Proteus penneri and Urinary Calculi Formation

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The clinical significance of Proteus penneri, a newly described species, is unknown. A case report is presented, which is to the best of our knowledge the first description of this organism causing a urinary tract infection and bladder calculi.

Recent revisions in the classification of the Proteae, a tribe of bacteria belonging to the family Enterobacteriaceae, recognized three genera, namely, Proteus, Providencia, and Morganella (3). In the genus Proteus, three species were identified. These included the well-known P. vulgaris and P. mirabilis species. A third, P. myxofaciens, was proposed for an organism isolated from gypsy moth larvae (Portheitia dispar), but is not of clinical importance. Bacteria formerly in the genus Proteus and previously classified as Proteus rettgeri and Proteus morganii were reassigned to the genera Providencia and Morganella, respectively. Subsequent studies of 20 indole-negative strains generally grouped with P. vulgaris led to the finding that they constituted a separate species (8). The name given to this species was Proteus penneri (10). Although strains of this species have been reported to be isolated from urine, stool, and blood specimens, their clinical significance is largely unknown (8). With the report of this new species, more attention was given to the precise classification of the Proteus species in our laboratory. This species may be differentiated by tests for esculin hydrolysis, salcin, and indole (all negative at 48 h) which are readily performed in clinical laboratories. This approach has led to the diagnosis of an infection caused by P. penneri. We present in this paper a case report that, to our knowledge, describes the first detailed account of such an infection.

Case report. An 84-year-old man was admitted to the hospital in 1974 after a cerebrovascular accident. He developed a nosocomial urinary tract infection with Escherichia coli and Klebsiella pneumoniae. Subsequently, he was transferred to a chronic care facility where he remained for the next 8 years. His course was punctuated by symptomatic urinary tract infections with a variety of gram-negative bacilli, managed with appropriate antimicrobial therapy. For the last 3 years, he had no bacteriuria.

In August 1982, the patient was noted to have painless, foul-smelling hematuria. Otherwise, he was asymptomatic. Urinalysis revealed 30 to 40 erythrocytes and 3 leukocytes per high-power field, trace protein, no glucose, pH 9, and a specific gravity of 1.011. Urine culture demonstrated a pure growth of \( >10^5 \) CFU of P. penneri per ml (isolate no. 1). Treatment was instituted with appropriate antibiotics; however, hematuria persisted, and a urological consult was obtained. On 24 September 1982, the patient underwent cystoscopy which revealed a severely inflamed and hemorrhagic bladder mucosa with diverticuli. On 21 October 1982, urine culture again yielded pure growth of \( >10^5 \) CFU of P. penneri per ml. Two variants, one hemolytic and the other nonhemolytic, were identified (isolates 2 and 3, respectively).

Once again antimicrobial therapy was ineffective in clearing the infection, since on 4 November 1982, midstream urine culture revealed three strains of \( >10^5 \) CFU of P. penneri per ml (isolates no. 4, 5, 6, respectively). A kidney-ureter-bladder X ray demonstrated three stones in the bladder. These were removed surgically, and a pure growth of P. penneri was isolated from the center of one stone (isolate no. 7). Subsequent urine cultures were negative for P. penneri, and the hematuria resolved. The stones were composed of a mixture of uric acid and magnesium ammonium phosphates.

In an attempt to identify the reservoir of P. penneri in the patient, swabs of the rectum, perineum, scrotum, penile shaft, and abdominal skin were cultured. These were negative for P. penneri. Urine cultured from each of the five other patients that shared the same room were negative for P. penneri.

Urinary tract infections caused by P. mirabilis and P. vulgaris have been described on numerous occasions (1, 5, 12–14). Some of these may have been due to organisms that would have been classified as indole-negative P. vulgaris. Little, if any, significance would have been attached to the negative indole reaction as it would most likely have been considered to be a biochemical variation. However, since these bacteria are now known to constitute a separate species (10), it may be expected that certain biological properties, other than the ones that are defined readily in the microbiology laboratory, may be different from those of P. vulgaris or P. mirabilis, such as differences in pathogenicity. More infections need to be assessed and compared with P. vulgaris infections to demonstrate such differences.

