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Case report

Invasive infection from *Kingella kingae*: Not only arthritis

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ABSTRACT

Kingella kingae is a known pathogen for osteoarticular infections in young children. However other invasive infections such as pneumonia in immunocompetent patients are scarcely described in literature. We present an unusual case of bacteremia and lower respiratory tract infection in a previously healthy infant, the first one described in Greek pediatric population. The pathogen was identified using both culture and molecular techniques

Introduction

During the last years *Kingella kingae* is recognized as a cause of invasive infections within pediatric population. It is, from clinical point of view, the most important species of *Kingella* genus. *K. kingae* is a slowly growing Gram- coccobacillus and a member of the *Haemophilus* spp, *Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae* (HACEK) group. For many years it has been referred as a rare human pathogen. However, due to improved culture methods, greater experience in terms of identification and the wide use of molecular methods, *K. kingae* is recently recognized more often as a pathogen in invasive infections, mainly osteoarticular, bacteremia and rarely endocarditis, in children younger than 4 years old [1]. Although *K. kingae* asscosiated osteoarticular infections are well described in literature, pneumonia due to this bacterium is rarely noted. Between 1988 and 2013 only 5 cases of pneumonia have been described among 143 children with invasive disease due to *Kingella* [2,3].

Herein we present an unusual case of bacteremia and pneumonia in a previously healthy infant, the first one described in Greek pediatric population. The clinical presentation, that is a lower respiratory tract infection, is dealt with very often in every day practice, however the pathogen is a rare cause of pneumonia and is mainly connected to bone-joint infections in young children.

Case report

An 8-month-old, previously healthy female infant was admitted to our clinic due to high fever up to 39.4 °C with concurrent cough and nasal congestion for 3 days. On admission she was in respiratory distress with diffuse bilateral rales, retractions of intercostals spaces and SatO2 95 % in air. The rest of physical examination was normal. The laboratory evaluation showed CBC and biochemistry within normal limits apart from a slightly increased CRP (26 mg/L). She was initially started on inhaled bronchodilators. Six hours later, the infant was significantly deteriorated with hypotonia, paleness, tachypnea, tachycardia, and remained febrile. A second lab test revealed leucocytosis (WBC 17800/mL, N/67 %, L/28 %), CRP 173 mg/L and ESR 48 mm/h. The chest X-ray showed pulmonary opacities by the right heart border and the right upper lung as well as the left retrocardiac area. She was started empirically on IV ceftriaxone and fluids.

On the 3rd day after admission, a short Gram-negative bacterium was detected in blood cultures by the Bactec (BD, USA) automated system. The blood culture vials were subcultured to Trypticase-soy agar supplemented with 5% hemoglobin, chocolate agar and MacConkey agar. After 48 h incubation, in 35 °C, in aerobic conditions, there was a growth of a bacterium on the blood agar medium, on chocolate agar (the 5% CO_2 atmosphere improved its growth) but no growth on MacConkey agar. The colonies were small (0,5–1 mm,48 h), with beta hemolysis and characterized by marked pitting of the agar surface. The bacterium was non motile, non-spore forming, exhibited negative catalase, urease and indol tests, had positive oxidase activity and produced acid from glucose and maltose. The Phoenix automated system

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(BD, USA) identified it as *Kingella Kingae* and the identification was confirmed by sequencing of 16Sr-RNA gene. Susceptibility testing to antimicrobials was performed according to EUCAST instructions. The production of β-lactamase was negative.

Following pathogen identification further investigation with transesophageal heart echo was carried out with normal findings. The clinical examination with emphasis on bones and joints showed no sign of arthritis, thus no imaging was done. The infant responded well to treatment and remained afebrile after the 3rd day of hospitalization, while repeated blood cultures were all sterile. The baby was discharged from hospital after 12 days of treatment in excellent general condition.

