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Fourteen (14) cases of acute focal bacterial nephritis in children

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To investigate clinical features, laboratory, and imaging characters in Chinese children, we conducted a retrospective study on 14 children with acute focal bacterial nephritis (AFBN) admitted in Beijing Children's Hospital during January 2005 to December 2009. Six girls and eight boys with a mean age of 4.7 years (range: 0.3-11.4 years) were followed up on average 1.7 years (range: 0.5-3.5 years). Leukocyturia was found in 10/14 children. Urine cultures were positive in 10/14 cases; *E. coli* was the most common cause of AFBN. A combination of nephromegaly and focal mass was found in 11/14 patients. Urinary tract anomalies were found in 8 children. Two boys had underlying disease of acute lymphatic leukemia under chemotherapy. AFBN resolved on average 3-12 weeks after therapy. Ultrasound and enhanced CT were not necessary in cases of fever of unknown origin, even if pyuria nor urine culture is positive. Vesicoureteral reflux (VUR), malignancy and renal vascular malformation are potential risk factors of AFBN; careful radiological investigations should be performed.

Key words: Acute focal bacterial nephritis, vesicoureteral reflux, children.

INTRODUCTION

Acute focal bacterial nephritis (AFBN) is a localized bacterial infection of the kidney presenting as an inflammatory mass not containing drainable pus. AFBN typically involves one or more renal lobules. Rosenstein originally called it acute lobar nephronia (ALN) (Rosenfield et al., 1979). The first report of AFBN in children was published in 1985 (Lawson et al., 1985). Pathological examination reveals hyperemia, interstitial edema, and infiltration of leukocytes, but not necrosis or liquefaction (Montejo et al., 2002). Septicemia due to respiratory tract infections or ascending infection of the lower urinary tract is suspected. For the majority of children, the pathogenesis may be related to ascending infection. The most common pathogen is *E. coli*, although other bacteria can cause it as well.

AFBN is being diagnosed with increasing frequency due to increasing awareness and advances in imaging. Ultrasonography (US) and computerized tomography (CT) scanning may serve as an arbiter when the diag-

nosis of AFBN is unclear despite clinical and laboratory evaluation. It is not a rare condition. It is probably an underdiagnosed disease entity. Previous reports have revealed that pre-existing malformative uropathy, especially vesicoureteral reflux (VUR), is common in pediatric patients with AFBN (Uehling et al., 2000; Siegel and Glasier, 1981). It has potential for parenchymal renal scarring.

However, there is little report on AFBN among Chinese children. To investigate clinical features, laboratory and imaging characters, we conducted a retrospective study on AFBN children admitted.

MATERIALS AND METHODS

Subjects

We evaluated 14 children diagnosed with AFBN during January 2005 to December 2009 admitted in Beijing Children's Hospital,

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China. Six girls and eight boys with a mean age of 4.7 years (range: 0.3-11.4 years) were followed up on average 1.7 years (range: 0.5-3.5 years). The patients with AFBN comprised 3.2% of the children with UTI and 2.7% of those with VUR.

Methods

Clinical features, predisposing factors, laboratory findings, imaging results, treatment and outcome were investigated. All patients underwent urinalysis and urine and blood cultures. Positive urine cultures were defined as a minimum of 10^5 colony-forming units (CFU) per milliliter of a single pathogen isolated in fresh, midstream urine samples.

Blood and urine cultures were taken from all patients before treatment in our hospital. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and white blood cell count (WBC) were raised in all children; serum creatinine levels and glomerular filtration rates determined by Schwartz formula (Schwartz et al., 1976) were calculated in all cases.

