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Association of *Pseudomonas maltophilia* with Malignant Lesions

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Infections caused by nonfermentative, gram-negative, rod-shaped bacteria (NFGNR) in 564 patients were reviewed. For comparison, 227 patients with *Serratia marcescens* infections were also studied. Among the patients with NFGNR infections, 24% had some form of malignant solid tumor, and 9% had leukemia and lymphoma. Among the patients with *S. marcescens* infections, 22% had some type of malignant solid tumor, and 8% had leukemia and lymphoma. The frequency of various species of NFGNR (except *Pseudomonas maltophilia* and *S. marcescens*) in patients with a malignancy at the site from which the specimens had been obtained was 5 to 24%. However, 39 of 82 patients (48%) with *P. maltophilia* infections had a malignancy at the site from which *P. maltophilia* had been isolated. There were significantly more *P. maltophilia* infections at the sites of malignant lesions than there were other NFGNR or *S. marcescens* infections ($P < 0.05$).

Pseudomonas maltophilia has been regarded as having relatively little pathogenicity in humans but has been isolated from well and river water, sewage, and various animal by-products. It is clinically linked to wound infections, septicemia, eye infections, and pneumonia (7–9). Nonfermentative, gram-negative, rod-shaped bacteria (NFGNR) (7, 15) and *Serratia marcescens* (4) have been given more attention in selected patients, especially those with neoplastic (17) or hematological diseases (2). I now report the clinical features of patients infected with these strains and the high frequency of *P. maltophilia* in tumor-involved organs.

Japanese patients admitted to or cared for in the outpatient clinics of Kyoto University Hospital and from whom NFGNR or *S. marcescens* were isolated from 1 April 1980 through 31 March 1983 were included in this survey. The records of the patients were reviewed to obtain pertinent clinical data, including age, sex, diagnosis, antibiotic therapy, and any instrumentation associated with the source of infection. Because NFGNR and *S. marcescens* were frequently isolated from patients with mixed infections, it was difficult to determine whether their presence represented a primary, secondary, or commensal role. Therefore, I reviewed only the clinical histories of patients from whom NFGNR or *S. marcescens* was cultured in a pure culture or was the predominant organism in a mixed culture. Each organism was repeatedly isolated from pathological lesions in the presence of objective signs of infection which were ameliorated after appropriate treatment. Multiple isolates from the same patient were counted only once. These organisms were identified by standard laboratory procedures (9, 13).

I studied 564 isolates of NFGNR and 227 isolates of *S. marcescens*, distributed almost evenly throughout the year. Table 1 summarizes findings related to factors known to play a role in individuals from whom NFGNR and *S. marcescens* are isolated. The most important conditions preceding the isolation of NFGNR and *S. marcescens* were malignancy and postoperative status. For NFGNR, 24% of the patients had an underlying malignant solid tumor, 9% had underlying leukemia and lymphoma, and 19% had undergone surgery. For *S. marcescens*, 22% of the patients had a malignant solid tumor, 8% had leukemia an lymphoma, and 20% had undergone surgery (Table 1). The frequency of malignancy in those from whom NFGNR had been isolated was not significantly different from that in patients from whom *S. marcescens* had been isolated.

Table 2 shows the frequency of isolation of various species of NFGNR and *S. marcescens* from malignant lesions, in situ or from specimens in which exudates from malignant lesions were included. Contamination from the malignant lesions was based on positive Papanicolaou stains of the specimens for malignant cells and clinical confirmation of the presence of enough advanced malignant lesions to contaminate exudates from malignant lesions. Of the 82 patients with *P. maltophilia* infections, 39 (48%) had a malignancy at the site from which *P. maltophilia* had been isolated. In these patients, *P. maltophilia* was not cultured from other sites. The number of *P. maltophilia* in malignant lesions was significantly higher than the numbers of other NFGNR and *S. marcescens* in malignant lesions ($P < 0.05$). Clinical information on all 39 patients from whom *P. maltophilia* had been isolated from malignant lesions is as follows (number of patients in parentheses). The sites or types of infection were urinary tract (15), respiratory tract (9), cancerous fistula (5), effusion from cancer (4), carinomatous peritonitis (2), endometritis (1), empyema (1), ulcer on an osteosarcoma (1), and pile-like lesions in the oral cavity (1). The sources of specimens were urine (15), pus (12), bronchial sputum or tracheal aspirate (9), ascites fluid (2), and drainage from empyema (1). The underlying conditions were cancer of the urinary bladder (6), uterus (6), tongue and palate (5), esophagus (4), larynx (4), lung (5), kidney (3), thyroid gland (1), prostate gland (1), rectum (1), pancreas (1), and liver (1) and osteosarcoma (1).

P. maltophilia was isolated directly from pus in the malignant lesions of 14 patients. In one of the patients, the recurrence of cancer after surgery for pharyngeal cancer was detected 1 month after *P. maltophilia* had been isolated from the fistula at the surgical site. In another patient, *P. maltophilia* was isolated directly from the pus on the surface of the osteosarcoma-related ulcer (Fig. 1).

