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ORIGINAL ARTICLE

Urinary tract infection and antibiotic use around ureteral stent insertion for urolithiasis

Bérénice Souhail[1] · Patrick Charlot[2] · Gilles Deroudilhe[3] · Yves Coblentz[2] · Gregory Pierquet[3] · Pierre Gimel[4] · Nathalie Challut[4] · Thierry Levent[5] · Stéphane Cusumano[6] · Véronique Dautezac[6] · Pierre-Marie Roger[1,7,8]

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Abstract

Urolithiasis is the main indication for a ureteral JJ stent. Our aim was to determine the incidence of urinary tract infections (UTIs) after a JJ stent for urolithiasis, with an emphasis on antibiotic use. Prospective, multicenter, cohort study over a 4-month period including all of the patients with urolithiasis requiring JJ stent insertion. The clinical and microbiological data and therapeutic information were recorded until removal of the JJ stent. Two hundred twenty-three patients at five French private hospitals were included. A urine culture was performed for 187 patients (84%) prior to insertion of a JJ stent, 36 (19%) of which were positive. One hundred thirty patients (58%) received an antibiotic therapy during surgery: 74 (33%) prophylaxis and 56 (25%) empirical antibiotic therapy, comprising 17 different regimens. The rate of prophylaxis varied according to the center, from 0 to 70%. A total of 208 patients were followed-up until removal of the first stent. The rate of UTIs was 6.3% (13/208); 8.1% of the patients who did not receive a prophylaxis had a UTI versus 1.4% of those who did receive a prophylaxis ($p = 0.057$). Seven empirical antibiotic regimens were used to treat these 13 patients. Another large panel of antibiotic prescriptions was observed at the time of JJ stent removal. The incidence of a UTI after JJ stent insertion for urolithiasis was 6.3%, in part due to a lack of prophylaxis. An unwarranted diversity of antibiotic use was observed at each step of care.

Keywords Urolithiasis · Ureteral stent · Urinary tract infection · Healthcare-associated infection · Antibiotic therapy

Introduction

The first indication for use of a ureteral stent (or a double pigtail stent or JJ stent) is complications from urolithiasis, making it a daily occurrence for urological surgeons [1]. The complications of urolithiasis are urinary tract infection (UTI), and/or anuria, and/or intolerable pain. These are urological emergencies as they require urgent decompression of the collecting system [2]. Ureteral stents and percutaneous nephrostomy catheters are two options for decompression of the renal collecting system [1].

The French Society of Anesthesiology and Intensive Care (Société Française d'Anesthésie Réanimation SFAR) updated its recommendations regarding antibiotic prophylaxis in surgery and interventional medicine in 2018 [3]. In endourology surgery, it is recommended to perform a urine culture before the procedure and a documented antimicrobial treatment should be administrated in case of bacteriuria [1, 4]. If the urine culture before the procedure is sterile, the SFAR recommends antibiotic prophylaxis treatment during the endoscopic treatment of urolithiasis (ureteroscopy, percutaneous

✉ Bérénice Souhail
souhail.b@chu-nice.fr

1 Réso-Infectio-PACA-Est, Nice, France
2 Elsan, Clinique Inkermann, 84 Rte d'Aiffres, 79000 Niort, France
3 Elsan, Clinique Saint Augustin, 114 Ave d'Arès, 33000 Bordeaux, France
4 Elsan, Clinique Saint-Roch 5 Rue Ambroise Croizat, 66330 Cabestany, France
5 Elsan, Clinique Vauban, 10 Avenue Vauban, 59300 Valenciennes, France
6 Elsan, Clinique du Sidobre, Chemin de St Hyppolyte, 81100 Castres, France
7 Elsan, Clinique Les Fleurs,, Avenue Frédéric Mistral, 83190 Ollioules, France
8 Faculté de Médecine, Université Côte d'Azur, 28 Avenue de Valombrose, 06107 Nice, France

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nephrolithotomy, nephrostomy, and retrograde JJ stent insertion) by cefazoline, cefamandole, cefuroxime, or gentamicin in case of allergy [3]. There was no significant variation in this field compared to the previous recommendations (2010).

