Anaerobic bacteremia in a cancer center

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Abstract. Seventy-five episodes of clinically relevant anaerobic bacterial bacteremia observed in cancer patients were reviewed. Gastrointestinal (22.7%), hematological (22.7%) and female genital tract (18.6%) cancers were the most common underlying malignant diseases. Among 84 strains of strict anaerobic bacteria recovered in the 75 patients, gram-negative rods were isolated in 49 patients (58.3%), gram-positive rods in 29 patients (34.5%) and gram-positive cocci in 6 patients (8%). Bacteroides spp. and Clostridium spp. were the most frequent pathogens (85.7%). Twenty-one episodes of bacteremia were polymicrobial, aerobic gram-positive cocci being the most frequently associated pathogens. When identified, the primary sites were the gastrointestinal tract (40%), the female genital tract (17.3%), skin and soft tissue (14.6%), the oropharynx (12%) and the lower respiratory tract (6.7%). The source remained unknown in 7 cases (9.3%). The overall survival (evaluated 10 days after the occurrence of bacteremia) was 82.5%. There was no difference in mortality between patients with monomicrobial and polymicrobial bacteremia. Pulmonary complications were more frequent in patients with fatal outcome in comparison to patients who survived. The mortality rate of the patients adequately treated was 10.3% compared to 41% for the patients not treated or treated inadequately ($P=0.016, \chi^2$).

Key words: Anaerobes – Bacteremia – Cancer – Bacteroides – Clostridium

Introduction

Anaerobic bacteria account for an important part of the endogenous human microflora and are recognized as relatively common causes of infection. Upper airways and the gastrointestinal and female genital tracts harbor a large number of these bacteria, and therefore are considered as the most frequent portals of entry for anaerobic infections.

Tissue necrosis and breaches of the mucosal barriers are two features frequently encountered in cancer patients producing an appropriate environmental milieu that will permit anaerobic bacteria to invade the host.

Despite these considerations, anaerobic bacteremia in cancer patients is a fairly infrequent event. The recovery of anaerobic bacteria ranges between 5% and 12% of positive blood cultures among unselected non-cancer patients with clinically significant bacteremia [2, 3, 7, 13, 14, 20]. Bacteremia due to strict anaerobes is particularly unusual in granulocytopenic patients representing less fewer 1% of all the bacteremic isolates [7, 8, 15]. From the comparison between previous studies published in the 1970s and early 1980s [11, 14, 17, 22] and those published more recently [7, 13], the incidence of anaerobic bacteremia seems to have declined.

In this study we are reviewing the episodes of anaerobic bacteremia occurring in a cancer hospital over 10 years. Clinical characteristics of the patients and microbiological data are analyzed.

Materials and methods

All records of blood cultures performed between 1979 and 1989 in the microbiology laboratory of the Institut Jules Bordet were reviewed. Over this period, 142 episodes of anaerobic bacteremia were documented, corresponding to 7% of all bacteremic episodes.

Eighty-four charts were available for review from the medical archives and were analyzed. Four patients were excluded because they had no cancer and 5 because bacteremia was caused by Propionibacterium acnes, which was considered to be clinically insignificant.

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Patients who had a strict anaerobic organism, alone or in association with other organisms, isolated from one or more blood-culture sets, were included and considered as significant providing they had clinical manifestations of bacteremia including fever, chills or septic shock, or an evident source of infection.

Multiple isolations of an identical organisms were considered to be single episodes. Brain/heart infusion (BHI) broth (Gibco) was used for anaerobic blood cultures. Specimens were inoculated on Columbia blood agar and incubated anaerobically using a Gaspack anaerobic system (BBB, Cockeysville). Pathogens recovered from blood cultures were identified according to standard procedures.

For susceptibility testing, we used the Neo-sensitabs agar-disk diffusion method (Rosco Diagnostic Teestrup, Denmark). The inoculum was prepared directly by picking up several colonies from a fresh agar plate and suspending them in the BHI medium to a final concentration of $10^7$-$10^8$ colony-forming units/ml.

After adjustment, the strains were applied with cotton swabs to the surface of Columbia blood agar. Neo-sensitabs were applied and the plates were incubated in anaerobic conditions. Zones of inhibition were measured after 24-48 h of incubation at $37^\circ$C and compared with two different interpretative zone standards, one for the fast-growing and another for the slow-growing anaerobic bacteria according to the manufacturer [4].

The underlying cancer disease, age, sex, predisposing factors, clinical characteristics, occurrence of granulocytopenia (polymorphonuclear neutrophils, PMN $<$1000/µl), primary site, types of associated pathogens, in vitro susceptibility, treatment and outcome were recorded.