AFBN diagnosis was made on the basis of positive US or CT findings. All patients underwent renal ultrasonography (Philips HD 11) after admission. US revealed variation in the pattern of echoes, which may range from hypoechoic to hyperechoic and may be heterogeneous. Renal parenchymal perfusion was examined by color power Doppler. Intravenous contrast medium-enhanced CT scanning (GE LightSpeed VCT 64) was performed in 10 patients. The findings on CT scanning included the appearance of a nonenhancing mass, usually within the kidney. The lesion was often wedge-shaped, had a low density, and did not have a clear margin. Urinary tract and renal vascular 3-dimensional reconstructions were performed in four patients suspected of homogenous infection. All children underwent voiding cystoureterography (VCUG) after successful antibiotic treatment. Four children were examined by dimercaptosuccinic acid (DMSA) scan due to sonographic suspicion of renal scarring.

Treatment

All children received intravenous antibacterial therapy for 19.5 days (range 17 to 28 days) on average. The particular choice of antibiotics was made on the basis of the sensitivity findings of the initial urine culture. Ten children were treated with cephalosporin (cefpiramide, ceftazidime, or ceftriaxone), and four with meropenem.

Follow-up

All patients were followed up to assess their clinical symptoms, urine culture results, and renal size by ultrasonography. Ultrasound was performed repeatedly after antibiotic therapy weekly until lesion resolution, followed by ultrasound controls every 3 to 6 months during the follow-up period. AFBN resolved on average 3 of 12 weeks after therapy.

RESULTS

Clinical and diagnostic findings

Clinical features, laboratory findings and predisposing factors are illustrated in Table 1. All patients had been febrile for 2 to 7 days before admission. Only four children older than 7 years had flank pain. Younger children (range: 0.3-3.2 years) presented unspecific symptoms such as vomiting, lethargy, and poor feeding or reduced

general condition. All of them were given antibiotics before admitted in our hospital. Two boys had underlying disease of acute lymphatic leukemia (ALL) under chemotherapy. No patient had diabetes or immunodeficiency.

Main laboratory findings on admission are summarized in Table 2. Glomerular filtration rates were normal in all cases. Leukocyturia was found in 10/14 children; 4/14 were negative in tests. Urine cultures were positive in 10/14 cases; *E. coli* was the most common, followed in frequency by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, and *Acinetobacter spp.* Four children had negative urine culture results.

Imaging results revealed AFBN of the right kidney in 6 children, of the left kidney in 4 children and of both kidneys in four patients. A combination of nephromegaly and focal mass were found in 13/14 (92.86%) patients. All children underwent VCUG. Urinary tract anomalies were found in 8 children, vesicoureteral reflux in 7 and PUJO in 1. Unilateral vesicoureteral reflux (VUR) was found in four children; bilateral refluxes were found in three children. Urinary tract anomalies, especially high grade of VUR was found predominately in children younger than 3 years old.

After initiation of antibiotic treatment, the clinical condition of all children improved; temperatures were back to normal within one to six days. Patients with underlying disease of ALL had longer fever duration after treatment, 5 or 6 days respectively. Urine and blood cultures were performed 5-7 days after treatment onset and were negative in all cases. In patients with VUR or pelviureteric junction obstruction (PUJO), intravenous therapy was followed by low dose prophylactic antibiotics with nitrofurantoin (six patients), cefixime (one patient), or cefaclor (one patient) for 6 weeks to 9 months until surgical interventions of the underlying cause was completed.

Case 4 had an episode of septicemia and meningitis, blood culture was positive for *Acinetobacter spp.* The ultrasounds showed both kidneys were normal. After 14 days of treatment, the cerebrospinal fluid tests were normal. The treatment stopped. One week later, the child had fever again, and the urine tests showed pyuria, urine culture was positive for the same organism (as determined by strain and antibiotic sensitivity), while blood culture was negative. The enhanced CT revealed that left kidney developed AFBN, while multiple renal abscesses formed in right kidney. The further investigation by 3-dimensional reconstruction revealed the malformation of renal artery. The right kidney is nourishing by several fine arteries derivatives from aorta instead of normal renal artery (Figure 1).

Follow-up

During the follow-up period of 1.7 years (range: 0.5-3.5 years), renal function and blood pressure were normal. Hematuria or proteinuria was not found. In our evaluation, scarring was found in one child and cysts in one child during follow-up.