In 2007, French societies of Urology (AFU) and of Infectious Diseases (SPILF) provided recommendations regarding HCAI UTI [4]. A urinary colonization or an asymptomatic bacteriuria should be treated according to the result of the urine cultures in patients with ureteral stent. In France, the empirical antibiotic treatment for HCAI pyelonephritis is firstly based on piperacillin/tazobactam because of its activity against *Pseudomonas aeruginosa* and enterococci [4]. In case of severe sepsis or septic shock, Amikacin should be added to the antibiotic regiment [4].

The epidemiology of multi-drug resistant (MDR) bacteria indicates their emergence especially in the context of a UTI. Thus, infectious complications due to a JJ stent could often result in difficult-to-treat bacteria. However, there is a paucity of up-to-date information regarding infectious complications following the placement of a JJ stent as well as in regard to the bacteria involved. Moreover, most of the studies to date did not differentiate bacteriuria and stent colonization from urinary infections [5, 6]. One randomized controlled trial in 1998 compared the efficacy and outcomes of percutaneous nephrostomy and ureteral stents for decompression in 42 patients [7]. The percentage of positive urine cultures with a retrograde ureteral JJ stent was 19%, but no data were presented about the clinical signs of infection [7]. In another prospective monocentric study conducted in Italy between 1998 and 2001, the rate of fever > 40 °C was 6.8% 24 h after stent insertion and 12.3% 30 days later [8], but no information was provided about the antibiotic therapy. Other studies have reported the rate of irritative bladder symptoms, bacteriuria, and flank pain that can only result from the presence of the JJ [9, 10], and accordingly, colonization versus UTI was not discussed [11–15]. Lastly, some studies have considered the outcomes after double pigtail insertion for various indications (e.g., malignancy, urolithiasis, fistula, etc.) and the results are difficult to interpret, notably those regarding infectious complications, because the populations were not homogeneous [16]. More data are available regarding UTI associated with a JJ stent placement in kidney transplantation surgery [17–19], but needless to say, these results are not relevant in the context of urolithiasis.

Therefore, our aim was to describe the microbiological and therapeutic aspects of infection related to JJ stents insertion for complicated urolithiasis.

Methods

This was a multicenter, prospective, cohort study undertaken at five French private hospitals that had the same electronic patient records system in common.

The antibiotic audits were sponsored by the French National Health Agency, and the patients or their relatives provided their written consent for computerization of their personal data for hospitalization purposes and potential clinical research. According to the French National Health Agency directives, in non-interventional studies, personal data should not be used if the patient does not wish to participate in the study. However, the patients provided their personal consent upon admission, and patient privacy was protected as no personal data were derived from the computerized files.

The characteristics of the participating centers are listed in Table 1. All of them had an emergency ward except center 2. Importantly, these five hospitals had the same internal consensus, promoting cefotaxime as empirical antibiotic therapy in case of community-acquired UTI and piperacillin/tazobactam treatment for healthcare-associated infections in the setting of urological surgery.

All of the adult patients who needed a retrograde ureteral stent insertion for a complicated urolithiasis (obstruction and/or major pain and/or fever) were included. Only primary stent placement for obstructing renal or ureteral stone was included. Patients who underwent stenting for another indication such as malignant obstruction or stent exchange were excluded from the analysis.

The inclusion period was 4 months for the five private hospitals, successively. The patients were registered exhaustively by using the pharmacist's register of sterile device deliveries. The patients were followed-up until the JJ catheter was removed.

The electronic patient records included the patient's entire medical history, their current medical file including the nurses' comments, all laboratory and radiological test results, and successive treatments. We specifically registered comorbidity, antibiotic allergies, UTI in the past 6 months, and stent insertion data: whether or not a urine culture was performed before stent insertion, results of the urine culture, antibiotic treatment, or prophylaxis during the stent insertion. Whether a urine culture was performed before the stent removal, the culture results, and the prescription of antibiotic before/during the removal were also noted.

An antibiotic prophylaxis was defined as an antibiotic regiment prescribed before or per procedure out of any context of UTI and/or bacterial documentation on a urine culture. We considered as curative antibiotic therapy every antibiotic regimen prescribed (i) in case of a clinical and/or biological suspicion of UTI (fever, pyuria, elevated CRP, or white blood cell count), (ii) for an asymptomatic bacteriuria documented on a urine culture before the JJ stent insertion.

