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Scientific letters

Gentamicin resistant *E. coli* as a cause of urinary tract infections in children☆

Resistencia a gentamicina en infecciones urinarias por E. coli *en niños*

Urinary tract infections (UTIs) are common in childhood, constituting 5–7% of cases of fever of unknown origin in infants under 2 years of age.[1,2] The early institution of adequate treatment is crucial in order to prevent kidney lesions.[3] *Escherichia coli* is the main uropathogen in childhood (70–90% of cases),[1,2,4] and it is thus important to understand its local resistance patterns in order to select the empirical antibiotic treatment.[5]

Various paediatric protocols consider gentamicin to be a first-line treatment for UTIs requiring parenteral antibiotic therapy.[1,2,6,7] We recently performed a retrospective review of UTI cases diagnosed at the children's emergency department of one tertiary hospital between January and December 2014. We included significant growths in urine collected using suprapubic aspiration (any amount), catheterisation (>10^4 colony-forming units [CFUs]), spontaneous urination (>10^5 CFUs) or an adhesive bag (>10^5 CFUs of the same germ in at least two bags) in children under 14 years of age, excluding untreated asymptomatic bacteriuria. In cases caused by gentamicin-resistant *E. coli*, we recorded the existence of factors that could favour this resistance,[6–8] such as a history of prematurity, nephro-urological malformations or other chronic diseases, recent hospital admissions, stays in intensive care, previous UTIs or receiving antibiotic prophylaxis. 78% of the isolates were caused by *E. coli* (201/258), 15% of which were gentamicin-resistant (30/201). 25 were considered UTIs with significant growth, 15 by spontaneous urination (60%), nine by catheterisation (36%) and one in two urine collection bags (4%). The 25 episodes occurred in 21 children, with a median age of 12.4 months (interquartile range: 3.6–23.4), requiring hospitalisation on 13 occasions (52%). Resistance risk factors were observed in 13 patients (61%): 8 (38%) with nephro-urological disease, 7 (33%) had had previous UTIs, 5 (23%) were receiving antibiotic prophylaxis, 5 (23%) had been hospitalised in the six months prior, 3 (14%) were in intensive care and 5 (23%) had other diseases (encephalopathy, Down's syndrome, congenital CMV infection and heart disease). 57% (12) presented more than two risk factors, and 28% (6) presented more than three. 44% of the isolates combined resistances to amoxicillin/clavulanic acid and cefuroxime (11), 36% to cefotaxime (9) and 32% to ciprofloxacin (8). 28% (7) produced extended-spectrum beta-lactamases (ESBL) and 8% (2, from the same patient) VIM-type carbapenemases. 90% of the resistant strains subjected to a susceptibility analysis were sensitive to amikacin (9/10).

If this trend were confirmed in children with risk factors, gentamicin might no longer be the empirical treatment of choice in UTI cases among these patients as, in order to select an empirical treatment, we must consider that potential aetiological agents may not present resistances of over 10–20%.[5]

We noted that these strains combined resistances to drugs such as cephalosporins and ciprofloxacin, as mentioned previously in other studies.[6–9] The increase in cephalosporin resistances is particularly relevant as they constitute the routine outpatient treatment and the treatment administered to children with kidney failure.[2]

Rising rates of ESBL-producing strains have recently been published in community UTIs.[9–11] As in our series, these resistances are observed in patients with risk factors.[6–8,12] Similarly, other authors have observed high rates of gentamicin resistance in community-acquired UTIs caused by *E. coli*.[6]

However, hospitals in our geographical area have published high rates of gentamicin sensitivity in *E. coli* strains that cause community UTIs in children (95.6%).[2] As our hospital is a referral centre for certain paediatric diseases, the patients treated at our emergency department often present with comorbidities, histories of long hospital stays and exposure to broad-spectrum antibiotics. In view of our results and those presented by other groups, it is becoming increasingly important to adapt antibiotic strategies according to these risk factors.

In our study, we observed that amikacin could be an excellent empirical UTI treatment option in these patients within our setting. Other authors have already proposed the use of amikacin in this population, given its adequate coverage for other common uropathogens and its excellent diffusion to the renal parenchyma.[7,9]

In conclusion, we consider it essential to continue the epidemiological surveillance of UTI-causing strains in risk populations. These factors must be assessed on establishing an empirical treatment to avoid complications and treatment failures.

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Micafungin in the treatment of invasive fungal infection in an infant with extracorporeal

Micafungina como tratamiento de la infección fúngica invasiva en un paciente con oxigenación por membrana extracorpórea

The use of extracorporeal membrane oxygenation (ECMO) life support systems has increased in recent years. They can be colonized by several microorganisms, particularly fungi, giving rise to nosocomial infections, such as invasive fungal infection (IFI), in the form of central line-associated bloodstream infection (CLABSI) and circuit infection. These microorganisms, moreover, can develop a biofilm that perpetuates their existence.