Urease production is a characteristic of P. penneri (8) which is therefore similar to other species in the genus Proteus. The enzymatic breakdown of urea results in increased urinary alkalinity and bicarbonate and ammonia concentrations, all of which favor the precipitation of magnesium, ammonium, phosphate, and carbonate apatite (6, 7, 10).

Urinary tract infections range in severity from simple bacterial growth in the urine without symptoms (asymptomatic or covert bacteriuria) to massive bilateral renal infection resulting in chronic renal failure (4). In the untreated patient, whether symptomatic or asymptomatic, counts of more than \( 10^5 \) CFU per ml of urine are indicative of infection (2).

Our patient in whom P. penneri was isolated in pure culture on three separate occasions (\( >10^5 \) CFU per ml) would be classified as having a urinary tract infection (2). Therefore, urinary tract stone formation as found in our patient infected with P. penneri is consistent with struvite

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stone formation with other members of the \textit{Proteae} group of organisms. The isolation of \textit{P. penneri} from the center of the stone in our patient suggests that a urinary tract infection by this urea-splitting organism preceded the formation of bladder calculi. These calculi then traumatized the bladder mucosa, resulting in hematuria. The paucity of leukocytes on urinalysis requires further comment. Pyuria (the presence of at least 3 to 10 leukocytes per high-power field) has not been found to be a reliable guide to the presence of infection; indeed, only about 50% of patients with significant bacteriuria will have the usual 3 to 10 leukocytes per high-power field that are often considered meaningful (9, 11). In addition, it is well known that alkaline urine, as found in our patient, very rapidly lyse leukocytes (15).

We could not identify any reservoir of \textit{P. penneri} in our patient or his environment. Clearly, further studies with larger groups of patients are needed to elucidate the ecology of this organism.

Biochemically, all seven isolates from our patient were negative for the following reactions: indole (24 h, 48 h), Voges-Proskauer, Simmons citrate, \textit{L}-lysine, \textit{L}-arginine, \textit{L}-ornithine, malonate, arabinose, adonitol, cellobiose, dulcitol, inositol, lactose, mannitol, melibiose, raffinose, rhamnose, salicin, sorbitol, trehalose, amygdalin, esculin (24 h, 48 h), oxidase, and \textit{o}-nitrophenyl-\textit{D}-galactopyranoside. The following reactions were positive for all seven strains: methyl red (24 h, 48 h), hydrogen sulfide, urea, phenylalanine, maltose, and sucrose.

These biochemical characteristics are identical with those of the strain of \textit{P. penneri} in the American Type Culture Collection (ATCC 33519) (8). There were strain variations among our seven isolates. On sheep blood agar, isolates 3 and 6 were nonhemolytic whereas isolates 2, 4, 5, and 7 were beta-hemolytic (37°C, 24 h). Isolates 1, 2, and 6 were xylose positive, with the others being xylose negative. The gelatin reaction was negative for all of our seven isolates but was positive for strain ATCC 33519 (8). All seven isolates of \textit{P. penneri} were inhibited by ampicillin at a concentration > 16 μg/ml, chloramphenicol at ≥32 μg/ml, cefazolin at >64 μg/ml, and cefamandole at >64 μg/ml. All strains were inhibited by gentamicin at concentrations ranging from 1 to 4 μg/ml, tobramycin at <0.5 to 8 μg/ml, and amikacin at 4 to 32 μg/ml. The minimal inhibitory concentration against cefoxitin ranged from 2 to 8 μg/ml; however, a third-generation cephalosporin, ceftaxime, was less active with minimal inhibitory concentrations ≥32 μg/ml.

Therefore, asymptomatic bacteriuria, with bladder calculi formation causing traumatic hematuria, may be manifestations of infection with \textit{P. penneri}. Additional patients with \textit{P. penneri} infections need to be studied to define the full spectrum of disease.

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**LITERATURE CITED**


