

Case report

Multifocal Invasive Group A Streptococcus Infection in a Previously Healthy 17-Month-Old Child: A Rare Case Report

Ysaline Marchione, Marc Hainaut

CHU Saint-Pierre, Department of Pediatrics, Université Libre de Bruxelles, Brussels, Belgium.

ysaline.marchione@ulb.be

Keywords

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Abstract

Group A β -hemolytic *Streptococcus* is a highly pathogenic organism with multiple virulence factors enabling it to invade a wide range of sterile sites. Multifocal dissemination of infection is not uncommon. However, urinary tract infection is very rarely reported.

We describe an atypical case of a 17-month-old boy in whom a streptococcal urinary tract infection delayed the diagnosis of a multifocal invasive infection with more classic joint involvement.

Case Report

Group A β -hemolytic *Streptococcus* (GAS), also known as *Streptococcus pyogenes*, is a human-restricted gram-positive bacterium that colonizes epithelial surfaces. It can lead to asymptomatic carriage or cause a wide spectrum of clinical presentations ranging from local infections such as pharyngitis to invasive disease including streptococcal toxic shock syndrome (STSS) (1). Indeed, this pathogenic organism possesses multiple virulence factors that allow it to invade many sterile sites (2). Invasive group A streptococcal infection (iGAS) is defined by the isolation of GAS from a normally sterile body site (3). iGAS can manifest as bacteremia without focus, severe pneumonia, osteoarticular infection, endocarditis, meningitis, necrotizing fasciitis, STSS, etc. However, urinary tract infections (UTI) due to GAS are exceptionally reported. Necrotizing fasciitis and STSS are both associated with the production of exotoxins that act superantigens inducing an exaggerated immune response resulting in a severe clinical picture (1,4,5). Over the past forty years, the incidence and severity of iGAS has steadily increased worldwide (1,2). Although it can affect individuals of all ages, the highest rates are found in children under the age of 5 and adults over the age of 60 (1,5,6). The clinical manifestations of iGAS in children differ from those in adults. Pediatric patients have a lower rate of STSS and necrotizing fasciitis. Osteoarticular infections are uncommon but, in contrast, more frequent than in adults, accounting for 4.5% to 24% of pediatric patients with iGAS (1,4,5). Most cases of iGAS occur in otherwise healthy children without chronic conditions. The main points of entry are the respiratory tract and the skin (6). Surgical wounds, skin lesions and chickenpox are therefore some of the known predisposing risk factors, although nearly half of affected children have none (5,6). The overall case fatality rate for iGAS is 8-19%, corresponding to an estimated 160,000 deaths per year worldwide and it rises to nearly 50% when the infection is complicated by a STSS (4,6,7,8). In all studies, the mortality rate in children is at least half that of adults (1,5,7,8). However, iGAS is often severe in children, accounting for approximately 40% of intensive care unit admissions (5).

We present the case of a previously healthy 17-month-old boy who developed an iGAS with an unusual multifocal presentation: upper urinary tract infection, hip arthritis and bacteremia.

Case presentation

A 17-month-old boy presented to the emergency department with a 2 day history of fever up to 39.6°C and intermittent episodes of vomiting.

Since the previous day, his general condition had deteriorated with a decreased feeding and avoidance of standing and walking. He had no contributing medical history other than recurrent acute otitis media. His vaccinations were up to date. Vital signs were within normal limits (heart rate = 137 bpm, oxygen saturation = 96%, blood pressure = 101/70 mmHg). On physical examination, the toddler was pale, with pharyngeal erythema and showed signs of discomfort. He refused to stand up, remaining in a sitting position. Mobilization of both hips appeared to be painful, but without range of motion limitation, joint swelling, warmth or erythema. Laboratory tests revealed a severe inflammatory syndrome (white blood cell (WBC) count = 32.12 x10e9/L with an absolute neutrophil count = 25.6 x10e9/L and C-reactive protein = 359 mg/L). A urine sample obtained by transurethral bladder catheterization showed leukocyturia with >800 WBC/ μ L. The patient was admitted and started on intravenous antibiotics with temocillin 50 mg/kg/day in 2 doses, given the diagnosis of urinary tract infection. The day after admission, a limp in the left lower limb was noted. In contrast to the previous day, the patient had now markedly restricted range of motion of the left hip, but still no associated local signs of inflammation. Ultrasound imaging confirmed a left hip joint effusion, and an evacuating joint aspiration was promptly performed. The macroscopic purulent appearance and the microscopic analysis of the synovial fluid were consistent with bacterial arthritis. Therefore, on the first day of hospitalization, the antibiotic therapy was changed to a broad-spectrum antibiotic, ceftriaxone 100mg/kg/day in a single dose. The patient became afebrile on the same day. Blood, urine and joint fluid cultures all showed the presence of *Streptococcus pyogenes*, leading to the final diagnosis of multifocal iGAS with bacteremia, upper urinary tract infection, and left hip arthritis. Antibiotic susceptibility testing revealed that the bacterium was susceptible to penicillin-G, erythromycin, clindamycin, levofloxacin and vancomycin. On the third day of hospitalization, the patient was switched from broad-spectrum antibiotic coverage with ceftriaxone to dual therapy with intravenous amoxicillin (200mg/kg/day in 4 doses) and clindamycin (30mg/kg/day in 3 doses). Despite the absence of hemodynamic instability, a potentially toxic erythematous rash developed, justifying the addition of clindamycin without requiring intravenous immunoglobulin. The patient's gait gradually improved, albeit with a residual limp. Magnetic resonance imaging of the left lower extremity performed on the ninth day of hospitalization showed no osteomyelitis associated with septic arthritis. Abdominal ultrasound showed no deep focus of infection between the bladder and the left hip