When a UTI was suspected, the information gathered comprised the clinical signs, the time between the stent insertion and the beginning of the infection, the empirical antimicrobial treatment, the microbiological documentation, the documented antimicrobial treatment and its length, the need for stent removal due

Table 1 The main patient characteristics, including JJ management, from insertion to removal

	Total $n = 223$ (%)	Center 1 $n = 89$	Center 2 $n = 38$	Center 3 $n = 33$	Center 4 $n = 15$	Center 5 $n = 48$
Center characteristics						
Number of beds	1019	283	189	152	225	170
Number of urologists	27	8	9	3	4	3
Patient characteristics						
Age (years)[a]	57 ± 16	57 ± 16	59 ± 17	57 ± 17	51 ± 15	58 ± 17
Sex ratio (Male/Female)	1.7	1.7	2.4	1.2	1.5	3
Charlson comorbidity index[a]	0.9 ± 1.3	0.6 ± 0.9	0.8 ± 1.2	2 ± 1.6	0.7 ± 0.9	0.8 ± 1.5
History of urolithiasis	76 (43)	34 (63)	13 (34)	11 (33)	3 (20)	29 (60)
History of UTI in the past 6 months	24 (1)	7 (8)	2 (5.3)	5 (15)	0	10 (21)
Retrograde JJ stent insertion						
Urine culture performed before insertion	187 (84)	86 (97)	31 (82)	22 (67)	12 (80)	36 (75)
Positive urine culture	36 (19)	14 (16)	4 (13)	8 (36)	2 (17)	8 (22)
Antibiotic prophylaxis	74 (33)	0	26 (68)	23 (70)	0	25 (52)
Curative antibiotic therapy	56 (25)	19 (21)	6 (16)	6 (18)	3 (20)	23 (48)
No antibiotic treatment	93 (42)	70 (79)	6 (16)	4 (12)	12 (80)	0
UTI after JJ stent insertion						
Number	13 (6.3)	5 (5.7)	3 (11)	1 (3)	1 (6.7)	3 (6.8)
Hospitalization	10 (77)	4 (80)	1 (33)	1 (100)	1 (100)	3 (100)
Intensive care requirement	2 (15)	0	1 (33)	0	0	1 (33)
JJ stent removal						
Lost to follow-up	15 (6.7)	1 (1.1)	10 (26)	0	0	4 (8.3)
Duration of JJ stent treatment (days)[a]	20 ± 12	19 ± 14	16 ± 9	22 ± 10	23 ± 8	19 ± 13
Urine culture performed	90 (43)	11 (12)	15 (54)	28 (85)	4 (27)	32 (70)
Positive urine culture	15 (17)	2 (18)	0	12 (43)	0	1 (3.1)
Antibiotic when removed	59 (28)	3 (3.4)	19 (68)	26 (79)	0	11 (24)

UTI urinary tract infection

[a] Mean ± std.dev

to the infection, and the outcome: out-patient care, conventional hospitalization, intensive care unit, or death.

A positive urine exam before the JJ stent insertion was defined by the isolation of a bacterial species (Kass $\geq 10^3$ CFU/mL) irrespective of the white and/or red blood cell counts as all of the patients presented with urolithiasis, which altered the urine analysis.

A healthcare infection due to a ureteral stent was defined by local and general clinical signs occurring after the stent insertion possibly confirmed by a positive urine culture and/or a positive blood culture. A bacteriuria threshold $\geq 10^5$ CFU/mL was chosen, as recommended [4] in the presence of endourological catheter.

All five of the affiliated laboratories used the same technique and materials for urine culture analysis. A polymicrobial urine culture was considered to be contaminated.

Statistical analysis

The data were analyzed with StatView version 5.0 software, and statistical significance was established at $\alpha = 0.05$. The continuous variables were compared with the Student's *t* test or the Mann–Whitney non-parametric test. Proportions were compared with the χ^2 statistic or Fisher's exact test when appropriate.

Results

Patient characteristics

From December 2017 to September 2018, a total of 223 patients were included and followed-up until removal of the JJ stent. Their main characteristics are shown in Table 1. As the sole indication for JJ insertion was obstructive urolithiasis, there were mostly young males without comorbid conditions and the JJ stent insertion was performed within 24 h after the hospital admission.

Microbiological tests and antibiotic therapy at the time of JJ stent insertion

A urine culture was obtained for 187 patients (84%), ranging from 67 to 97% depending on the center. The urine culture was positive for 36/187 patients (19%). The isolated bacteria were mostly Enterobacteriaceae ($n = 17.47\%$), comprising *E. coli* (33%), *P. mirabilis* (8%), and *Enterobacter spp.* (6%), followed by *Streptococcus spp.* (14%), *E. faecalis* (3%), and *S. aureus* (3%). Of note, the urine cultures were polymicrobial in 12 cases (33%).

