

Pyuria and microbiology in acute bacterial focal nephritis: a systematic review

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Abstract

INTRODUCTION: presentation and imaging findings of acute focal bacterial nephritis, a localized renal infection not containing drainable pus, have been extensively addressed. The aim of this review was to assess the prevalence of cases without pyuria or bacteriuria and the spectrum of microorganisms underlying this condition. **EVIDENCE ACQUISITION:** we conducted a systematic review of the literature in the National Library of Medicine and Excerpta Medica databases. For the final analysis, we retained 54 reports published between 1981 and 2018 describing 251 patients affected by focal bacterial nephritis, who have been specifically investigated with respect to urinalysis and standard bacterial cultures. They were 177 (102 females and 75 males) subjects ≤ 20 and 74 (57 females and 17 males) > 20 years of age. **EVIDENCE SYNTHESIS:** Pyuria and bacteriuria were absent in 33 cases, while pyuria was not associated with bacteriuria in 5 further cases. The vast majority of culture-positive cases were caused by Enterobacteriaceae (slightly less than 80%) and Pseudomonas species (approximately 10%). Enterococcus species and Staphylococcus aureus were isolated in slightly more than 10% of the cases. **CONCLUSIONS:** a large subset of patients affected by focal bacterial nephritis present without pyuria and significant bacteriuria. The initial management consists of broad-

spectrum antimicrobials with high tissue penetration, active against Enterobacteriaceae, Pseudomonas species, Enterococcus species and Staphylococcus aureus.

Key words: Kidney diseases • microbiology • pyuria • urinalysis • lobar nephronia • abscess

Abbreviations

None

Introduction

Acute urinary infections include both infections of the urinary tract and infections of the kidney [1, 2]. The latter spans continuously from pyelonephritis to frank abscess [1-3]. Among this suite of renal infections, acute focal bacterial nephritis, also known as lobar nephronia, is a localized area of renal infection not containing drainable pus, which typically involves one, or less frequently, more lobes [3]. In this rather uncommon condition with unknown prevalence, clinical presentation and imaging findings have been extensively addressed [4].

The initial assessment for subjects with suspected urinary infection includes urinalysis and culture [1, 2]. Pyuria and significant bacteriuria are usually necessary to make the diagnosis. Some patients affected by acute bacterial focal nephritis have negative urinalysis and culture. This fact results in delays in diagnosis and, consequently, management. Furthermore, there is so far limited information about the microorganisms causing this infection.

The aim of this review was to assess the prevalence of cases without pyuria or bacteriuria and the spectrum of microorganisms underlying this condition.

Methods

Literature search strategy

We recently conducted a search with no date limits of the Medical Subject Headings terms "focal bacterial nephritis" OR "acute focal nephritis" OR "acute lobar nephronia" OR "acute nephronia" in the National Library of Medicine and Excerpta Medica databases. The literature of each included article was also screened. The review was performed according to the Economic and Social Research Council guidance on the conduct of narrative synthesis and on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

Selection criteria

We selected original articles reporting cases of acute focal bacterial nephritis, which specifically address urinalysis and microbiological findings. Reports published in Spanish, Portuguese, Italian, German, French, English and Dutch were eligible. For the final analysis, we included apparently immunocompetent subjects of both genders and a poorly defined, irregularly margined focal mass with hyper-, iso-, or hypoechogenicity or a generalized kidney enlargement on imaging [3, 4]. Pyuria and bacteriuria were not a prerequisite for inclusion. Cases with sterile pyuria possibly unrelated to the urinary tract were excluded.

Data extraction

Results of imaging tests completed in the original reports to support the diagnosis of acute focal bacterial nephritis were

reviewed using recognized criteria [2-4]. From each reported case, the following information was sought, in addition to results of imaging studies, by means of a predefined database: 1) demographics; 2) urinalysis; 3) standard bacterial cultures; and 4) pre-existing renal conditions.