Table 1. Clinical features, predisposing factors and laboratory findings of patients with AFBN.

Age (year)	Gender	Associate disease	Fever before treatment (day)	Fever after treatment (day)	Affected kidney(s)	Urinary tract anomalies	Urine culture	Blood culture
0.3	M	Pneumonia	5	3	Right	Right VUR grade III	<i>Escherichia coli</i>	Negative
0.5	M	None	4	3	Right	Right VUR grade II	<i>Klebsiella pneumoniae</i>	Negative
0.7	F	Pneumonia	6	2	Left	Left PUJO	Negative	Negative
1.0	M	Meningitis Septicemia	5	4	Bilateral	None	<i>Acinetobacter spp</i>	<i>Acinetobacter spp</i>
1.1	M	Perianal abscess	7	4	Right	Left VUR grade I and right grade III	<i>Escherichia coli</i>	Negative
1.7	F	Pneumonia	4	2	Left	Left VUR grade III	<i>Klebsiella pneumoniae</i>	Negative
2.3	F	None	6	2	Right	Left VUR grade IV and right grade II	<i>Escherichia coli</i>	Negative
3.2	M	ALL Septicemia	5	6	Bilateral	None	<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>
7.4	F	None	8	2	Left	Left VUR grade I	Negative	Negative
7.6.	M	ALL Septicemia	6	5	Bilateral	None	<i>Enterococcus faecalis</i>	<i>Enterococcus faecalis</i>
8.1	F	None	7	2	Right	None	Negative	Negative
9.4	F	None	4	2	Bilateral	None	<i>Escherichia coli</i>	Negative
10.4	M	None	2	1	Right	None	<i>Escherichia coli</i>	Negative
11.4	M	None	3	1	Left	Bilateral VUR grade I	Negative	Negative

DISCUSSION

AFBN is a nonsuppurative focal form of acute bacterial infection. The typical presentations of ALN include fever, flank pain, leukocytosis, pyuria, and bacteriuria. Only older children with AFBN presented specific findings of flank pain or symptoms related to urinary system. Diagnosis of

AFBN is often delayed due to nonspecific symptoms (Kline et al., 1988). All children in our study were admitted with fever. Young children were presented with poor feeding, dehydration, or lethargy, symptoms that could easily be attributed to other more common causes. In our group, before admission, four children were suspected of fever of unknown origin, three of pneumonia, and

three of septicemia. AFBN should be considered as a differential diagnosis in children presenting persisting fever and rapid deterioration of clinical condition despite antibiotic treatment.

Clinical and laboratory findings of all children suggested acute infection. Elevated CRP and ESR usually were found. Among the 14 patients in this study, *E coli* was the most common pathogen

Table 2. WBC count, CRP, ESR and Leukocyturia of patients with AFBN

Parameter	Mean (range)	Number
White blood cell count ($10^9/l$)	20.8 (12.2-47.3)	14
C-reactive protein (mg/l)	103.2 (55-236)	14
Erythrocyte sedimentation rate (mm/h)	89.8 (45-130)	14
Leukocyturia (WBC/HP)	64 (15-200)	10 4 (Negative)

Figure 1. Enhanced CT (A) AFBN in left kidney, renal abscesses in right kidney, (B) reconstruction of AFBN in left kidney, renal abscesses in right kidney, (C) vascular reconstruction illustrates abnormal right renal artery.

of previous studies (Montejo et al., 2002; Klar et al., 1996; Cheng et al., 2006), followed in frequency by *K. pneumoniae*, *P. aeruginosa*, *E. faecalis*, and *Acinetobacter* spp. The incidence of bacteremia in our study was low: only three patients proved to have bacteremia. Negative urine culture and lack of leukocyturia in AFBN have been reported previously (Montejo et al., 2002; Kline et al., 1988). Although AFBN was confirmed, (4/14) patients in our group, neither pyuria nor urine culture was positive. We suggest that an early examination of enhanced CT and US are necessary in cases with fever of unknown origin, considering the possibility of AFBN even if neither pyuria nor cultures of urine are positive.

