Microbial Surveillance for Sources of Sepsis in Burned Patients: One Year Prospective Study

SALAH NASSER, M.D.*; KARIM KHALIL EL-LAMIE, M.D.*; KHALID M. EL-SHERBINY, M.D.*; AHMED F. EL-SHERIF, M.D.*; ABD EL-AZIZ HANAFY, M.D.* and RANDA R. MABROUK, M.D.**
The Departments of Plastic & Reconstructive Surgery* and Clinical Pathology**, Faculty of Medicine, Ain Shams University.

ABSTRACT

The aim of this one year prospective study was to investigate the potential sources of sepsis in burned patients. One hundred and fourteen consecutively admitted patients with moderate and severe burns were included in the study. Extensive microbial work up was performed for suspected cases of sepsis where samples from surface swabs, biopsy of wounds with local signs of infection, sputum, catheter tips of central lines, blood samples and urine samples were collected and examined. The surface swabs were found to be positive in 111 cases (98.1%); pseudomonas aeruginosa was isolated in 77.2% of cases. Sepsis was suspected clinically in 53 patients but confirmed microbiologically in 46 (40.35%) patients only. Pneumonia was found to be the most prevalent source of sepsis in these patients. Invasive burn wound sepsis followed by catheter-associated infection was next in frequency as sources of sepsis. Blood stream infection diagnosed by positive blood cultures in 13 cases was found to be secondary to catheter-associated infection in 9 cases and invasive wound infection in four. This study showed that, the incidence of invasive burn wound infection has declined with increase in pneumonia and catheter-associated sepsis in our burn unit. In conclusion, this work has defined the specific sites that should be monitored in burned patients and emphasized the need for routine surveillance procedures for expected different sources of sepsis, to provide early identification of organisms and to guide perioperative or empiric antibiotic therapy.

INTRODUCTION

Sepsis remains a significant factor affecting morbidity and mortality in burned patients [1]. Infection is directly or indirectly responsible for 95% of deaths that occur more than two days after burn injury [2]. Plastic surgeons are concerned more with invasive burn wound sepsis predisposed to by destruction of the natural protective barrier and immune system dysfunction [3,4]. It can occur in non-excised and granulating burn wounds [5,6]. Early excision of the burn wound has resulted in invasive wound infection now being less likely to be the primary source for sepsis in burns patients. Over the last two decades, sepsis has been more often secondary to catheter-related infection or pneumonia rather than a result of the burn wound itself [7]. The American Burn Association Consensus Conference on 2007 considered sepsis as a presumptive diagnosis where antibiotics are usually started and a search for a cause of infection should be initiated [8]. Specific sites of infection that are particularly important for burn patients include, burn wound infection, bloodstream infection, pneumonia and urinary tract infection. To ensure early and appropriate therapy in burn patients while sparing most patients exposure to unnecessary antibiotics, a frequent surveillance of microorganisms in the burn wound, blood stream, sputum, urine and intravascular devices and a regular update of their antibiotic resistance pattern are essential to maintain good infection control programs in the burn unit. In this prospective study we investigated the potential sources of sepsis in burned patients.

MATERIAL AND METHODS

This one year prospective study was conducted at the Burn Unit, Plastic Surgery Department, Ain-Shams University Hospitals during the period from the first of January to 31 of December 2008. A total number of 138 consecutive patients were admitted according to our burn unit criteria [9]. Of these 114 patients of both sexes, with moderate and severe thermal burns were included. Neonates and elderly above the age of 60 years, patients with electrical or chemical injuries and patients who died in the first 48 hours of admission were excluded from the study.

All patients were resuscitated based on Parkland’s formula guidelines using crystalloids in the first 24 hours. Plasma was given from the second day. Nutritional and metabolic support was initiated with early enteral feeding based on the body weight and surface extent of burn, using Curreri’s formula for adults and Sutherland’s formula for children.
A wide pore peripheral line is inserted, preferably in non-burned area [11]. Central venous catheters or arterial lines were inserted by the intensive care specialist when indicated. These catheters were not changed routinely and were removed if there was no further indication and in cases of displacement or suspected catheter infection.

Endotracheal intubation is done for patients with inhalation injury diagnosed with fiberoptic bronchoscopy or to bypass obstruction caused by supraglottic edema. It is also done for patients who develop adult respiratory distress syndrome (ARDS) requiring ventilatory support [12].

Urinary catheterization for monitoring urine output was done for all patients during the resuscitation phase and in cases admitted to the ICU for cardiopulmonary support.