When IFI is confirmed in a patient on ECMO, the circuit should be changed or even removed, depending on the patient's condition. The use of antifungal drugs with activity against biofilm could allow IFI treatment to continue without removing the circuit.

We present the case of an infant on ECMO support who suffered a CLABSI when the circuit was infected by *Candida.* The patient was treated with micafungin without ECMO being changed or removed.

A female infant of 20 months of age, weighting 12 kg, with a body mass index of 0.6, with no relevant personal or family history, was admitted to the pediatric intensive care unit (PICU), following referral from another center to receive ECMO support. Diagnosis was necrotizing pneumonia by *Streptococcus pneumoniae*, with acute respiratory distress syndrome and septic shock.

Initial symptoms on admission were a 5-day history of fever up to 40 °C, accompanied by respiratory and heart failure.

Community-acquired left lobar pneumonia was diagnosed, with ipsilateral pleural effusion and septic shock, requiring intubation and mechanical ventilation. Broad-spectrum antimicrobial treatment was started with cefotaxime and vancomycin. Vancomycin was withdrawn following isolation of cephalosporine-susceptible serotype 7F/A from culture.

After day 6, her respiratory symptoms worsened, with pneumothorax, which was drained, and serious respiratory destabilization. As a result, high-frequency ventilation was started, with poor response. A new broad-spectrum antimicrobial treatment was started with piperacillin-tazobactam and amikacin, due to the possibility of ventilator-associated pneumonia, and inotropic support (consisting of dopamine up to 16 mcg/kg/min and adrenaline up to 0.8 mcg/kg/min) was required.

On day 7, due to poor evolution and response to treatment given so far, she was transferred to our PICU. Considering the seriousness of the patient, who had a Pediatric Risk Score of Mortality III (PRISM-III) of 25, oxygenation index of 38, an alveolar arterial difference of 590, 15 mmol/L lactate and echocardiographic signs of severe pulmonary hypertension (60–70 mmHg), ECMO was started.

The previously started inotropic therapy was maintained, and a steroid treatment for relative suprarenal insufficiency in the context of septic shock was started. Other treatments were sedation with fentanyl and midazolam, neuromuscular blockade and parenteral nutrition with gastric protection. Fig. 1 shows radiologic examination at the time of starting ECMO.

The patient made good progress, with removal of inotropic support after 4 h on ECMO. Respiration also improved, and she was gradually weaned from ventilator support, with radiologic and analytical improvements.

However, after 5 days after admission to our PICU, the patient's condition deteriorated, with febricula and altered analytical parameters (leukocytosis 16,000 l/mm^3, C-reactive protein 148.7 mg/L and procalcitonin 1.5 ng/mL, normal lactate). Several cultures were taken from the patient (blood, urine and

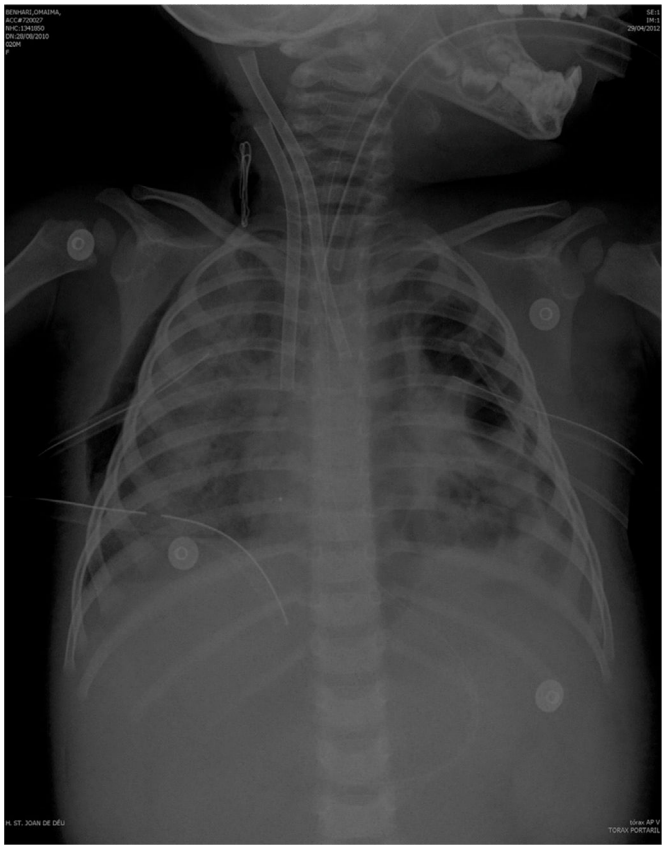

Fig. 1. Radiologic examination at day 7, at the time of starting ECMO.