

The bacteriology of infected malignant ulcers

VO ROTIMI,* FA DUROSINMI-ETTI†

From the Departments of *Microbiology and †Radiotherapy, College of Medicine, Lagos University Teaching Hospital, PMB 12003, Lagos, Nigeria

SUMMARY Infected ulcerated malignant tumours are often foul smelling and covered with necrotic tissue. We have studied 70 patients with infected ulcers; 30 of the underlying lesions in these patients were carcinoma of the breast, and 19 were a variety of skin cancers. Anaerobes were the predominant organisms isolated from individual ulcers. Of the 179 anaerobes isolated, 37 were *Bacteroides asaccharolyticus*, 31 each were *B melaninogenicus* and anaerobic streptococci, 29 *B fragilis*, and 17 *B ureolyticus*. Among the facultative organisms *Escherichia coli* was the commonest and was isolated mainly from patients with carcinoma of the breast. Most infections were mixed, yielding both anaerobes and aerobes and this made interpretation of the role of individual pathogens difficult to assess.

Infected ulcers superimposed on malignant lesions are usually characterised by dirty greyish necrotic sloughs, inflamed margins, and very offensive odour. A number of studies on the role of anaerobes in the aetiology of these infections have provided, indirectly through antibiotic trials, an insight into the type of bacteria that may be present in these lesions.¹⁻⁶

Although anaerobes together with some facultative bacteria can be isolated from these infected ulcers, it is doubtful whether their presence often leads to bacteraemia and subsequent septicaemia.^{7*} However, the isolation of *Bacteroides* spp from blood culture, as an initial finding, may be indicative of some deep malignant lesions, particularly carcinoma of the colon.⁹ As far as we know detailed studies on the bacteriology of infected ulcers superimposed on peripheral malignant lesions have not been reported. In order to provide base line data, we have studied bacteriologically all patients with infected ulcers with underlying malignant lesions admitted to the radiotherapy ward of the hospital.

Material and methods

SPECIMENS

Specimens were obtained from infected ulcers in 70 consecutive patients admitted to the radiotherapy ward for management of malignant lesions which had become secondarily infected and eroded.

Albumin coated cotton wool swabs (Exogen Ltd, Dumbarton Road, Glasgow) were used to obtain wound swabs. They were then broken into Amies transport medium and transported immediately to the anaerobe research laboratory of our hospital. Where feasible, pieces of debrided necrotic tissues were taken into sterile universal bottles and also into steamed cooked meat broth. All specimens were processed within 20 min of taking by a carefully controlled procedure. A set of blood cultures was obtained from the antecubital vein from all patients within the first 24 h of admission.

CULTURE

All specimens were cultured for anaerobic and aerobic organisms using standard laboratory methods. A set of freshly prepared and prerduced selective and non-selective media was used for isolation of the anaerobes: these included cooked meat broth, blood agar (Oxoid), blood agar plus neomycin (100 µg/ml); and BM agar made selective by the addition of kanamycin (75 µg/ml) and 2.5 µg/ml vancomycin.¹⁰ For the isolation of aerobes the following media were used: blood agar (Oxoid), MacConkey agar (Oxoid), Mannitol-salt agar (Oxoid), and crystal violet blood agar. Media used for blood culture were those routinely used in our clinical bacteriology laboratory—that is, brain heart infusion broth (Oxoid) and thioglycollate broth (Oxoid).

INCUBATION

The aerobic plates were incubated in air plus 10% CO₂ at 37°C for 24 h initially and then 48 h when

Table 1 Characteristic features of the cancer patients with infected ulcers

General features of patients						No of patients with the following clinical features				
Site of ulcer	Underlying lesion	No of patients	Mean age (yr)	No of females	No of males	Foul smelling ulcers	Normal body temperature	Temperature of $\geq 38^{\circ}\text{C}$	Leukocytosis (≥ 9000)	Bacteraemia
Breast Skin	Carcinoma	30	43.5	30	0	30	23	7	2	1
	Malignant melanoma	3	40.5	1	2	3	3	0	0	0
	Sarcomas	12	61.7	3	9	11	11	1	0	0
External genitalia	Rodent ulcers	4	40.5	1	3	4	4	0	0	0
	Ca penis	1	60	0	1	0	1	0	0	0
	Ca cervix	5	50.5	5	0	5	4	1	0	0
Axilla	Ca vulva	2	30.0	2	0	2	1	0	0	0
	Carcinoma	4	40.7	2	2	2	4	0	0	0
Antrum	Carcinoma	1	30	0	1	1	1	0	0	0
Oral cavity	Ca tongue	1	17	0	1	1	1	0	0	0
Eye	Retinoblastoma	4	9.5	1	3	3	2	2	1	0
Mandible	Carcinoma	3	36.5	0	3	3	3	0	0	0