Discussion

K. kingae was first characterized in 1968 as *Moraxella kingii* [4]. Thirty years later it was identified as a leading cause of septic arthritis in young children, on the ground of improved culture techniques and increasing familiarity of microbiologists with its identification. The bacterium was found to be part of the pharyngeal flora of young children. Pharyngeal colonization prevalence differs between studies based on age, day care attendance, sampling season, previous antimicrobial consumption or different microbiologic techniques. In general, up to 12 % of children aged 0–36 months are colonized while attendees of child care centers have much higher rates up to 73 % and even higher during outbreaks [2,3].

Connection to disease has been shown only with a few distinct clones with organisms showing enhanced tissue invasive capacity and virulence. Among the 32 genotypically distinct clones only 5 (B, H, K, N, P) are responsible for the vast majority of invasive infections, with K, N and P relating to bacteremia, osteoarticular infections and endocarditis respectively [5].

Another co-factor in *K. kingae* disease is simultaneous or previous viral infections. It has been shown that a viral upper respiratory infection especially with rhinovirus, enterovirus or HSV most of the times precede or coincide with *K. kingae* disease. It seems that the respiratory epithelial cell damage from the virus favors the microbes' invasion to the blood stream and subsequent secondary infections [2].

K. kingae invasive infections are encountered mainly in children 6–36 months old with no underlying medical conditions. In older children infection is mostly seen in patients with chronic health problems such as primary or secondary immunodeficiencies, cardiac, renal and hematologic conditions [6]. In an Israeli study by Dubnov-Raz et al. 81 % of children with *Kingella* bacteremia had no underlying diseases, 80 % were between 5 and 18 months old and 79 % presented with concurrent viral infection of the respiratory or digestive system [6]. The same applies to our case, a previously healthy infant, with initial symptoms compatible with respiratory viral infection.

Septic arthritis due to *Kingella* is especially common in children below 4 years old. It was the most common agent in joint infections of young children in Israel after the inoculation of samples in blood culture vials, and the most common in France on the ground of combined blood culture vials and a DNA-amplification technique [7,8]. Skeletal infection was the most common entity also in nine outbreaks in childcare centers between 2003 and 2014 in USA, Israel and France [3].

Occult bacteremia represents up to 43,6% of *K. kingae* invasive infections in children according to a nationwide collaborative study in Israel [9]. In *K. kingae* bacteremia as in osteoarticular infections symptoms are often mild and there is only a slight increase in inflammation markers with WBC often lower than 15000/mL [6]. On the contrary in more severe cases such as endocarditis there is high fever >39 °C and increased acute phase reactants [1]. In 10 % of bacteremic cases endocarditis is also encountered, that is why further investigation with heart echo is imperative. HACEK organisms are responsible for 6 % of all cases of endocarditis in the general population [2]. In our case the combination of high acute phase reactants with severe clinical picture favored a more complicated diagnosis than bacteremia. Although endocarditis had to be excluded the whole picture was justified from the second nidus of infection in the respiratory tract.

Kingella pneumonia is also scarcely described in children with no underlying disease. The case of a Spanish 10 year old child with pneumonia was published in 2001, while in Israel only 5 cases of pneumonia have been described among 143 children with invasive disease due to *Kingella* between 1988 and 2013 [2,10].

Our case is the first one described in Greece with *Kingella* bacteremia and LRTI and the second one overall with *Kingella* invasive infection. The previous case report was that of a 16-month-old child with *K. kingae* arthritis [11]. Unfortunately there are no available epidemiological data on kingella prevalence in Greek pediatric series with bacteremia or septic arthritis. This might reflect the issue of technical difficulties in isolating the pathogen from blood and joint fluid cultures. Another explanation is that on the ground of mild symptoms and the lack of marked leucocytosis, blood cultures are not routinely drawn from outpatient febrile children between 6–36 months old, thus making occult bacteremia diagnosis gone unrecognized.

In terms of diagnosis, it is nowadays well known that direct inoculation of clinical samples in solid cultures does not lead to the isolation of *K. kingae.* On the contrary inoculation in blood culture vials increases significantly the possibility of isolation, since the inhibitory effect of factors that are highly concentrated in samples such as synovial fluid is significantly decreased after being diluted in blood culture vials. The identification can be currently made with various commercial systems such as the quadFERM + kit, Phoenix, API NH, Vitek 2, matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) and molecular methods such as PCR 16SrRNA, NAA *cpn60(*chaperonin60) and NAA *rtxA* (RTX toxin) [2]. In our case *K. kingae* was diagnosed by Phoenix.