Local wound care is done by daily topical application of 1% silver sulphadiazine cream. Early excision and skin grafting was performed within the first 5 days for full thickness and deep dermal burns of the hands and for 5-10% of the burned areas per session when the patient is hemodynamically stable. Otherwise, staged excision and grafting is done. Coverage is done by autografts, allograft and/or amniotic membrane depending on the condition of the wound bed and donor site availability. Wounds were inspected daily during dressing change for the amount of discharge and for any change in the wound character, early eschar separation, or skin graft loss.

Prophylactic empirical antimicrobial therapy was given for severely burned patients in the form of cephalothin, amikin and metronidazole from the first day of admission. Otherwise, antimicrobials were given only in the perioperative period. The empiric antimicrobial therapy is based on the burn unit antibiogram. Specific antibiotic is given once the pathogen is isolated from the source of sepsis.

**Sepsis in burned patients is diagnosed by the presence of at least 5 of the following systemic criteria [13]:**

- Tachypnea (>40/minute in adults).
- Hypotension.
- Oliguria.
- Hyperthermia (>38.5°C) or hypothermia (<36.5°C).
- Leukocytosis (>15 000/mm³) or leucopenia (<3 500/mm³).
- Thrombocytopenia (<50 000/mm³ or if falling rapidly).
- Prolonged paralytic ileus.
- Altered mental status.
- Unexplained acidosis, hyperglycemia, or hypoxia.
- Progressive renal failure or pulmonary dysfunction.

**All suspected infections were registered and followed carefully by extensive microbial work-up:**

- A surface swab is taken routinely every week and whenever there were local or systemic signs of sepsis. Wound biopsy is taken for bacterial count and histological examination if there are local signs of invasive infection and systemic signs of sepsis. Invasive burn wound infection is diagnosed if bacterial count exceeds 1x10⁵/gm of tissue and bacteria are detected in the viable tissues [14].
- All central venous catheter tips were cultured if there is sepsis with unidentified source and the central venous catheter was in place for 48 hours. Catheter related infection is diagnosed by isolation of pathogenic bacteria with simultaneous positive blood culture for the same pathogen from a separate vein [8].
- Sputum samples were collected by sterile aspiration catheters and cultured in cases of pneumonia diagnosed clinically and radiologically [15]. Adequacy of the samples was confirmed by microscopic screening for saliva [16].
- Urine samples for cultures were collected from the rubber catheter for all cases requiring catheterization for more than 72 hours [17]. Urosepsis is diagnosed if bacterial count exceeds 1x10⁵/ml and pus cells exceed 3 / high power field.
- At least two blood cultures are done in the presence of signs of sepsis and suspected blood stream infection whether primary or secondary to infection in another site [8].

**RESULTS**

The study was conducted on 114 patients with moderate to severe thermal burns, 64 males and 50 females. Thirty one patients (27.2%) had smoke inhalation injury. The median age for the included patients was 21.8 years (range 1-59). Median TBSA burn was 23.3% (range 13-95%), with median length of hospital stay 13 days. All these patients exhibited signs of systemic inflammatory response syndrome (SIRS). The outcome of surface swabs taken from the wounds of these patients is shown in Table (1). Swabs were positive with bacterial
colonization in 111 cases (98.1%) at a time during their stay in the unit. Pseudomonas aerogenosa was isolated either separately or in association with another pathogen in 88 cases (77.2%).

Sepsis was suspected clinically in 53 patients. Microbial work-up was done for isolation of pathogenic bacteria from wound biopsy, the central venous catheter, sputum, urine or blood. More than one source was investigated in each patient. Sepsis was confirmed microbiologically in 46 (40.35%) patients. The sources of sepsis were the burn wounds in 10 cases, the central venous catheters in 9 cases and pneumonia in 27 cases including ventilator associated pneumonia (VAP) (Table 2, Fig. 1).

Patients with invasive burn wound infection exhibited typical local signs of sepsis (Figs. 2,3). Invasive infection was documented in these cases by wound biopsy bacterial counts exceeding $1 \times 10^5$/gm of tissue and histological detection of bacteria in the viable tissues (Fig. 4). Pseudomonas aerogenosa was isolated from all biopsies. Blood stream infection was secondary to invasive burn wound infection in 4 cases and catheter related infection in 9 cases. Although 51.02% of examined urine samples were positive for pathogenic bacteria, none of these satisfied the criteria of urosepsis.

<table>
<thead>
<tr>
<th>Isolated organism(s)</th>
<th>Number of patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>74</td>
<td>64.91</td>
</tr>
<tr>
<td>Pseudomonas +</td>
<td>12</td>
<td>10.53</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>2</td>
<td>1.75</td>
</tr>
<tr>
<td>Pseudomonas +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph. Aureus</td>
<td>11</td>
<td>9.65</td>
</tr>
<tr>
<td>Klebsiella + Pneumococci</td>
<td>2</td>
<td>1.75</td>
</tr>
<tr>
<td>E.Coli</td>
<td>2</td>
<td>1.75</td>
</tr>
<tr>
<td>Staphylococcus Aureus</td>
<td>8</td>
<td>7.03</td>
</tr>
<tr>
<td>Negative cultures</td>
<td>3</td>
<td>2.63</td>
</tr>
</tbody>
</table>

Table (1): Microorganisms isolated from the surface swabs of burn wounds.