Ca = carcinoma.

necessary. The anaerobic plates were incubated anaerobically in the presence of 90% H₂ and 10% CO₂ generated by Gas pak (Oxoid) using the gas generating kit system and anaerobic jars, each equipped with one satchet of 4 g room temperature catalysts (Oxoid Ltd, Basingstoke, England). The jars were controlled biologically using Simmon citrate agar slope seeded with *Pseudomonas aeruginosa* and incubated at 37°C for 48 h and extended for 72 h if necessary. The blood culture bottles were incubated in air at 37°C for 24 h, subcultured, and incubation was then continued for up to seven days with daily inspection.

IDENTIFICATION

All the aerobic micro-organisms isolated were identified by the methods of Cowan¹¹ and API₂₀ system (API System, SA, La Balme Les Grottes, Montalier, Vercieu, France). Representative colonies of the anaerobes were Gram stained and subcultured on to fresh blood agar and BM agar with kanamycin and vancomycin on which metronidazole (5 µg)

discs were placed. They were identified by initial sensitivity to the metronidazole disc and confirmed and speciated by methods already described.^{12,13} All isolates were quantified by a semi-quantitative method previously described.¹⁴

Results

A total of 70 swabs or necrotic tissue specimens obtained from 70 patients were cultured; each patient provided a single specimen. Seventy blood cultures were also investigated.

The general features and clinical characteristics of the patients are summarised in Table 1. All infected ulcers were peripheral, and the underlying lesions were as follows: cancer of the breast (30/70), skin cancers (19/70), cancer of the external genitalia, including exocervix (8), and a miscellaneous group of cancers—axilla (4), eye (4), mandible (3), mouth (1), and antrum (1). Sixty five (92.8%) of the 70 infected ulcers were foul smelling. The body temperature was normal (37.5°C) in 58 (82.9%) of the 70 patients while a temperature of $\geq 38^{\circ}\text{C}$ was recorded in the remaining 12 patients. Only three patients had a leucocytosis. All but one of the blood cultures were negative and that grew *Staphylococcus aureus*.

The micro-organisms, anaerobes and aerobes—isolated from the infected ulcers are shown in Table 2. Anaerobes were the predominant micro-organisms, with a mean score of 4⁺ on a scale of 1⁺–5⁺ estimated by the semi-quantitative method, while the aerobic micro-organisms had a mean score of 3⁺ on the same scale. Of a total of 282 bacterial isolates, anaerobic micro-organisms accounted for 179 (63.3%).

The commonest anaerobe was *Bacteroides asaccharolyticus*, which made up 21% of the 179 anaerobes and 13% of the total 282 isolates.

Table 2 Isolation rate of anaerobes and aerobes from all patients

Species of anaerobes	No of isolates	Species of aerobes	No of isolates
All anaerobes	179	All aerobes	103
<i>B melaninogenicus</i>		<i>E coli</i>	21
<i>ss melaninogenicus</i>	10	<i>Klebsiella</i> spp	3
<i>ss intermedius</i>	21	<i>Pr mirabilis</i>	14
<i>B asaccharolyticus</i>	37	<i>Pr morgani</i>	5
<i>B ureolyticus</i>	17	<i>Ps aeruginosa</i>	8
<i>B fragilis</i>	29	<i>Ps fluorescens</i>	2
<i>B thetaiotaomicron</i>	7	<i>Acinetobacterium</i> spp	3
<i>B ovatus</i>	6	<i>Enterobacterium</i> spp	5
<i>B bivius</i>	4	Group A streptococci	6
Anaerobic streptococci	31	Group G streptococci	2
<i>Eubacterium</i> spp	8	<i>Staph aureus</i>	18
<i>Fusobacterium</i>		<i>Staph albus</i>	13
<i>necrophorum</i>	2	<i>Str faecalis</i>	3
<i>Bacteroides</i> spp	7		

Table 3 Isolation of anaerobes and aerobes from infected ulcers of patients with cancer

