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Clinical Significance and Antibiotic Resistance Patterns of *Leminorella* spp., an Emerging Nosocomial Pathogen

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Although *Leminorella* spp., members of the family *Enterobacteriaceae*, were previously isolated from feces and urine specimens, clinical correlates have not been studied. We conducted a retrospective study to investigate the clinical significance and disease spectrum of these organisms, as well as their antibiotic susceptibility patterns. Identification and susceptibility testing were performed by an automated system. Eighteen cases were identified retrospectively during a 28-month period (1/97 to 4/99), representing an incidence of 11 cases per 100,000 patient admissions. The medical records of 14 patients were reviewed. The average patient age was 67 years, and 78% were males. Patients had multiple and diverse underlying conditions which might have predisposed them to infection. *Leminorella* spp. were classified as definite pathogens in 43% of the cases, probable pathogens in 29%, and possible pathogens in 21%. In one case of asymptomatic bacteriuria, the isolate had no clinical significance. All infections but one were nosocomial. Clinical syndromes included urinary tract infection in six patients, surgical site infection in three patients, and primary bacteremia, peritonitis, respiratory tract infection, and soft tissue infection in one patient each. Isolates were uniformly susceptible to imipenem. Other beta-lactam agents had poor activity against the isolates. We conclude that *Leminorella* spp. are significant nosocomial pathogens that are capable of causing a variety of clinical syndromes and are resistant to multiple antibiotic agents.

The genus *Leminorella* consists of gram-negative bacilli belonging to the family *Enterobacteriaceae* and was first described as enteric group 57 in 1982. The generic name is derived from Leon Le Minor, a French microbiologist who has made many contributions to enteric bacteriology as the head of the National Salmonella Center of France. Although strains of *Leminorella* spp. share the general properties of *Enterobacteriaceae*, they exhibit only 3 to 16% DNA homology to other bacteria in this family. Based on genetic differences, they are divided into three taxa: *Leminorella grimontii*, *L. richardii*, and *Leminorella* sp. strain 3 (2).

Strains of *Leminorella* spp. are easy to culture and identify. They are facultative anaerobes which grow on sheep blood and MacConkey agar and are negative for D-mannose fermentation and positive for tyrosine hydrolysis, hydrogen sulfide production, and L-arabinose fermentation.

The clinical significance of *Leminorella* spp. is not clear. There are no reports of infections caused by *Leminorella* spp., and their incidence in clinical specimens is unknown. We initiated this study to investigate the occurrence, clinical significance, infection spectrum, and antimicrobial susceptibility of *Leminorella* spp. in a tertiary care hospital.

MATERIALS AND METHODS

The study was conducted in the Tel Aviv Sourasky Medical Center, a 1,150-bed tertiary care teaching hospital with approximately 70,000 patient admissions per year. The microbiology laboratory processes over 82,500 clinical specimens annually. Identification of gram-negative organisms (including *Leminorella* spp.) and susceptibility testing were performed by an automated system (Microscan; Dade Behring Inc., West Sacramento, Calif.) using a combined gram-negative identification panel and an automated microbroth dilution method (Neg/Urine Combo Panel; Microscan). Criteria for identification acceptance were >85% agreement (in accordance with manufacturer recommendations). Identification of blood isolates was also confirmed by API 20. Criteria for resistance were evaluated in accordance with National Committee for Clinical Laboratory Standards guidelines. Records of the Microbiology Laboratory for the period spanning 1 January 1997 to 30 April 1999 were searched retrospectively for recovery of *Leminorella* spp. from clinical specimens. The medical records of patients identified by this search were reviewed, and data were entered into a prepared questionnaire. To define infections, we used a modification of Centers for Disease Control and Prevention guidelines (modified to include community-acquired infections and exclude asymptomatic bacteriuria) (1). An isolate was classified as a definite pathogen if the patient had symptoms and signs of infection at the site of isolation and no other pathogen was isolated from that site, as a probable pathogen if the patient had symptoms and signs of infection at the site of isolation but the culture yielded polymicrobial growth or if the *Leminorella* sp. was a single isolate but the signs and symptoms of infection were not definitely related to the site of isolation, as a possible pathogen if signs and symptoms of infection were evident but not clearly related to the site of isolation, and as a nonpathogen if there was no evidence of infection at the time of isolation.

RESULTS

During the 28 months surveyed, *Leminorella* spp. were identified in clinical specimens from 18 patients, representing an incidence of 11 cases per 100,000 patient admissions. There was no clustering of cases by time or place. The medical records of 14 of the patients were available for review. The mean age was 67 (range, 10 to 88) years, and 78% of the patients were male. In 12 of 14 cases, *Leminorella* spp. were isolated after more than 72 h (average, 11 days) in the hospital. In one case, they were isolated from a patient undergoing chemotherapy who had intensive contact with the health care system, and in one case, the isolate appeared to have been community acquired.