Fig. (1): Incidence of different types of secondary sepsis in the study group.

Fig. (2): Blackish discoloration of the burn eschar caused by invasive wound infection.

Fig. (3): Blackish spots of infection in excised burn wound.

Fig. (4): Pseudomonas aeruginosa, identified as Gram-negative bacilli invading viable tissues [Gram-stain and 1000 X magnification].
DISCUSSION

Despite recent advances in the use of topical and parenteral antimicrobial therapy and the practice of early tangential excision, bacterial infections remain a major problem in the management of burn victims today [18]. Most burn related deaths in modern burn units occur because of septic shock and organ dysfunction rather than hypovolemic shock [1]. Infectious complications in patients with severe burns are due to thermal destruction of the skin barrier, depression of local and systemic host cellular and humoral immune responses, the possibility of gastrointestinal translocation and the presence of invasive catheters and tubes [3,4,11]. Burn sepsis is differentiated from the (SIRS) in the presence of an identifiable source of sepsis and from septic shock by the response to adequate volume resuscitation [19]. In this study, sepsis was suspected clinically in 53 patients while identifiable cause of sepsis was documented only in 46 (40.35%) patients, probably because most of the burn patients exhibited the criteria of (SIRS). These criteria are non-specific and can be elicited in the absence of infectious causes [8,20].

The burn wound surfaces are sterile following thermal injury. Eventually, they become colonized within the first 48 hours by gram positive bacteria located in hair follicles and sweat glands. After an average of 5 to 7 days, these wounds become colonized by gram negative bacteria derived from the host’s gastrointestinal and respiratory tracts and/or from the hospital environment [21-23]. Invasion of microorganisms into the tissue layers below the dermis may result in bacteremia, sepsis and multiple organ dysfunctions [24-26]. Clinical diagnosis of invasive burn wound sepsis relies on regular monitoring of the vital signs and daily wound inspection during dressing change [14]. In this study, surface swabs were positive in 98.1% of cases. Pseudomonas aerogenosa was the prevailing microorganism, being isolated in 77.2% of surface swabs and 100% of wound biopsies. Invasive burn wound sepsis was diagnosed clinically in 10 cases. This number represents 8.7% of the studied burn patients and 21.7% of cases of sepsis. Clinical diagnosis was confirmed by biopsy counts and histological examination. It was demonstrated that quantitative culture of 1x10^5 or more bacteria per gram of tissue correlated with high (75-83%) mortality rate [26-28]. Mortality among patients with invasive burn wound sepsis in our study was 90% which correlates with previous studies. Invasive burn wound sepsis is life-threatening and requires urgent wound excision, despite of the risk of dissemination of infection and blood loss [8,11].

Pulmonary complications are common in patients with inhalation injury. Burned patients with severe inhalation injury requiring prolonged intubation are at risk of developing ventilator associated pneumonia (VAP), usually caused by antibiotic-resistant bacteria [29,30]. This was defined as pneumonia that develops more than 48 hours in mechanically-ventilated patient without clinical evidence of pneumonia at the time of intubation [13]. It was recommended to do bacterial count of the bronchoalveolar lavage fluid and to confirm the presence of VAP if more than 1x10^4 colony forming units (CFU) were detected [31]. We relied upon clinical diagnosis of pneumonia and confirmed by isolation of the pathogen. In our study, the incidence of pneumonia was 23.7% (n=27) and cultures for sputum and endotrachial tubes were positive for pathogenic bacteria in 81.8% of examined cases (n=27/33). This figure falls within the range of incidence of nosocomial pneumonia (10-65%) in the intensive care units [15,32]. Invasive diagnostic bronchoalveolar lavage did not change the overall

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Source of sample</th>
<th>Number of samples</th>
<th>Positive cultures</th>
<th>Negative cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Number</td>
<td>Percent</td>
</tr>
<tr>
<td>Invasive burn wound infection</td>
<td>Burn wound biopsy</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Catheter related infection</td>
<td>C.V. catheter</td>
<td>14</td>
<td>9</td>
<td>64.28</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Sputum</td>
<td>33</td>
<td>27</td>
<td>81.8</td>
</tr>
<tr>
<td>Blood stream infection</td>
<td>Blood</td>
<td>35</td>
<td>13</td>
<td>37.14</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>Urine</td>
<td>49</td>
<td>25</td>
<td>51.02</td>
</tr>
</tbody>
</table>

Table (2): Different sources of sepsis in the studied group of burns patients.
mortality from VAP [33]. Detection of pathogenic bacteria in the sputum guides antimicrobial therapy. Isolation of pathogenic bacteria from the endotracheal tube after extubation helps in identifying the prevailing bacteria in the ICU, determining the empirical antimicrobial and the infection control policy [34]. However, quantitative lavage may help to differentiate pneumonia from SIRS or ARDS [8].