Micro-organisms isolated	No of isolates from infected ulcers in the following sites							
	Breast (n = 30)	Skin (n = 19)	External genitals (n = 8)	Eye (n = 4)	Antrum (n = 1)	Axilla (n = 4)	Mouth (n = 1)	Mandible (n = 3)
<i>B fragilis</i>	12	9	5	3	0	0	0	0
<i>B asaccharolyticus</i>	23	11	0	0	0	0	0	3
<i>B melaninogenicus</i> *	19	6	4	0	0	0	1	1
<i>B ureolyticus</i>	13	1	0	0	1	2	0	1
Anaerobic streptococci	16	9	3	2	0	1	0	0
<i>B thetaiotaomicron</i>	7	0	0	0	0	0	0	0
<i>B ovatus</i>	6	0	0	0	0	0	0	0
<i>Bacteroides</i> spp	7	0	0	0	0	0	0	0
<i>Eubacterium</i> spp	8	0	0	0	0	0	0	0
<i>Fusobacterium</i> spp	0	0	0	0	0	0	1	2
<i>B bivius</i>	0	0	4	0	0	0	0	0
<i>E coli</i>	11	4	1	0	0	2	0	0
<i>Pseudomonas aeruginosa</i>	7	3	0	0	0	0	0	0
<i>Proteus</i> spp	9	8	1	0	0	1	0	0
<i>Staph aureus</i>	5	5	3	2	1	0	0	2
<i>Staph albus</i>	7	6	0	0	0	0	0	0
Group A streptococci	5	1	0	0	0	0	0	0
Group G streptococci	2	0	0	0	0	0	0	0
<i>Ps fluorescens</i>	2	0	0	0	0	0	0	0
<i>Kleb aerogenes</i>	3	0	0	0	0	0	0	0
<i>Acinetobacter</i> spp	2	1	0	0	0	0	0	0
<i>Enterobacterium</i> spp	4	1	0	0	0	0	0	0
<i>Str faecalis</i>	0	0	3	0	0	0	0	0

**B melaninogenicus* ss *melaninogenicus* and ss *intermedius*.

Anaerobic streptococci, *B melaninogenicus*, *B fragilis*, and *B ureolyticus* were also common.

Escherichia coli was the most frequent facultative micro-organism, accounting for 20.4% of the 103 aerobic bacteria isolated and 7.5% of the 282 total isolates. *Proteus* spp and *Staph aureus* were frequently isolated.

Table 3 details the distribution of bacterial isolates from infected ulcers associated with particular sites.

Discussion

The results of this study demonstrate the complex bacterial population isolated from infected ulcers superimposed on malignant lesions. These localised infections, although not associated with bacteraemia in this study, represent an interesting model for understanding anaerobic infections. Anaerobes were isolated from all the foul smelling infected ulcers. Most of these anaerobes were black pigmented *B asaccharolyticus* and *B melaninogenicus*, *B fragilis*, *B ureolyticus*, as well as anaerobic streptococci, all of which are known opportunistic pathogens.¹⁵⁻¹⁷ When anaerobes were found in the relatively odourless ulcers they were usually either anaerobic streptococci alone or in combination with *B ureolyticus*.

Mixed anaerobes were present in about 87% of the 70 patients in the present study. The commonest combination was *B asaccharolyticus*, *B*

melaninogenicus, anaerobic streptococci and/or *B fragilis*, and a facultative bacteria. This combination was commonly seen in patients with cancer of the breast or skin. *B fragilis*, anaerobic streptococci, and *B ureolyticus* was the next most common combination.

The finding of facultative organisms, particularly Gram negative bacilli, in association with anaerobes in most of these infections makes the precise role of the anaerobes in ulcers difficult to assess, especially when concurrent associated bacteraemia could not be shown. Most reports presented by other workers on a series of related studies accord well with this observation.^{5,7,8} Investigations by Finegold,⁹ McHenry *et al*,¹⁸ and Finegold *et al*¹⁹ have, however, emphasised the importance of bacteroides bacteraemia as a potentially life threatening condition in patients with cancer. Because these patients are already severely compromised by their advanced lesions, anaerobic bacteraemia may easily develop, especially if any form of surgery is undertaken.

Anaerobic infections in malignant ulcers may represent a specific infective syndrome, like Melleney's synergistic gangrene or necrotising ulcerative gingivitis, from which anaerobes and aerobes can be isolated to the exclusion of anaerobic bacteraemia. Treatment of these types of infection with specific or broadspectrum antianaerobic agents is justified and there have been good clinical responses to these antibiotics in a number of controlled clinical trials already conducted on patients with cancer.¹⁻⁶ The

results of this study may be useful to our clinical colleagues, many of whom have at present no alternative to empirical antibiotic treatment, lacking adequate bacteriological base line data.

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Requests for reprints to: Dr VO Rotimi, Department of Microbiology, College of Medicine, University of Lagos, PMB 12003, Lagos, Nigeria.