and no urinary tract abnormalities were found on abdominal ultrasound. Laboratory tests gradually returned to normal, and a baseline immune blood workup was unremarkable. On the 10th day of hospitalization, after 7 days of intravenous antibiotic therapy with amoxicillin and clindamycin, considering the criteria of clinical improvement and resolution of the inflammatory syndrome, oral amoxicillin (100mg/kg/day) was continued for 14 days, while clindamycin was discontinued. At the two-month follow-up visit, the limp was completely resolved.

Discussion

Since the mid-1980s, iGAS has increased in incidence and severity worldwide. It may be partly attributed to the emergence of new virulent strains (1,9). In high-income countries, the reported annual incidence ranges from 1.6 to 3.8/100,000 (6,8). This is at least two to three times higher than the incidence of invasive meningococcal disease in Europe. Indeed, due to the development of vaccines against childhood pathogens such as *Neisseria meningitidis* and their introduction into immunization programs, iGAS has become an emerging cause of severe infection in children (7). After a period of reduced incidence related to the lockdown during the COVID-19 pandemic in 2020-2021, several European countries have reported a new increase in the number of iGAS cases since September 2022, especially in children younger than 10 years (10).

In our case of multifocal iGAS, although bacteremia and arthritis are classic manifestations, UTI is exceptionally reported. In children, we found only one observational study conducted in Kenya from 1998 to 2011 that revealed that UTI could be one of the manifestations of iGAS, identifying 6 patients with UTI among 369 cases of pediatric iGAS (4). In addition, the propensity of GAS to disseminate to multiple sites can complicate management. In our patient, because of the early diagnosis of upper UTI on admission, the clinical signs of limping, highly suspicious for osteoarticular infection, were ignored and delayed the diagnosis and appropriate treatment of hip arthritis (i.e., joint cavity drainage and appropriate antibiotic therapy).

The adjunction of an antitoxin antibiotic such as clindamycin to conventional beta-lactam therapy is widely recommended in the literature for the treatment of iGAS, particularly in case of necrotizing fasciitis, STSS or clinical signs suggestive of toxin production (rash, gastrointestinal signs, hemodynamic disturbances) (9,11). In our patient, the addition of clindamycin was justified by the appearance of an erythematous-macular rash, which raised concern of a toxic rash. Clindamycin is a lincosamide that inhibits protein synthesis and thus exotoxin production. Compared to penicillin, in addition to its antitoxin activity, clindamycin has a superior post-antibiotic effect, better tissue penetration and activity against bacteria in stationary phase, so it is not affected by inoculum size or growth stage (9). However, clindamycin should not be used alone as a small proportion of GAS are resistant to it (5-10% in Belgium but almost 30% in the USA), whereas there is no resistance to penicillin to date (1,2). Nevertheless, GAS strains with unusually high minimum inhibitory concentrations for ampicillin and amoxicillin have recently been reported in the United States, although they are still clinically susceptible to β -lactams (12). The optimal total duration of antibiotic therapy for iGAS is unclear because data are limited. Without specifying the minimum intravenous duration, most authors recommend a minimum of 10 to 14 days of treatment, to be tailored to each patient's situation. The occurrence of septic arthritis in our patient's clinical picture explains the total duration of amoxicillin treatment of 21 days. Intravenous immunoglobulins are generally recommended for all hemodynamically unstable patients and/or patients admitted to intensive care and/or those with STSS or necrotizing fasciitis (9,11). Since our case did not meet any of its severity criteria, immunoglobulins were not required. There is no international consensus regarding secondary chemoprophylaxis for contacts. In a systematic review published by Laho et al. in 2021, the authors recommend prophylaxis with first-generation cephalosporins for all household members of the patients and for contacts at high risk of complications related to iGAS (11).

Conclusion

Given its increasing incidence and severity, early recognition of iGAS is imperative to ensure prompt and appropriate treatment. However, the initial clinical presentation is often non-specific, may even be unusual and plurifocal as in our patient, and therefore challenging to diagnose. Despite decades of research, the development of an effective vaccine for the prophylaxis of GAS infections remains a major issue and has been declared a priority by the World Health Organization (WHO) in 2018 (13).

Conflict of interest

The authors have no conflicts of interest to declare.

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