

An Unexpected Agent in a Child with Urinary Tract Infection: *Haemophilus influenzae*

Üriner Sistem Enfeksiyonu Olan Bir Çocukta Nadir Görülen Bir Etken: *Haemophilus influenzae*

ABSTRACT

Haemophilus influenzae, particularly in children, causes local and systemic infections such as meningitis, pneumonia, epiglottitis, otitis media, sinusitis and bacteremia. This bacterium has rarely been implicated as the causative agent of urinary tract infections (UTIs) in children. Most of the reported cases on UTIs due to *H. influenzae* were associated with urinary tract abnormalities and/or recurrent UTIs. Because of the inability of *H. influenzae* to grow in standard media commonly used for urine cultures, the true incidence of UTIs due to this potential pathogen is unknown. In this report, we present a case of UTI caused by *H. influenzae* in a 17-year-old boy with bilateral nephrolithiasis and hydronephrosis. To our knowledge, this is the first reported case of UTI caused by *H. influenzae* in Turkey.

KEY WORDS: *Haemophilus influenzae*, Urinary tract infections, Urine

ÖZ

Haemophilus influenzae, özellikle çocuklarda, menenjit, pnömoni, epiglottit, otitis media, sinüzit ve bakteriyemi gibi lokal ve sistemik enfeksiyonlara yol açmaktadır. Bu bakteri, çocuklarda üriner sistem enfeksiyonlarının (ÜSİ) etkeni olarak nadiren izole edilmiştir. *H. influenzae*'ye bağlı olarak gelişen ÜSİ ile ilgili bildirilen olguların çoğu, üriner sistem anormallikleri ve/veya tekrarlayan ÜSİ ile ilişkilendirilmiştir. *H. influenzae*'nin idrar kültürleri için yaygın olarak kullanılan standart besiyerlerinde ürememesi nedeniyle, bu potansiyel patojene bağlı olarak gelişen ÜSİ'nin gerçek insidansı bilinmemektedir. Bu raporda, bilateral nefrolitiazisi ve hidronefrozu olan 17 yaşındaki bir erkek çocukta *H. influenzae*'ye bağlı olarak gelişen ÜSİ olgusunu sunuyoruz. Bildiğimiz kadarıyla, Türkiye'de bildirilen *H. influenzae*'nin etkeni olduğu ilk ÜSİ olgusudur.

ANAHTAR SÖZCÜKLER: *Haemophilus influenzae*, Üriner sistem enfeksiyonları, İdrar

INTRODUCTION

Urinary tract infections (UTIs) are among the most common infectious diseases in childhood (1). The vast majority of UTIs are caused by bacterial agents, the most important of which are the Enterobacteriaceae, a family of gram-negative bacilli. Although *Klebsiella* spp. are more common in neonates, and *Proteus* spp. among boys over one year of age, *Escherichia coli* accounts for 80-90% of UTIs in children (1-3). Some bacterial species that have low virulence factors for the urinary tract could also grow in children with malformation or dysfunction of the

urinary tract (3). *Haemophilus influenzae* is a small, non-motile, facultative anaerobic, pleomorphic, gram-negative coccobacillus which cannot be isolated in the standard urine culture (4). There are few reports in the literature on UTIs caused by *H. influenzae* in children. We report here a rare case of UTI caused by *H. influenzae* in a child. To our knowledge, this is the first reported case of UTI caused by *H. influenzae* in Turkey.

CASE REPORT

A 17-year-old boy was admitted to our clinic with abdominal pain, malodorous urine and dysuria. There was no vomiting

Mümtaz Cem ŞİRİN¹
Cengiz Han ELMAS²
Neval AĞUŞ¹
Caner ALPARSLAN²
Nisel YILMAZ¹
Önder YAVAŞCAN²

- 1 İzmir Tepecik Training and Research Hospital, Department of Medical Microbiology, İzmir, Turkey
- 2 İzmir Tepecik Training and Research Hospital, Department of Pediatric Nephrology, İzmir, Turkey



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Correspondence Address:

