the rates of axillary lymph node dissection in clinically node negative breast cancer by 70%, and thus should reduce the risks of erysipelas [11]. For patients with recurrent erysipelas authors recommend antibioprohylaxis as the effective preventive measure, but clinician should be aware that prophylaxis does not prevent erysipelas in all cases [12].

Although the outcome was favorable in all our patients, the recurrence occurred in three patients during the three years period of follow up.

Based on our and previous findings, surgeons, oncologists, and primary care physicians should be aware of the danger of erysipelas, especially in patients with lymphedema, increased body mass index, arterial hypertension, and should give recommendation to the patients how protect themselves against any injury.

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