The distinguishing morphological, physiological, and serological features of *P. maltophilia* were first reported by Hugh and Ryschenkow in 1961 (10). Data on *P. maltophilia* infections in relation to malignant lesions have apparently been given no attention. In recent years, there has been an increased frequency of infections caused by NFGNR in patients with malignant lesions (6). This increased incidence

TABLE 1. Clinical data on 564 patients with NFGNR infections and 227 patients with *S. marcescens* infections

Underlying pathology	No. (%) of patients with:	
	NFGNR	*S. marcescens*
Malignant solid tumor	136 (24)	50 (22)
Leukemia and lymphoma	50 (9)	18 (8)
Central nervous system lesions	62 (11)	40 (18)
Postoperative status		
Malignancy	68 (12)	28 (12)
Other	39 (7)	19 (8)
Renal failure	23 (4)	6 (3)
Other	161 (33)	66 (29)

of NFGNR, however, has been reported in relation to the use of cytotoxic drugs, adrenal corticosteroids, and antibiotics as well as to impaired host defenses and leukopenia in patients with malignant lesions.

Data obtained in the present study showed that 50 of the 82 patients from whom *P. maltophilia* had been isolated had an associated malignant disease; in 39 patients (48%), there was a striking association with the malignant lesions in situ, an area from which *P. maltophilia* had been isolated. The frequency of various species of NFGNR (except of *P. maltophilia*) in patients with a malignancy was 5 to 24%. These studies raised interesting questions concerning the diagnostic value of tests for malignant lesions. When a *P. maltophilia* infection develops in patients in the absence of certain predisposing factors for NFGNR (such as a history of prior instrumentation at the site from which the organisms were isolated or long-term antecedent antibiotic therapy), the possibility that the patients may have an associated malignant lesion, occult or manifest, in the infected lesion cannot be neglected.

The following case was characteristic of the striking association between malignant lesions and *P. maltophilia* isolation. The patient, a 46-year-old man, was referred for oral surgery to Kyoto University Hospital because of fungus-like lesions on his palate. Whitish, coated, pile-like lesions were present on the floor of the mouth, and materials from these lesions were cultured. The abundant *P. maltophilia* isolated suggested a malignant lesion, in the absence of the predisposing factors for NFGNR infections. A biopsy of the pile-like lesions led to a diagnosis of squamous cell carcinoma. In this case, the isolation of *P. maltophilia* proved to be a valuable diagnostic tool.

TABLE 2. Frequency of isolation of NFGNR and *S. marcescens* from malignant-tumor-involved organs

Organism	Total no. of isolates	No. (%) of isolates from malignant-tumor-involved organs
Pseudomonas maltophilia	82	39 (48)
Pseudomonas aeruginosa	157	24 (15)
Acinetobacter anitratum	145	7 (5)
Acinetobacter lwoffii	21	5 (24)
Flavobacterium sp.	50	4 (8)
Pseudomonas cepacia	31	2 (7)
Pseudomonas putida	21	3 (14)
Pseudomonas alcaligenes and *Alcaligenes* sp.	26	2 (8)
Achromobacter sp.	20	1 (5)
Serratia marcescens	227	32 (14)

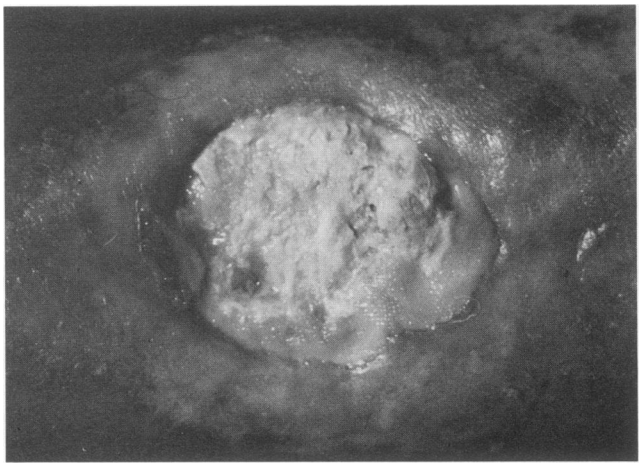

FIG. 1. Appearance of lesions in an osteosarcoma-related ulcer from which *P. maltophilia* had been isolated.

The effect of bacteria on neoplasms is an interesting aspect of the problem of cancer therapy, as microorganisms may be involved in tumor destruction (14, 16). Anaerobic glycolysis is significantly increased in tumor tissue, with a resulting accumulation of lactic acid in this tissue and in the in vivo environment. Spores of nonpathogenic *Clostridium* spp. localize and germinate in neoplasms and produce extensive lysis of tumors without concomitant effects on normal tissue. The poor vasculation of the tumor may provide favorable conditions for the multiplication of anaerobic or microaerobic *Clostridium* spp. (12). Clostridial septicemia from an infection within tumor lesions has been reported (1, 3). *Streptococcus bovis* may be present in fecal cultures from patients with carcinoma of the colon. Klein et al. (11) recommended that patients with *S. bovis* endocarditis be carefully evaluated for possible carcinoma of the colon. Further studies are warranted.

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