Mümtaz Cem ŞİRİN
İzmir Tepecik Eğitim ve Araştırma Hastanesi,
Tıbbi Mikrobiyoloji Laboratuvarı,
İzmir, Turkey
Phone : +90 232 469 69 69
E-mail : drmcemsirin@yahoo.com

or fever. He had been followed at our clinic for a diagnosis of bilateral multiple nephrolithiasis in conjunction with bilateral grade two hydronephrosis on double collector system of the left kidney since he was seven years old. The family history revealed that his brother had an ectopic kidney and his sister had a diagnosis of nephrolithiasis. His past medical history revealed open kidney surgery for stone removal at seven years of age, and further percutaneous nephrolithotomy when he was 16 years old. After the percutaneous nephrolithotomy, ultrasonography showed no stone and hydronephrosis. He had numerous UTIs. The most commonly growing microorganism had been *E. coli* and treated with appropriate antibiotics. The urine culture taken a week ago was negative by standard culture methods but the patient remained symptomatic. On physical examination there was bilateral tenderness at the costovertebral angle but the rest of the physical examination was unremarkable. Laboratory findings were as follows; serum urea 34 mg/dl, creatinine 0.9 mg/dl, sodium 138 mmol/l, potassium 4.5 mmol/l, chlorine 105 mmol/l, calcium 9.4 mg/dl, leukocyte 18.500/mm³, hemoglobin 13.2 g/dl, platelet 297.000/mm³, C-reactive protein 59 mg/l. Nitrite test and leukocyte esterase were positive in the urinalysis and microscopy of urine showed many leukocytes and leukocyte clusters. After obtaining urine culture, an oral antibiotic (cefixime, 8 mg/kg/day) was started empirically. Urine culture from the patient showed growth of *H. influenzae* with a bacterial load of 10⁵ colony forming units per milliliter (CFU/ml). Initially, *H. influenzae* was isolated from blood agar by satelliting around a few *Staphylococcus aureus* colonies. Then repeat urine culture was taken from the patient, and chocolate agar was used to isolate *H. influenzae*. Identification of the oxidase-positive, dewdrop-like colonies that revealed gram-negative coccobacilli was carried out by using Vitek 2 Compact NH ID card (bioMérieux, France), and antibiotic susceptibility testing was performed by the Kirby-Bauer disk diffusion method according to the Clinical Laboratory Standards Institute (CLSI) criteria. The strain was resistant to ampicillin, ampicillin-sulbactam, amoxicillin clavulanate, cefaclor and susceptible to cefixime, ceftriaxone, ceftazidime, cefepime, trimethoprim-sulfamethoxazole, ciprofloxacin, levofloxacin. The beta-lactamase test was positive by nitrocefin disk (Becton Dickinson, USA). The strain was classified as serotype b by *H. influenzae* capsular typing antisera (Denka Seiken, Tokyo, Japan). When we queried the patient history in more detail, we learned that he had not previously been vaccinated against *H. influenzae* type b. According to the antibiogram report, the patient continued to receive oral cefixime for 10 days. He showed clinical improvement with no complaints. Urinalysis was normal and urine culture showed no growth.

DISCUSSION

H. influenzae is part of the normal flora of the upper respiratory tract and may cause epiglottitis, acute tracheobronchitis, pneumonia, meningitis, otitis media, and sinusitis in children (4). Evidently, this bacterium does not have the properties to

invade and colonise the urinary tract under normal conditions. However *H. influenzae* has rarely been implicated as the causative agent of UTIs in children and most of the cases were associated with anatomical or functional urinary tract abnormalities (3-6). The first report in children was probably in 1960, when Rogers et al. (7) described eight patients with UTIs caused by *H. influenzae*. Six of these had hydronephrosis, calculus or congenital abnormalities of the urinary tract. In 1979 Schuit (6) detected only one case among 877 urine samples in order to determine the frequency of isolation of *H. influenzae*. In 1984 Burns et al. (5) described seven children, aged from five months to eight years, with *Haemophilus* spp. isolated from urine. In all children, the significant infections were associated with abnormalities of the urinary tract and histories of recurrent infections. Of the seven isolated strains, three were identified as *H. influenzae*. In our case, the patient had bilateral multiple nephrolithiasis and bilateral grade two hydronephrosis on double collector system of kidney. These abnormalities, to our opinion, most likely increased susceptibility to UTI due to this bacterium.

