Small risk of osteoarticular infections in children with asymptomatic oropharyngeal carriage of Kingella kingae

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Abstract

The aim of this study was to evaluate the absolute risk for children younger than 4 years of age with asymptomatic oropharyngeal carriage of Kingella kingae to sustain an osteoarticular infection. The rate of K. kingae carriage in the oropharyngeal mucosa was 9% among healthy children, and the risk for an asymptomatic carrier to develop an osteoarticular infection due to K. Kingae was estimated to be lower than 1%.

Reference


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that in our case, the source of his infection was likely to be from his mother because the child had no contact with animals. The infant’s mother reported a history of a persistent cough before the infant’s birth, but this cough resolved before the child had his first positive culture.

The mother was not screened for Bordetella bronchiseptica infection due to asymptomatic respiratory carriage has not demonstrated an incidence of invasive disease.

We conducted this study to investigate the genetic susceptibility to osteoarticular infection caused by K. kingae and to estimate the prevalence of osteoarticular infection caused by K. kingae. In addition, we assessed the correlation between asymptomatic carriage and the subsequent incidence of osteoarticular infection due to K. kingae, including the probability for an asymptomatic carrier to sustain an osteoarticular infection due to this pathogen.

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Kingella kingae is the major bacterial cause of osteoarticular infection in children less than 48 months of age. 1-3 This organism is a frequent component of the oropharyngeal flora of young children and is readily transmitted from person to person. 4-6 There is evidence suggesting that it colonizes the oropharynx before penetrating the bloodstream and invading distant organs, 4 such as joint and bone. 3 Administration of a short antibiotic course has been recently recommended for contacts between 6 and 48 months of age when disease clusters are detected, 7 but investigations of the epidemiologic features of asymptomatic respiratory carriage have not demonstrated any correlation between the pattern of carriage of K. kingae and the incidence of invasive disease. 3 We conducted this study to investigate the genetic susceptibility to osteoarticular infection caused by K. kingae. In addition, we assessed the correlation between asymptomatic carriage and the subsequent incidence of osteoarticular infection due to K. kingae, including the probability for an asymptomatic carrier to sustain an osteoarticular infection due to this pathogen.

METHODS

Study Design and Patients

In this prospective, consecutive study, we collected the data of all children aged 6–48 months admitted to the emergency department of the Geneva Children’s Hospital (111-bed tertiary pediatric hospital) with a suspicion of osteoarticular infection between January 1, 2008, and December 31, 2011. Eligible subjects underwent a clinical evaluation and blood analysis, and magnetic resonance imaging was performed on patients presenting clinical or laboratory findings suggestive for an osteoarticular infection and analyzed for signs of infection according to established criteria. 8 Arthrocentesis or bone aspiration was performed under fluoroscopy guidance in the operating room for cases where imaging suggested osteoarticular infection. In parallel, healthy children aged between 6 and 48 months were screened for asymptomatic oropharyngeal carriage of K. kingae during the same period. Oropharyngeal specimens were obtained by rubbing a cotton swab on the tonsils and subsequently analyzed by real-time polymerase chain reaction (PCR) for K. kingae as described earlier. Recruited children were either hospitalized for clean surgery, were attending our orthopedic outpatient clinic or visiting the emergency department for minor problems; children of hospital staff were also screened. Exclusion criteria were the presence of invasive diseases and the administration of antimicrobial drugs during the previous months.

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Analysis of aspirates included a Gram stain (aerobic/anaerobic) culture and PCR assays. All biologic samples (oropharyngeal swabs, synovial fluid, bone biopsy specimen, peripheral blood) were analyzed with a new real-time PCR assay specific to *K. kingae*. Each PCR analysis was performed in duplicate. If the specific *K. kingae* PCR assay was negative, osteoarticular samples were submitted to broad-range PCR assay.

The diagnosis of osteoarticular infection caused by *K. kingae* was established when cultures and/or specific PCR assays were positive for this microorganism in blood, synovial fluid or bone aspirate samples. Osteoarticular infection caused by other microorganisms was defined by the presence of bacterial growth other than *K. kingae* on synovial fluid, blood or bone aspirate cultures and/or by a positive result in the broad-range PCR. The diagnosis of presumed osteoarticular infection was assigned when joint fluid/bone samples were not obtained for diagnostic bacterial culture or PCR assay or when cultures were negative, but magnetic resonance imaging demonstrated conclusive signs of infection. The diagnosis of osteoarticular infection was excluded when there were no positive bacterial findings or signs of osteoarticular infection on magnetic resonance imaging, or when improvement occurred without treatment.

The protocol was approved by the local institutional review board (09-029R, Mat-Ped 09-008R), and the study was conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki.