Cancer disease was considered to be evolutive if rapid clinical or laboratory progression was evident within 2 weeks and not evolutive if only localized or no progressive disease was detected.

Only systemic cancer chemotherapy (including steroid treatment) and surgical treatment performed within 30 days before the onset of anaerobic bacteremia were considered as predisposing factors.

The determination of the primary source of bacteremic isolates was mainly based on clinical data and, whenever available, confirmed by microbiological data.

Bacteremia was considered polymicrobial if two or more bacterial species were isolated from blood cultures within a 24-h period [16].

Breakthrough bacteremia was defined as persistent isolation of organisms for 5 days or recurrent bacteremia within 10 days of treatment end that occurred despite appropriate antimicrobial therapy [21].

Patients were considered to be in septic shock when they had signs and symptoms of hemodynamic instability with systolic blood pressure below 90 mm Hg (12 kPa) or a decrease of at least 40 mm Hg (5.3 kPa) from baseline despite adequate fluid infusion and without evidence of hemorrhage.

Antimicrobial therapy that includes at least one antibiotic proven to be active in vitro against the anaerobic organism was considered to be adequate. In 12 cases where no sensitive tests were performed, appropriateness of therapy was judged on the sensitivity pattern of various anaerobic species isolated at the Institut Jules Bordet.

Death was considered to be related to bacteremia if occurring within 10 days of the onset of bacteremia unless clinical a pathological data clearly suggested another reason.

**Results**

The mean incidence of anaerobic bacteremia during this study was 3/1000 admissions (range: 1.5-5.6/1000). Anaerobic bacteremia represented 7% of all bacteremic episodes in our hospital.

The characteristics of the patients are shown in Table 1, stratified according to the granulocyte count at the time of bacteremia.

As indicated in Table 1, among 75 patients studied, 51% were female and 49% were male. Their age ranged from 20 to 84 years (mean age 54.4 years).

Thirty-three patients (44%) received chemotherapy and 27 patients (36%) had surgery during the last month preceding anaerobic bacteremia.

Seventeen patients (23%) were profoundly granulocytopenic (PMN $\leq$100/µl) on the day of onset of bacteremia. In 16 patients, granulocytopenia was secondary to systemic antineoplastic chemotherapy and in 1 patient it was consequence of the underlying malignancy.

Three patients (4%) were receiving immunotherapy and 6 patients (8%) corticosteroids. The most common underlying malignancies were gastrointestinal (22.7%), genital (18.7%) and hematological (22.7%). Cancers of the head and neck, lung, urinary tract, breast, skin and soft tissue and miscellaneous cancers accounted for the other 36%.

Malignant disease was considered to be evolutive in 81.3% of the patients and not evolutive in 18.7%.

Among clinical manifestations of bacteremia, fever ($T>$38$^\circ$C) was documented in 61 patients (81.3%) and chills in 20 patients (26.7%). Septic shock occurred in 11 patients (14.7%).

The most probable sources of bacteremia are shown in Table 1. The gastrointestinal tract was predominant (40%), followed by the female genital tract (17.3%), skin and soft tissue (14.7%), the oropharynx (12%) and the lower respiratory tract (6.7%). Only 7 patients (9.3%), all with hematological malignancy, had no source identified.

The site of malignancy correlated well with the source of bacteremia in 80% of patients.

Breakthrough bacteremia was found in 8 patients (10.7%). Among the 17 patients with profound granulocytopenia, 7 (41.2%) had polymicrobial bacteremia.

Antimicrobial therapy included at least one antibiotic proven to be active in vitro against the anaerobic organism was considered to be adequate. In 12 cases where no sensitive tests were performed, appropriateness of therapy was judged on the sensitivity pattern of various anaerobic species isolated at the Institut Jules Bordet.

Death was considered to be related to bacteremia if occurring within 10 days of the onset of bacteremia unless clinical and pathological data clearly suggested another reason.

The distribution of the pathogens identified is shown in Table 2.

Eighty-three strains of anaerobic bacteria were isolated in 75 patients. Gram-negative bacilli were found in 49 episodes (58.3%), gram-positive bacilli in 29 episodes (34.5%) and gram-positive cocci in 6 episodes (7.2%).

*Bacteroides* spp. occurred in 51.2% of the 75 episodes and *Clostridium* spp. in 31%. A similar distribution was seen in gastrointestinal, breast and gynecological cancer while, in patients with female genital tract malignancy, the *Bacteroides* group accounted for 87% of the cases and the *Clostridium* group for only 6.7%.

*Bacteroides* spp. and *Clostridium* spp. accounted for