Careful radiological investigations are a valuable tool in the evaluation of these patients (Kline et al., 1988; Cheng et al., 2004). It may reveal a causative or contributory factor to the infection such as VUR or renal vascular abnormalities, either of which may alter therapeutic management. A combination of nephromegaly and a focal mass was found in 13/14 patients in the study; the same as that reported by Cheng et al. (2004). Cheng et al. (2004) reported that severe nephromegaly in combination with a focal mass were very useful diagnostic criteria for AFBN; a systematic imaging evaluation for patients suspect that AFBN should be a combination of renal ultrasonography and CT scanning and early stages of the AFBN can be detected.

US findings ranged from hypoechoic to hyperechoic and may be heterogeneous (Cheng et al., 2004; Farmer et al., 2002). Our observation suggests that the sonographic appearance can alter according to the time of we

perform US examination. CT is currently recognized as the most sensitive and specific imaging modality for diagnosing selected cases, because the initial examination by ultrasonography does not always provide a definitive diagnosis (Farmer et al., 2002).

The findings on enhanced CT scanning include the appearance of a mass effect, usually within the kidney. The lesion is often wedge-shaped, has a low density, and does not have a clear margin. The use of intravenous contrast during CT evaluation not only improves anatomic detail but may also provide functional information about the kidney. Development of the CT scanning processed in multiple imaging planes with three-dimensional reconstruction capabilities has further improved sensitivity for detecting underlying renal abnormalities. In case 4, AFBN and renal abscesses were caused by hematogenous spread of bacteria. This different inflammatory process may not be determined by bacterial strains or genetic immune response differences of the host as in other patients. We speculated that the renal artery malformation factor played a leading role that affected the different speed of disease progression. The kidney with normal blood supply stayed in AFBN phase, while lesion of the kidney with multiple fine arteries deteriorated rapidly into renal abscesses. Low speed of blood circulation caused by renal artery malformation may induce more bacteria dwell and rapid proliferation in kidney. Renal vascular malformation should be considered as a risk factor of progression in patients with AFBN. 3-dimensional reconstruction of renal vascular is recommended if enhanced CT scanning is performed. But we should consider the

high radiation burden that would be put on the group of children.

Intravenous antibiotic therapy is recommended. Treatment duration has been discussed controversially (Klar et al., 1996; Cheng et al., 2006; Shimizu et al., 2005). The clinical condition of all children improved rapidly within one to six days after treatment onset. We suggest that a 3-week antimicrobial-therapy protocol for patient without immunodeficiency.

In our evaluation, urinary tract abnormalities were found in 8 children, mainly vesicoureteral reflux (7) followed by PUJO (1). VUR was noted in half of the children with ALN in this study, a figure comparable to that in several previous studies (Uehling et al., 2000; Siegel and Glasier, 1981; Mutari et al., 2002; Rathore et al., 1991). AFBN is a result from ascending bacterial infection of the urinary tract. This explanation is supported by experiments in which the disease was produced when vesicoureteral reflux was induced in pigs infected with *E. coli*. VUR may be a prerequisite for the development of AFBN (Uehling et al., 2000). Another group of children at increased risk for this disease are those with malignancy. Except for two boys with ALL, none of the children had underlying systemic diseases such as diabetes, which is known as a main predisposing factor for AFBN in adults (Boam and Miser, 1995).

Residual lesions after AFBN, such as renal scarring or cysts, have been described previously (Siegel and Glasier, 1981; Klar et al., 1996; Seidel et al., 2007). Renal scarring might be present in some of the patients despite antibiotic treatment; DMSA scans should be performed regularly in long-term follow-up. Because this study is retrospective, limitation on DMSA scan evaluation cannot be avoided in present study.

AFBN should be considered in patients with a renal mass detected during an episode of urinary infection. Due to the diverse clinical presentations and low incidence of AFBN in children, prospective studies are difficult to perform; therefore, multicenter studies are required to solve the questions of pathogenesis, optimal therapy, and long-term outcome of AFBN in children.

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