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Endotoxemia and Bacteremia in Patients Following Ultrasonic Lithotripsy

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Summary. The incidence of endotoxemia was studied in 17 patients who underwent ultrasonic lithotripsy (USL), and compared with the incidence in 11 patients who underwent transurethral resection (TUR) and in 8 patients who underwent other operations. Fourteen of 17 patients (82%) who underwent ultrasonic lithotripsy had endotoxemia. The incidence of endotoxemia after USL was significantly higher than that after TUR (9%) or after other operations (12.5%). Only 2 of the 17 patients (12%) who underwent USL had bacteremia. The organisms isolated were *P. mirabilis* and *S. sanguis*, respectively. Six of the 14 patients with endotoxemia after USL suffered high fever. These data suggest that endotoxemia is a factor which causes high fever after USL.

Key words: Endotoxemia, Bacteremia, Ultrasonic lithotripsy.

Introduction

Recently ultrasonic lithotripsy has become more widespread as a treatment for urolithiasis. We noted high fever followed this procedure in many cases. Postoperative bacteremia was suspected, and blood cultures were taken twice in 25 cases who underwent this procedure from January to May 1985. However, the cultures were negative for bacteria. Therefore, to detect blood endotoxin which is a known pyrogen limulus tests were performed on subsequent patients who underwent USL.

Materials and Methods

We studied 17 patients who underwent ultrasonic lithotripsy from September 1985 to March 1986.

The eleven women and six men ranged in age from twenty to seventy-six years, with a mean age of forty-six years. Of these patients 10 had renal calculi (5 solitary calculi, 4 multiple calculi and 1 had a staghorn calculus) underwent percutaneous nephrolithotripsy (PNL) and 7 with a mid or lower ureteral calculus underwent transurethral ureterolithotripsy (TUL). PNL consisted of a 1-stage technique. After PNL a nephrostomy tube was left in place in all patients. Stone fragmentation and extraction were performed with an ultrasonic lithotriptor. There was only one complication of ureteric perforation in a patient who underwent TUL. We also studied 11 patients who underwent TUR and 8 patients who underwent other operations (Table 1). Preoperatively, and 2 h and 18 h postoperatively venous samples were collected in plastic, heparinised, pyrogen-free syringes for assays of endotoxin. Blood cultures were performed 2 h and 18 h after operation. The limulus test was performed as described by Levin et al. [4]. For detection of endotoxin

Table 1. Summary of patients on whom the limulus tests were performed

Procedures	No. pts.
Ultrasonic lithotripsy	
PNL[a]	10
TUL[b]	7
Subtotal	17
TUR	
TUR-P	5
TUR-Bt	6
Subtotal	11
Other Operations	
Simple nephrectomy	1
Radical nephrectomy	1
Open prostatectomy	2
Cutaneous ureterostomy	1
Percutaneous nephrostomy	2
Adrenalectomy	1
Subtotal	8

[a] percutaneous nephrolithotripsy
[b] Transurethral ureterolithotripsy

Table 2. The incidence of preoperative and postoperative endotoxemia in patients who underwent various urological procedures

Procedures	Incidence of endotoxemia[a]	
	Preop. (%)	Postop. (%)
Ultrasonic lithotripsy		
PNL	0/6 (0)	8/10 (80)
TUL	0/4 (0)	6/7 (86)
Subtotal	0/10 (0)	14/17 (82)[b,c]
TUR		
TUR-P	0/3 (0)	1/5 (20)
TUR-Bt	0/2 (0)	0/6 (0)
Subtotal	0/5 (0)	1/11 (9)[b]
Other operations	0/5 (0)	1[d]/8 (12.5)[c]

[a] The ratio indicates the number of patients with positive endotoxemia/total number of patients
[b,c] $P < 0.01$ by the χ^2-test
[d] a patient who underwent radical nephrectomy

Table 3. The incidence of bacteremia after various urological procedures

Procedures	Total no. pts.	Bacteremia no. pts. (%)
Ultrasonic lithotripsy		
PNL	10	1[a] (10)
TUL	7	1[b] (14)
Subtotal	17	2 (12)
TUR	7	0 (0)
Other Operations	6	0 (0)

[a] *S. sanguis* was isolated from the blood
[b] *P. mirabilis* was isolated from the blood

Table 4. Relationship between endotoxemia and postoperative fever in patients who underwent ultrasonic lithotrispy

Endotoxemia	Total no. pts.	Postop. fever no. pst. (%)
Positive	14	6 (43)
Negative	3	0 (0)

Table 5. Relationship between endotoxemia and preoperative bacteriuria in patients who underwent ultrasonic lithotripsy

Endotoxemia	Total no. pts.	Preop. bacteriuria no. pts. (%)
Postitive	14	4 (29)
Negative	3	0 (0)

we used Pyrosate™ kits (Green Cross Co., Ltd. Japan) in which the limulus amebocyte lysate (U.S. Haemochem Co., Ltd.) was used. By comparison with standard *E. coli* endotoxin, we were able to detect concentrations of endotoxin as low as 0.075 ng/ml. Cases which had a positive test on more than one assay were judged to be a positive case. All patients received antibiotic treatment; after 2 h postoperatively venous samples were taken.