One hundred thirty patients (58%) received an antibiotic therapy at the time of the JJ stent insertion, including antibiotic

prophylaxis for 74 patients (33%) and curative antibiotic therapy for 56 patients (25%, see Tables 1 and 2).

There was a substantial variation for antibiotic prophylaxis use between the centers, ranging from 0 to 70%. Cefuroxime and cefazoline were the main drugs used for prophylaxis, in 65% and 34% of the cases respectively. There was an association between whether or not a urine culture was performed and the absence of antibiotic prophylaxis treatment: 91% versus 70% ($p < 0.001$).

Of the 56 patients who received an empirical antibiotic therapy for curative purpose, 31 patients (55%) received a single therapy based on 13 different compounds, and 25 patients (45%) received a combination therapy with 4 different options (see Table 2). The duration of the antibiotic treatment varied between the centers, with a median of 5 days, range 3-23 days.

Follow-up and infectious events

Fifteen patients (6.7%) were lost to follow-up, with their JJ stent still in place. For the remaining 208 patients, the mean length of time that the JJ stent was in place was 20 ± 12 days.

Thirteen patients (6.3%) exhibited a healthcare-associated infection after insertion of the JJ stent. Twelve patients (8.1%) who did not receive an antibiotic prophylaxis had a UTI versus 1 of the patients (1.4%) who had received a prophylaxis ($p = 0.057$). Of note, 4 of the 13 patients (31%) had a positive urine culture when the ureteral catheter was inserted, and all 4 of these patients received an antimicrobial therapy during the retrograde stent insertion.

The microbial and therapeutic data for these 13 patients infected due to JJ stent insertion are shown in Table 3. Due to antibiotic therapy before hospital readmission, the urine culture was positive in 9/13 cases (69%), with one isolation of an ESBL *E. coli* strain and one cephalosporinase-overexpressing *E. aerogenes* strain. Of note, 3 urine cultures were positive for *E. faecalis*. The antibiotic therapies were variable and not always active against the bacterial strain involved in the infection (Table 3).

Ten of the thirteen patients (77%) were hospitalized, including two in an intensive care unit. None of the patients died. In 3 cases (23%), the JJ stent had been removed due to the infection.

JJ stent removal

A urine culture was performed for 90 patients (43%) before JJ stent removal, ranging from 12 to 85% depending on the center. The urine culture was positive for 15 patients (17%), mostly polymicrobial ($n = 9$, 60%), while *E. coli* and *E. faecalis*

Table 2 The antibiotic treatments during stent insertion and removal. A total of 223 patients underwent a JJ stent insertion for urolithiasis, of whom 15 (6.7%) were lost to follow-up. As listed below, the empirical antibiotic therapies used for the urinary tract infections occurring in the setting of urological surgery were heterogenous, outside the internal guidelines that recommended cefotaxime or ceftriaxone in case of community-acquired infections and piperacillin + tazobactam in case of healthcare-associated infections (in both cases + amikacin when the criteria for severity were observed)

Antibiotic treatment during stent insertion		Antibiotic treatment during stent removal	
No antibiotic	93 (42%)	No antibiotic	149 (72%)
Antibiotic prophylaxis	74 (33%)	Antibiotic prophylaxis	40 (19%)
Empirical antimicrobial treatment	56 (25%)	Empirical antimicrobial treatment	19 (9%)
Single therapies ($n = 13$)		Single therapies ($n = 7$)	
Ceftriaxone	8	Cotrimoxazole	5
Ciprofloxacin	5	Ciprofloxacin	4
Ofloxacin	4	Amoxicillin	2
Cotrimoxazole	3	Piperacillin/tazobactam	2
Amoxicillin/clavulanic acid	2	Amoxicillin/clavulanic acid	1
Piperacillin/tazobactam	2	Nitrofurantoin	1
Gentamicin	1	Ofloxacin	1
Amoxicillin	1		
Amoxicillin/clavulanic acid	1		
Cefixime	1		
Cefotaxime	1		
Nitrofurantoin	1		
Pivmecillinam	1		
Combination therapies ($n = 5$)		Combination therapies ($n = 3$)	
Ceftriaxone + amikacin	17	Amikacin + levofloxacin	1
Ceftriaxone + gentamicin	6	Piperacillin/tazobactam + ciprofloxacin	1
Piperacillin/tazobactam + ciprofloxacin	1	Imipenem + vancomycin	1
Ceftriaxone + ofloxacin	1		

were isolated in 2 cases each and *S. haemolyticus* and *S. agalactiae* in one case each.