Patients' characteristics and clinical syndromes are summarized in Table 1. Signs and symptoms of infection were evident in 13 of the 14 patients studied. Site-specific signs and symptoms included dysuria in patients with urinary tract infections (UTI), purulent sputum production, rales on physical exami-

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TABLE 1. Patients' characteristics and clinical syndromes

Patient no.	Age (yrs)	Sex[a]	Site of isolation	Comorbidity[b]	Syndrome[c]	Infection
1	10	M	Blood	AML, recent chemotherapy	Primary bacteremia	Definite
2	75	M	Peritoneal fluid	DM, mesenteric vascular event	Peritonitis	Definite
3	79	F	Sputum	Anoxic brain damage, mechanical ventilation	LRTI	Probable
4	43	M	Wound	Fractured tibia, IHD	SSI	Definite
5	56	M	Wound	Pyoderma gangrenosum	Soft tissue infection	Possible
6	85	F	Wound	Fractured hip, IHD, sideroblastic anemia	SSI	Possible
7	59	M	Wound	IHD, sternal osteomyelitis	SSI	Probable
8	19	M	Urine	Mental retardation	UTI	Definite
9	27	F	Urine	Recent normal delivery	UTI	Possible
10	59	M	Urine	Carcinoma of rectum, recent abdominoprineal resection	UTI	Probable
11	88	M	Urine	Carcinoma of bladder, recurrent UTI	Definite	
12	72	M	Urine	Prostatic hypertrophy, stroke, DM	UTI	Definite
13	69	M	Urine	Carcinoma of rectum, abdominoperineal resection, heal conduit, recurrent UTI	Asymptomatic bacteriuria	No
14	71	M	Urine	Prostatic hypertrophy, DM, IHD	UTI	Probable

[a] M, male; F, female.
[b] AML, acute myelocytic leukemia; DM, diabetes mellitus; IHD, ischemic heart disease.
[c] LRTI, lower respiratory tract infection; SSI, surgical site infection.

nation of patients with lower respiratory tract infections, and purulent drainage, localized tenderness, and redness in patients with soft tissue infections. The systemic signs and symptoms of infection were as follows: fever in 57% leukocytosis in 43%, and leukopenia in 7% of the patients at the time that the *Leminorella* sp. was present. In 43% of the cases, *Leminorella* spp. were isolated from polymicrobial cultures. Three patients had an additional focus of infection other than the site of isolation of *Leminorella* sp. Using clinical criteria, *Leminorella* sp. was classified as a definite pathogen in six (43%) cases, a probable pathogen in four (29%) cases, and a possible pathogen in three (21%) cases. In one case (7%), *Leminorella* spp. had no clinical significance.

Urine was the most common site of isolation. In all cases, urine colony counts were >100,000 CFU/ml. In six of the seven patients, pyuria was present (>25 erythrocytes per high-power field). In three of the seven cases, *Leminorella* sp. was classified as a definite pathogen. Three patients had an indwelling urinary catheter, and two had recurrent UTI. Indeed, the most common clinical syndrome caused by *Leminorella* spp. was UTI, which occurred in six patients (43%). In five cases, it was the only pathogen isolated from urine and one patient had a polymicrobial UTI in which the copathogen was *Acinetobacter baumanii*.

In four patients, *Leminorella* sp. was isolated from wounds. Three of these patients had undergone surgical procedures prior to isolation of the organism. Two had surgical site infections following orthopedic surgery (not in a cluster). The first was a 43-year-old man who developed a wound infection with *Leminorella* spp. 7 days following repair of a fractured tibia. The second was an 85-year-old female who developed a wound infection 18 days after repair of a fractured hip. In the latter case, both *Leminorella* spp. and coagulase-negative staphylococci were isolated from the wound. The other two patients with wound infections were a 59-year-old man with post coronary artery bypass graft *Staphylococcus epidermidis* sternal osteomyelitis who developed a superinfection with *Leminorella* spp. and a 56-year-old man with pyoderma gangrenosum who had a soft tissue infection of a lower limb ulcer. In this case, *Leminorella* spp., *S. aureus*, and a group A beta-hemolytic streptococcus were isolated from the wound and the *Leminorella* sp. was classified as a possible pathogen.

The only case of bacteremia was that of a 10-year-old boy with acute myeloid leukemia who had postchemotherapy neutropenia and fever. No other pathogen was isolated at that time, and no localizing signs or symptoms were present. *Leminorella* sp. was isolated from two out of the three sets of blood samples drawn. We defined this case as primary bacteremia, and *Leminorella* sp. was classified as a definite pathogen.

A case of secondary peritonitis occurred in a 75-year-old male with diabetes mellitus who had been operated on for a mesenteric vascular event and had a leak from the anastomotic site. The patient developed signs and symptoms of peritonitis and underwent a "second-look" laparotomy. *Leminorella* sp. was the only organism isolated from the peritoneal fluid.

A case of lower respiratory tract infection involved a 79-year-old female with anoxic brain damage after a myocardial infarction. The patient was mechanically ventilated for a prolonged time. She produced copious amount of purulent sputum in association with fever and leukocytosis. Her chest radiograph was clear, and her sputum grew *Leminorella* spp., *Klebsiella pneumoniae*, and coagulase-negative staphylococci.