K. kingae isolates are almost always susceptible to most of the antimicrobials that are usually given to children. However oxacillin, clindamycin and daptomycin are not effective, while all strains are highly resistant to glycopeptides [1,2]. Thus empiric monotherapy for osteoarticular infections with antibiotics targeting mainly *S. aureus* are inadequate in *Kingella* cases. In 2013 beta-lactamase producing clones were identified [12]. However the enzyme seems to be detected only in around 1% of isolates in patients with invasive disease [2]. In our case the child responded well to treatment with ceftriaxone in terms of clinical picture and repeated lab investigation.

K. kingae infection may be underdiagnosed and underreported due to technical difficulties regarding isolation of the pathogen and the mild clinical picture that renders lab investigation unnecessary most of the times. The true burden of the disease is still unknown in many countries including Greece.

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Garyfallia Syridou: Conceptualization, Writing - original draft. **Panagiota Giannopoulou:** Investigation, Writing - original draft. **Nikoletta Charalampaki:** Investigation. **Joseph Papaparaskevas:** Investigation, Writing - review & editing. **Paraskevi Korovessi:**

Resources. **Sophia Papagianni:** Investigation. **Athanassios Tsakris:** Investigation, Writing - review & editing, Supervision. **Eleftheria Trikka-Grafakou:** Investigation, Writing - review & editing, Supervision.

Declaration of Competing Interest

None.

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References

[1] Principi N, Esposito S. *Kingella kingae* infections in children. BMC Infect Dis 2015;15:260, doi:http://dx.doi.org/10.1186/s12879-015-0986-9.
[2] Yagupsky P. *Kingella kingae*: carriage, transmission, and disease. Clin Microbiol Rev 2015;28:54–79.
[3] El Houmami N, Minodier P, Dubourg G, et al. Patterns of *Kingella kingae* disease outbreaks. Pediatr Infect Dis J 2016;35:340–6.
[4] Henriksen SD, Bovre K. Moraxella kingie sp. nov., a haemolytic saccharolytic species of the genous Moraxella. J Gen Microbiol 1968;51:377–85.
[5] Amit U, Porat N, Basmaci R, et al. Genotyping of invasive Kingella kingae isolates reveals predominant clones and association with specific clinical syndromes. Clin Infect Dis 2012;55:1074–9.
[6] Dubnov-Raz G, Scheuerman O, Chodick G, et al. Invasive *Kingella kingae* infections in children: clinical and laboratory characteristics. Pediatrics 2008;122:1305–9.
[7] Yagupsky P, Bar-Ziv Y, Howard CB, et al. Epidemiology, etiology, and clinical features of septic arthritis in children younger than 24 months. Arch Pediatr Adolesc Med 1995;149:537–40.
[8] Moumile K, Merckx J, Glorion C, et al. Osteoarticular infections caused by *Kingella kingae* in children: contribution of polymerase chain reaction to the microbiologic diagnosis. Pediatr Infect Dis J 2003;22:837–9.
[9] Dubnov-Raz G, Ephros M, Garty B-Z, et al. Invasive pediatric *Kingella kingae* infections. A nationwide collaborative study. Pediatr Infect Dis J 2010;29:639–43.
[10] Gómez-Garcés JL, Oteo J, Garcia G, et al. *Kingella* kingae pneumonia:a rare pathology or a pathology rarely diagnosed? Clin Microbiol Newsl 2001;23:192–3.
[11] Grivea IN, Michoula AN, Basmaci R, et al. *Kingella kingae* sequence type-complex 14 arthritis in a 16-month-old child in Greece. Pediatr Infect Dis J 2015;34:107–8.
[12] Basmaci R, Bonacorsi S, Bidet P, et al. Genotyping, local prevalence and international dissemination of β-lactamase-producing Kingella kingae strains. Clin Microbiol Infect 2014;20:O811–7.