We also studied the relationship between endotoxemia and preoperative bacteriuria, and postoperative fever in patients who underwent ultrasonic lithotripsy.

Results

1. The Incidence of Endotoxemia

The incidence of preoperative and postoperative endotoxemia in patients who underwent various urological procedures is shown in Table 2. Fourteen of 17 patients (82%) who underwent ultrasonic lithotripsy had endotoxemia while only one of 11 patients (9%) who underwent TUR and only one of 8 patients (12.5%) who underwent other operations had endotoxemia. The incidence of endotoxemia in patients who underwent ultrasonic lithotripsy was significantly higher than that in patients who underwent TUR or other operations ($p < 0.01$ by the χ^2-test).

However, only two of the 14 patients with endotoxemia after ultrasonic lithotripsy were positive by two tests. No patients had endotoxemia preoperatively.

2. The Incidence of Bacteremia

The incidence of bacteremia after various urological procedures is shown in Table 3. Only 2 of the 17 patients (12%) who underwent ultrasonic lithotripsy had bacteremia. No patients who underwent TUR or other operations had bacteremia. The incidence of bacteremia in patients who underwent ultrasonic lithotripsy was not significantly higher than that in patients who underwent TUR or other operations ($p > 0.05$ by the χ^2-text).

Of these two patients with bacteremia, *P. mirabilis* and *S. sanguis* were isolated from the two hour postoperative venous samples, but not in samples taken 18 h later. The patient with bacteremia due to *P. mirabilis* had preoperative urinary infection with *P. mirabilis* and *E. faecalis*. This patient suffered ureteric perforation during TUL, and had endotoxemia and high fever postoperatively. The other patient with bacteremia due to *S. sanguis* had sterile urine preoperatively. This patient had negative endotoxemia and no symptoms after PNL.

3. Relationship Between Endotoxemia and Postoperative Fever in Patients Who Underwent Ultrasonic Lithotripsy

Six of the 14 patients (43%) with endotoxemia after this procedure suffered fever (more than 38 °C) within the

first postoperative day while none of the 3 patients without endotoxemia suffered fever (Table 4).

4. Relationship Between Endotoxemia and Preoperative Bacteriuria in Patients Who Underwent Ultrasonic Lithotripsy

Four of the 14 patients (29%) with endotoxemia had preoperative bacteriuria (more than 10^4/ml) while none of the 3 patients without endotoxemia had bacteriuria. The organisms were all gram-negative rods except for a patient with a gram-positive rod (Table 5).

Discussion

Bacterial endotoxin is a component of the cell wall of gram-negative bacteria. Endotoxin has various biological effects, and causes fever, leukopenia, hypotension, and in some cases, fatality.

In 1967, Levin and Bang reported that extracts of amebocytes (the only type of cell found in the blood of *Limulus polyphemus,* the horseshoe crab) were gelled with low concentrations of bacterial endotoxin [3], and it has since been shown that endotoxemia occurs in a variety of septic and non-septic disorders.

In our study, the limulus tests were performed in order to reveal one of the causes of high fever after ultrasonic lithotrispy. Fourteen of 17 patients (82%) who underwent this procedure had endotoxemia. There was a significant difference between the incidence of endotoxemia in patients who underwent ultrasonic lithotripsy and that in patients who underwent TUR or other operations.

However, only two of the 17 patients (12%) who underwent ultrasonic lithotripsy had bacteremia and none of the 25 cases who underwent this procedure from January to May 1985 had bacteremia. Two of a total of the 42 cases (4.8%) had bacteremia.

The studies of Garibaldi et al. demonstrated a correlation between the concentration of bacteriuria in the urine of patients with indwelling catheters and the frequency of positive limulus tests in the blood [2]. According to the other reports, catheterization of the urinary bladder resulted in decreased peripheral vascular resistance, reduced level of pre-kallikrein and positive limulus tests [8]. From these reports, Levin described the escape of endotoxin from the genitourinary tract to the blood circulation [5].

In 1973, Thompson and Stamey cultured renal calculi and demonstrated bacterial growth in 77% of the removed caluculi [9]. Others also reported growth of bacteria in 14–42% of removed calculi. Most cultures yield gram-negative bacteria [1, 6, 7].

From these reports and our research data, it is suggested that bacteria not only in the urine but also within the calculi had been destroyed by ultrasound and that endotoxin, a component of the cell wall of gram-negative bacteria, had entered the circulation. Therefore it is suggested that the incidence of endotoxemia after ultrasonic lithotripsy is higher than following other procedures.

Six of the 14 patients (43%) with endotoxemia after this procecure suffered high fever (more than 38 °C) within the first postoperative day.

This suggests that endotoxemia is one of the factors leading to high fever after this procedure.

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