Antimicrobial susceptibility. The susceptibilities of the 18 isolates to 15 antimicrobial agents are summarized in Table 2. The isolates were uniformly susceptible to imipenem. Beta-

TABLE 2. Antimicrobial susceptibilities of 18 isolates of *Leminorella* spp.

Antibiotic agent(s)	% Susceptible	% Intermediately susceptible	% Resistant
Ampicillin	11	22	67
Amoxicillin-clavulanate	50	39	11
Piperacillin	39	0	61
Piperacillin-tazobactam	50	33	22
Ticarcillin-clavulanate	72	17	11
Aztreonam	33	17	50
Cefuroxime	6	11	83
Cefotaxime	43	17	45
Ceftazidime	61	33	6
Imipenem	100	0	0
Ciprofloxacin	45	0	55
Trimethoprim-sulfamethoxazole	28	0	72
Gentamicin	44	0	56
Tobramycin	72	11	17
Amikacin	94	6	0

lactam agents (with the exception of imipenem) had poor activity against *Leminorella* sp. isolates. One-half of the isolates or fewer were susceptible to the following agents: ampicillin, piperacillin (and their combination with a beta-lactamase inhibitor), expanded- and broad-spectrum cephalosporins (62% were susceptible to ceftazidime), and aztreonam. Similarly, the two fluoroquinolones which were tested (levofloxacin and ciprofloxacin) had poor activity. Over half of the isolates were resistant to gentamicin. In contrast, amikacin showed very good activity with intermediate susceptibility in only one isolate.

Three of four isolates tested were resistant to chloramphenicol; two of four were resistant to tetracycline.

DISCUSSION

Automated systems identify microorganisms based on multiple biochemical tests and computer analysis. Such systems are gaining popularity because of their ease of use and their ability to process a large number of specimens in a relatively short time. Taxa which were not identified to the species level in the past are now more frequently identified. For some of these "new" organisms, the lack of clinical correlates poses a clinical dilemma for the physician. *Leminorella* spp. are such species.

To date, *Leminorella* spp. have been recovered from stool and urine only, with no clinical correlates (2). Our study establishes *Leminorella* spp. as clinically relevant organisms causing primarily UTI, surgical site infection, peritonitis, bacteremia, soft tissue infection, and probably also lower respiratory tract infection.

Leminorella sp. was cultured almost exclusively after the patients were hospitalized for over 72 h, suggesting that it be considered a nosocomial pathogen. The organisms exhibited resistance to multiple antibiotic agents, with uniform susceptibility only to imipenem and amikacin.

Leminorella sp. infections tended to affect patients compromised by underlying conditions or those with invasive devices and procedures. Seventy-one percent of the patients from whose urine *Leminorella* spp. were isolated had an indwelling urinary catheter or recurrent UTI. Three of four patients from whose wounds *Leminorella* spp. were isolated had undergone a surgical procedure a few days before the culture was taken. *Leminorella* spp. were isolated from the sputum of only one patient. This patient has been mechanically ventilated for a long time before the isolation of *Leminorella* spp.

Retrospective study data should be viewed with caution. Isolates were not available for further investigation and identification to the species level. However, given the unique phenotypic profile of *Leminorella* spp. (hydrogen sulfide and L-arabinose positive, urea and lipase negative), errors in identification were very unlikely. Moreover, all of the isolates but one shared a typical antibiotic susceptibility pattern. *Salmonella* sp. is the only organism reported to be misidentified as a *Leminorella* sp. (3), but the clinical setting of our patients is not compatible with *Salmonella* sp. infection. Another limitation of a retrospective design is difficulty in distinguishing between infecting and colonizing organisms. To overcome this obstacle, we employed a set of suitable predefined criteria.

We conclude that *Leminorella* spp. should be considered significant nosocomial pathogens capable of causing a variety of clinical syndromes which could prove refractory to routine antimicrobial therapy.

REFERENCES

1. **Garner, J. S., W. R. Jarvis, T. G. Emori, T. C. Horan, and J. M. Hughes.** 1988. CDC definitions for nosocomial infections, 1988. Am. J. Infect. Control **16:** 128–140.
2. **Hickman-Brenner, F. W., M. P. Vohra, G. P. Huntley-Carter, G. R. Fanning, V. A. Lowery, 3rd, D. J. Brenner, and J. J. Farmer 3rd.** 1985. *Leminorella*, a new genus of *Enterobacteriaceae*: identification of *Leminorella grimontii* sp. nov. and *Leminorella richardii* sp. nov. found in clinical specimens. J. Clin. Microbiol. **21:**234–239.
3. **Kitch, T. T., M. R. Jacobs, and P. C. Appelbaum.** 1994. Evaluation of RapID onE system for identification of 379 strains in the family *Enterobacteriaceae* and oxidase-negative, gram-negative nonfermenters. J. Clin. Microbiol. **32:** 931–934.