Fifty-nine patients (28%) received an antibiotic treatment during the JJ stent removal. It was a prophylaxis in 40 cases (68%) and a curative treatment in 19 patients (32%) using a large panel of antibiotic compounds (see Table 2).

Discussion

Our study shows that during urolithiasis treatment, the HCAI rate was 6.3% by the time the first JJ stent was removed, with a trend towards a relationship between the absence of prophylaxis and the occurrence of an HCAI. Antibiotic-resistant Enterobacteriaceae and Enterococci were isolated in 4/13 cases of HCAI (31%). Furthermore, the antibiotic management was heterogeneous, with a mixture of prophylaxis and curative treatments, both when the JJ stent was inserted and when it was removed.

Our study has a number of limitations: 15/223 patients (6.7%) were lost to follow-up. Nevertheless, the restriction to urolithiasis as the sole reason for JJ stent insertion allowed for the recruitment of a homogeneous population of young patients without comorbid conditions such as cancer and/or immunosuppression. The infectious complications were, therefore, most likely the direct consequence of the insertion of a JJ stent.

The rate of HCAI we determined is not over evaluated in our study given that we included only primary stent placement for ureteral stone and stopped follow-up after the stent removal. Thus, considering the multitude of reasons for JJ stent insertion, a significant number of patients are likely to require successive rounds of ureteral insertion due to persistent ureteral obstruction, which may increase the rates of HCAI and of MDR bacteria.

Both the national and the European guidelines recommend systematic antibiotic prophylaxis before an endourological procedure [2, 3, 20]. However, 93 patients (42%) did not receive any antibiotic treatment during the retrograde stent insertion, with significant differences between institutions. Previous studies have reported varying levels of compliance in France and elsewhere with the guidelines for prophylaxis, possibly due to a low association with the risk for HCAI [20]. Also, several multicenter audits of antibiotic prescriptions have revealed large differences in practices between hospitals for a given pathology [21–24]. These results are probably the consequence of the current guidelines, which might be considered too exhaustive, thereby leading to heterogeneous and ultimately prejudicial clinical practices [24, 25].

Indeed, the most surprising result of our study was the heterogeneity of the empirical antibiotic therapy throughout the care process, from the JJ stent insertion to its removal (see Table 2). Furthermore, 7 different regimens for 13 HCAI were prescribed (see Table 3). To the best of our knowledge, this is the first study reporting such heterogeneous antibiotic use for a given pathology. Due to the large use of fluoroquinolone or third generation cephalosporins (see tables), our data may explain why the emergence of MDR bacteria is a relatively common occurrence in the urinary setting [26]. Interestingly, taking into account all of the isolated bacteria in HCAI, the use of piperacillin/tazobactam (+ amikacin in case of severe infection), which is recommended by the SPILF and our internal guidelines for HCAI after urological surgery, appears to be warranted. These data are in line with previous studies: (i) nearly half of all enterococcal bacteremia occurred after urological surgery, mostly due to *E. faecalis*, which is still susceptible to piperacillin [27], and (ii) amikacin has been associated with high in vitro antimicrobial activity against ESBL-secreting strains compared to gentamicin [28].

Finally, as it is known that urolithiasis can be recurrent [29], repeating such antibiotic practices, for prophylaxis and curative purposes, has a high likelihood of leading to MDR bacteria. Thus, our results provide ample reason for urgent cooperation between urologists and infectious diseases specialists to promote better antibiotic use.

Conclusion

The incidence of a UTI after a JJ stent insertion for urolithiasis was 6.3%, with a trend towards an association with the lack of antibiotic prophylaxis ($p = 0.057$), the latter depending on the institution. Our study also showed a high level of antibiotic use for a routine urological procedure and highlighted variable levels of adherence to the guidelines for antibiotic prophylaxis in retrograde JJ stent insertion for urolithiasis.

Collaborators Eve Montera, Pharmacy, and Thierry Vigier, Anesthesiologist, Clinique Saint-Roch, Cabestany, France; Nathalie Troadec, Pharmacy, and Anne Espinet, Infection Control, Clinique Saint Augustin, Bordeaux, France; Pierre Hacker, Urologist, Clinique Sidobre, Castre, France; Séverine Delobelle, Infection Control, Clinique Vauban, Valenciennes, France.