Analysis

The literature search and the data extraction were independently carried out by two of us (S.J. and S.R.). If the extracted data were incongruent, conflicts were resolved by reaching a consensus. Results are given either as median and interquartile range, or as frequency, as appropriate. The kappa-test was used to assess the agreement between investigators on the application of inclusion and exclusion criteria. The Fisher exact test was applied to compare frequency counts between groups. Statistical significance was assigned at $P < 0.05$.

Results

Search Results

The literature search process is summarized in Fig. 1. The chance-adjusted agreement between the two investigators was 0.89. For the final analysis, we retained 54 reports published between 1981 and 2018 [5-58]: twenty-four from Europe (Spain, N=13; United Kingdom, N=3; Belgium, N=2; Germany, N=2; Croatia, N=1; Greece, N=1; Italy,

N=1; Portugal, N=1), 17 from America (USA, N=13; Argentina, N=2; Chile, N=2), 12 from Asia (Japan, N=8; India, N=1; Taiwan, N=1; Thailand, N=1; Turkey, N=1) and 1 from Morocco. Thirty-six reports were published in English, 13 in Spanish, 2 in French, 2 in German and 1 in Portuguese.

Findings

The aforementioned reports described 251 patients (159 females and 92 males) affected by focal bacterial nephritis, who have been specifically investigated with respect to urinalysis and standard bacterial cultures. There were 177 (102 females and 75 males) subjects ≤ 20 and 74 (57 females and 17 males) > 20 years of age.

Pyuria and bacteriuria were absent in 33 cases, while pyuria was not associated with bacteriuria in 5 further cases (table 1). A negative bacterial culture was more common ($P < 0.02$) in the group of patients ≤ 20 years of age. Antimicrobial administration had preceded diagnostic urinary investigations in 14 of the 38 culture-negative cases, pointing out that 24 (10%) out of the 237 cases without antimicrobial pretreatment had an unexplained negative urine culture.

A total of 213 (85%) patients were culture-positive (regrettably, information about the identified germ was not available in 15 cases). The germs isolated in 198 patients are depicted in table 2. The vast majority of cases were caused by Enterobacteriaceae (almost 80%) and Pseudomonas species (approximately 10%). Enterococcus

species and *Staphylococcus aureus* were isolated in about 10% of cases. In 27 (14%) cases, the germ was isolated both in blood and urine. No case presented with a positive blood culture and a negative urine culture.

Since information on pre-existing renal conditions was found in <20 of the 251 cases, these data were deliberately not analyzed.

Discussion

Urinary findings and microbiology of urinary infections are well established [1, 2]. This analysis performed in acute focal bacterial nephritis suggests that 10% of the cases present without pyuria and significant bacteriuria. The study also points out that *Enterobacteriaceae* and *Pseudomonas* species are the predominant pathogens, followed by enterococci and staphylococci. The discussion will address the prevalence of cases without bacteriuria, the spectrum of microorganisms underlying this condition, and finally both the clinico-laboratory features and the management.

Since antimicrobial pretreatment of a urinary infection rapidly decreases the rate of culture-positivity [1, 2], this analysis points out that at least every tenth case of acute bacterial focal nephritis is culture-negative (more frequently children than adults). On the contrary, urine cultures are normally positive (and associated with a positive test for leukocytes and nitrites) in untreated children and adults with a febrile urinary tract infection

[1, 2]. In this severe infection, the rather common occurrence of both leucocyte- and culture-negativity suggests that this entity, like renal abscess, sometimes does not communicate with the urinary collecting system [3, 4]. Furthermore, we assume that, like renal and perirenal abscess, focal bacterial nephritis occurs as a complication of a urinary tract infection or secondary to an hematogenous spread [3, 4].