Since standard urine culture methods do not permit the growth of *H. influenzae*, it is not possible to determine the true incidence of UTIs with this potentially pathogen bacterium (3,6). Most clinical microbiology laboratories do not include an appropriate medium to support the growth of *H. influenzae* strains in their routine urine culture workup (8). *H. influenzae* requires preformed growth factors present in blood, particularly X factor (hemin) and V factor (nicotinamide adenine dinucleotide). The hemolysis of erythrocytes on blood agar by *S. aureus*, releases the necessary factor V for the growth of *H. influenzae*. Therefore, it grows poorly on ordinary blood agar unless streaked with *S. aureus*. Chocolate agar contains freely available X and V factors, and allows isolation of *H. influenzae*. The previous studies showed that this pathogen was isolated from chocolate agar or other rich culture media (3,4,6,9,10). Small, round, convex colonies which may be iridescent, develop in 5% CO₂ atmosphere within 24 hours on chocolate agar. In this case, *H. influenzae* colonies were initially discovered on blood agar by satelliting around *S. aureus* colonies. Then, in the repeat urine culture, we used chocolate agar to isolate *H. influenzae*.

Most of the invasive *H. influenzae* infections are caused by encapsulated strains belonging to serotype b (3). After the introduction of the *H. influenzae* type b vaccine, invasive *H. influenzae* type b diseases predominantly affecting children have decreased in many parts of the world. It has been reported that both encapsulated type b and noncapsulated (nontypeable) strains of *H. influenzae* might cause UTIs (6, 7, 11). In our case, the isolated strain was classified as serotype b. In the detailed history of our patient, we learned that he had not previously been immunized with *H. influenzae* type b vaccine.

In conclusion, UTI due to *H. influenzae* is very infrequent in children with normal urinary tract. But the incidence may increase if there is an underlying urinary tract abnormality. The

routine urinary culture techniques do not permit the isolation of *H. influenzae*. So, when recurrent UTIs appear in a patient with urogenital abnormalities, *H. influenzae* that does not grow in the standard urine culture should be considered and as in our case, other rich culture media like chocolate agar should be used.

REFERENCES

1. Stein R, Dogan HS, Hoebeke P, Kocvara R, Nijman RJ, Radmayr C, Tekgül S: Urinary tract infections in children: EAU/ESPU guidelines. *Eur Urol* 2015;67:546-558
2. Chang SL, Shortliffe LD: Pediatric urinary tract infections. *Pediatr Clin North Am* 2006;53:379-400
3. Hansson S, Svedhem A, Wennerström M, Jodal U: Urinary tract infection caused by *Haemophilus influenzae* and *Haemophilus parainfluenzae* in children. *Pediatr Nephrol* 2007;22:1321-1325
4. Demetrios P, Constantine B, Demetrios S, Nikolaos A: *Haemophilus influenzae* acute pyelonephritis in the elderly. *Int Urol Nephrol* 2002;34:23-24
5. Burns RT, Hinds BD, Hawkins E: *Haemophilus* organisms: urinary tract pathogens in children. *Diagn Microbiol Infect Dis* 1984;2:251-253
6. Schuit KE: Isolation of *Haemophilus* in urine cultures from children. *J Pediatr* 1979;95:565-566
7. Rogers KB, Zinnemann K, Foster WP: The isolation and identification of *Haemophilus* spp. from unusual lesions in children. *J Clin Pathol* 1960;13:519-524
8. Dingle TC, Clarridge JE: Clinical significance and characterization of *Haemophilus influenzae* type b genogroup isolates from urine samples in an adult male population. *J Clin Microbiol* 2014;52:1745-1748
9. Sturm AW: Isolation of *Haemophilus influenzae* and *Haemophilus parainfluenzae* from genital-tract specimens with a selective culture medium. *J Med Microbiol* 1986;21:349-352
10. Morgan MG, Hamilton-Miller JMT: *Haemophilus influenzae* and *H. parainfluenzae* as urinary pathogens. *J Infect* 1990;20:143-145
11. de Almeida AE, Caldeira NG, Schroeder LF, Batalha de Jesus AA, Serradas LR, da Costa AF, Lima CO, de Filippis I: Urinary tract infection caused by nontypable *Haemophilus influenzae* in the elderly. *J Med Microbiol* 2010;59:1132-1133