Data availability the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest all of the authors declare that they have no conflicts of interest.

Ethics approval Antibiotic audit are sponsored by the French National Health Agency.

Table 3 The microbial and therapeutic data for the thirteen patients with healthcare-associated UTIs. Seven different empirical antibiotic regimens were prescribed for 13 patients, illustrating the heterogeneity of the therapeutic means. Due to antibiotic therapy before hospital readmission, the urine culture was not always positive despite ongoing clinical symptoms and fever.

	Urine culture before JJ insertion	Urine culture result	Antibiotic treatment during JJ insertion	Time between JJ insertion and UTI (days)	Microbiological documentation	Empirical antimicrobial therapy (EAT)	EAT efficiency	Documented antimicrobial therapy
1	Yes	*E. coli*	Amoxicillin + clav.ac. 1 g × 3/day for 2 days then cefixime 200 mg × 2/day for 5 days	14	Negative	Ceftriaxone 1 g/d + amikacin 15 mg/kg/day for 1 day	Unknown	Cefixime 200 mg × 2/day for 7 days
2	Yes	Negative	Ceftriaxone 1 g/d + amikacin 15 mg/kg/day then cefixime 200 mg × 2/day for 15 days	24	Negative	Pipe/Tazo 4 g × 3/day + Amikacin 15 mg/kg/day for 6 days	Unknown	Cefixime 200 mg × 2/day for 10 days
3	Yes	Negative	Cefuroxime 1.5 g IV 1 day (per op)	15	*E. faecalis*	none	–	Amoxicillin 1 g × 3/day for 8 days
4	Yes	Negative	None	10	*K. pneumoniae* in urine and blood cultures	Amoxicillin/clav.ac. 1 g/day (clearance = 15 mL/min) for 2 days	yes	Amoxicillin/clav.ac. 1 g × 3 (normalization of renal function) for 10 days
5	Yes	*E. cloacae*	Ceftriaxone 1 g/day + ofloxacin 200 mg × 2/day for 10 days	3	Negative	Pipe/Tazo 4 g × 3/day for 6 days	Yes	None
6	Yes	Negative	None	3	Negative	Pipe/Tazo 4 g × 3/day for 3 days	Unknown	None
7	Yes	Negative	None	7	*E. coli*	Pipe/Tazo 4 g × 3/d for 3 days	Yes	None
8	No	–	Cefazoline 2 g	3	*E. coli*	Ceftriaxone 2 g + Amikacin 25 mg/kg/day for 1 day	Yes	Ciprofloxacin 500 mg × 2/day for 5 days
9	Yes	*E. faecalis*	Cefuroxime then nitrofurantoin for 10 days	11	*E. faecalis*	Levofloxacin 500 mg × 2/day + amikacin 1500 mg/day for 3 days	No	Levofloxacin 500 mg × 2/day for 8 days
10	Yes	Negative	None	6	*E. coli*	Ceftriaxone 2 g/day + gentamicin 500 mg/day for 3 days	Yes	Ofloxacin 200 mg × 2/day for 10 days
11	Yes	Negative	None	7	*E. coli*	Ofloxacin 200 mg × 2/day for 3 days	Yes	Ofloxacin 200 mg × 2/day for 4 days
12	Yes	Negative	Amikacin 8 mg/kg/day + ceftriaxone 1 g/day for 2 days	14	ESBL *E. coli*	Amikacin 8 mg/kg/d 1 day + Pipe/Tazo 4 g × 3/day for 3 days	Yes	Imipenem 500 mg × 2/day for 7 days then Ofloxacin 200 mg × 2/day for 7 days
13	Yes	*E. aerogenes*	Amikacin 15 mg/kg/day + ceftriaxone 1 g/day for 3 days	14	*E. aerogenes* hyperCase	Pipe/Tazo 4 g × 3/day for 3 days	Yes	Cotrimoxazole 800/160 × 2 /day + Amikacin 15 mg/kg/day for 3 days

Pipe/Tazo piperacillin/tazobactam; *Amoxicillin + clav.ac.* amoxicillin + clavulanic acid

Informed consent the patients or their relatives provided written consent for computerization of their personal data for hospitalization purposes and clinical research.

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