Enterobacteriaceae, most frequently *Escherichia coli*, are the predominant pathogens both in uncomplicated community-acquired urinary tract infection and focal nephritis [1, 2, 59, 60]. By contrast, *Pseudomonas*, *Enterococci* and *Staphylococci* appear to be more common in focal nephritis as compared with community-acquired urinary tract infection. *Pseudomonas* is usually identified in cases with history of urinary tract infections, anatomic abnormalities or use of antimicrobials [61]. *Enterococci* are relevant uropathogens in subjects with an anatomic abnormality or in hospitalized patients [62]. Finally, *Pseudomonas*, *Enterococci* and *Staphylococci* are recognized pathogens in catheter-associated urinary tract infection [61-63]. Regrettably, the results of this study do not allow to confirm (or infirm) whether focal bacterial nephritis caused by *Pseudomonas*, *Enterococci* and *Staphylococci* predominantly occurs in subjects with anatomic abnormalities or use of antimicrobials.

In patients with focal nephritis the diagnosis is often delayed, the duration of hospital stay prolonged and the risk of renal scar formation high, which emphasizes the importance of a high level of

suspicion.

This diagnosis should be considered in patients with or without altered urinalysis presented with prolonged fever, particularly if associated with flank pain and elevated inflammatory markers. In addition, the diagnosis should be suspected in pyelonephritis patients slow at responding to an appropriate antimicrobial therapy. Identification of focal bacterial nephritis on imaging confirms the suspicion. Echography carried out by an experienced examiner aware of the clinical suspicion using modern equipment is reliable for diagnosis. In many cases, however, computed tomography with contrast enhancement is used [4]. There is so far limited experience with magnetic resonance imaging with this condition.

There is no place for primary surgery in focal bacterial nephritis [3]. The mainstay of initial management consists of parenteral high-dose broad-spectrum antimicrobials with high tissue penetration, active against Enterobacteriaceae, Pseudomonas species, Enterococcus species and Staphylococcus aureus. In addition to the predicted infecting organisms, the choice is based on a combination of patient factors and local microbial susceptibility patterns. Limited but plausible data suggest a total of three weeks of initial intravenous and subsequent oral antimicrobial therapy tailored to the cultured organism's susceptibility [64].

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Notes

Authors contribution: SJ, GPM and MGB conceptualized and designed the study, and drafted the article. SJ, PBF, SR and SAGL performed the literature search, extracted and analyzed the data, and critically revised the manuscript. OG gave a significant contribution in the revision of the article. All authors approved the final version of the manuscript as submitted.

The authors would like to thank Alice Leblanc for careful revision of the English text.

Compliance with ethical standards

Ethics approval

The design of this systematic review of the literature was approved by the ethical committee of the hospital.

Conflict of interest

The authors declare that they have no conflict of interest.

Statement of financial support

Dr. Gregorio P. Milani is the current recipient of research grants from the Fondazione G. & D. de Marchi ONLUS.

Figure - Legend

Figure 1

Focal bacterial nephritis. Flowchart of the literature search process.

Table 1. Standard urine cultures in patients affected by focal bacterial nephritis.

Standard Urine Culture	Age (years)		
	All	≤20	>20
Culture-positive, N	213	151	62
Culture-negative, N	38	34	4*
Absent pyuria	33	31	2*
With antimicrobial pretreatment	14	13	1

*P<0.02

Table 2. Microorganisms isolated in 198 patients affected by acute bacterial focal nephritis. In 27 of the cases the germ was isolated both in blood and urine.

Microorganism	Urine (N=198)		Blood (N=27)	
	N	%	N	%
Enterobacteriaceae				
Escherichia coli	130	66	19	70
Klebsiella species	15	7.6	0	0.0
Proteus species	7	3.5	0	0.0
Enterobacter species	2	1.0	1	3.7
Serratia species	1	0.5	1	3.7
Pseudomonas species	19	9.6	2	7.4
Enterococcus species	15	7.6	1	3.7
Staphylococcus aureus	9	4.5	3	11