Burn patients are particularly susceptible to complications associated with prolonged insertion of intravenous and intra-arterial catheters and lines for monitoring, infusion and hyperalimentation [30,35,36]. They have high density of surface microorganisms and are liable to frequent episodes of bacteremia during wound manipulations [37,38]. It may not be possible to insert a catheter in a clean non-burned area in patients with extensive burns and it may be also necessary to cut down into a usable vein or artery through the burn wound itself [11]. Intravascular line or catheter-related sepsis is explained by adherence and migration of burn wound microorganisms along the catheter surface to the tip [39-41]. Catheter-related infections have been reported to affect from 8 to 57% of burn patients [38,39]. In our study, catheter related infection was suspected clinically in 14 burn patients with systemic signs of sepsis without an identifiable source. It was confirmed bacteriologically in 9 of them (64.28%) by simultaneous isolation of the same pathogen from the catheter tip and the blood. The overall incidence is 7.9% (9/114). However, the actual incidence may be higher if we include exit site infection, localized catheter colonization and thrombophlebitis in peripheral veins. Catheter is assumed to be the cause of sepsis if an invasive line is in place for at least 48 hours and the patient is septic, if signs of sepsis resolve within 24 hours after catheter removal, or if the patient has high-grade bacteremia without an obvious focus of infection [8,11]. Treatment of central catheter related infection is prompt institution of empirical systemic antibiotic therapy directed against the burn wound flora, removal of the infected line, relocation of another clean device in healthy non-infected area.

Burn patients may develop a urinary tract infection in association with prolonged bladder catheterization. Patients may develop significant bacteriuria after 72 hours of urinary catheter insertion. However, urosepsis is not a major contributor of sepsis in the burn population because of absence of stasis [42]. In this study, 51% of patients catheterized for more than 3 days had positive urine cultures for pathogenic bacteria but significant pyuria was detected in none of them. Sepsis in these patients was confirmed to result from sources other than the urinary tract. Urosepsis should be sought out in presence of high fever in burn patients and treated by changing catheter and initiation of antimicrobial therapy [8]. The urinary catheter should be removed after the initial period of fluid resuscitation and output monitoring [42].

Blood cultures are essential in determining septic episodes. Invasive burn wound infection leads to transient or intermittent bacteremia from seeding of microorganisms into the blood stream, but a positive blood culture is a late sign of sepsis [43]. Blood stream infection is diagnosed by the presence of at least one positive blood culture in the presence of signs of sepsis [8]. It can be primary or secondary. The later is diagnosed if there is another documented source of infection [44]. In this study, we had 13 cases of blood stream infection, all of which were secondary. These include 9 cases of catheter-related sepsis and 4 cases of invasive burn wound sepsis. The actual number of blood stream infections may be higher as in only 50% of cases of sepsis; there is documented bacteremia [11]. False negative results may be obtained if the specimen is collected at the time of the temperature spikes, if the patient was on antimicrobial therapy, or if the level of bacteria in the blood was low. Also, false positive results may be obtained if contamination occurs during collection of the blood sample [8,31].

This study did not consider bacterial translocation due to mucosal atrophy and gut barrier failure as a cause of sepsis. Specific infections with anaerobic bacteria, Candida (yeast) species and true fungi (mold) like Aspergillus, Mucor and Rhizopus, which have been associated with serious infections in burn patients, were not investigated as in all our patients there was a reliable explanation for the cause of sepsis with isolation of the causative organisms. We also relied on the qualitative cultures for diagnosis of catheter related infection, blood stream infection and pneumonia. Quantitative microbiological techniques which are more costly may lower the relative incidence of sepsis due to intravascular catheters and chest infection.

Summary: In this study, we investigated the various causes of sepsis in moderate and severe burn patients. The main cause of sepsis was pneumonia, including VAP. Burn wound sepsis due to invasive bacterial infection can be definitely diagnosed on clinical basis, especially because the
commonest pathogen is the gram-negative pseudomonas aerogenosa which needs prompt intervention in an attempt to save the life of the patients. Catheter related infection is as common as invasive burn wound infection and should be considered in any patient with systemic manifestations of sepsis, with an intravenous line in place for more than two days. We recommend introduction of quantitative microbiological techniques in our unit to fit the standard recommendations for the definition of sepsis and infection in burn patients.

REFERENCES