Statistical Analysis

The probability to sustain an osteoarticular infection due to *K. kingae* following a positive oropharyngeal PCR for *K. kingae* is equal to the positive predictive value (PPV) of the oropharyngeal PCR assay. The PPV can be derived from the sensitivity and specificity of the oropharyngeal PCR assay and the prevalence of osteoarticular infec

RESULTS

Between January 1, 2008, and December 31, 2011, 64 consecutive patients met the eligible criteria for osteoarticular infec

DISCUSSION

*K. kingae* is frequently isolated from the upper respiratory tracts of young children with a colonization rate ranging from 3.5% to 17.5%. Children usually first acquire *K. kingae* after the age of 6 months, the colonization rate then increases among infants aged between 12 and 24 months and finally declines among older children and adults. The present epidemiologic study confirmed a similar respiratory carriage rate in a Swiss pediatric population (9%), suggesting that asymptomatic colonization of the upper respiratory tract by *K. kingae* is probably a worldwide phenomenon. Similar to microorganisms such as *S. pneumoniae*, *H. influenzae* type b or *Neisseria meningitidis*, *K. kingae* is able to penetrate the bloodstream, disseminate and invade distant organs. Asymptomatic colonization of the upper respiratory tract is thus a strategy for *K. kingae* to survive and occasionally spread into the bloodstream under certain circumstances. A recent report described 3 patients with invasive *K. kingae* infections in whom the identical genotype isolate was recovered from the pharynx and the bloodstream. This observation supports the hypothesis that upper respiratory tract colonization represents the first step in the pathogenesis of invasive disease.

The correlation between asymptomatic carriage and the subsequent incidence of osteoarticular infection due to *K. kingae* remains unclear, even if prophylactic antibiotic administration has been recently recommended in an attempt to prevent further disease spreading during outbreaks of *K. kingae* among day-care center attendees. Nevertheless, previous investigations on the epidemiologic features of asymptomatic respiratory carriage have not demonstrated any correlation between the pattern of carriage of *K. kingae* and the incidence of invasive disease. The probability for asymptomatic children carrying *K. kingae* in the oropharynx to develop an osteoarticular infection due to this pathogen is probably lower than 1%. Oropharyngeal carriage of *K. kingae* does not imply the subsequent development of invasive infection and suggests that other cofactors may play a role in the pathogenesis of invasive *K. kingae* infections.

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REFERENCES


**POSTVARICELLA THROMBOSIS—REPORT OF TWO CASES AND LITERATURE REVIEW**


**Abstract:** Varicella (chickenpox) is a common disease of childhood, caused by varicella-zoster virus. Postviral thromboembolism is a rare complication of varicella-zoster virus in childhood. We describe 2 children who developed lower limb deep venous thrombosis shortly after varicella infection, along with a review of 130 previously reported cases.

**Key Words:** varicella, chickenpox, thrombosis, deep venous thrombosis, protein S deficiency, antiphospholipid antibody

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**FIGURE 1.** A and B, Doppler ultrasound demonstrating thrombus (A—arrows) in left common femoral vein (CFV), the left superficial femoral vein (SFV) and popliteal vein (POP) and its resolution (B).

Varicella-zoster virus (VZV) causes primary, latent and recurrent infections. The primary infection manifests as varicella (chickenpox) and results in establishment of a lifelong latent infection of the sensory ganglion neurons. Reactivation of the latent infection causes herpes zoster. Although often a mild illness in childhood, chickenpox can cause substantial morbidity and mortality in otherwise healthy children.

There have been few case reports of thrombotic complications including transient antiphospholipid syndrome, protein C and protein S deficiencies associated with varicella. Purpura fulminans is the most common thrombotic complication, and thromboembolism reported in association with varicella has been shown to be due to both arterial and venous thrombi, generally after the skin rash.

We report here 2 cases of postvaricella thrombosis and review the literature to explore the wide spectrum of presentations and the different underlying pathophysiologic mechanisms, treatments and outcomes.

**CASE REPORT**

**Case 1**

A 10-year-old girl presented with a 2-day history of increasing pain and swelling of the left leg. Two weeks before the present symptoms, she had fever and a characteristic chickenpox rash all over the body, lasting for a few days with subsidence of fever following scab formation. She had no previous history of bleeding tendency or thrombosis. The patient was not immobilized or incapacitated during the acute viral illness. Her siblings also had chickenpox. There was no history suggestive of collagen vascular disorder. The family history was negative for bleeding disorders, thrombosis or stroke, and the parents were not consanguineous.

On examination, she had low-grade fever of 38°C with otherwise normal vital signs. Her left leg was swollen, purplish, tender and warm with pitting edema and normal peripheral pulses. A healed maculopapular rash was observed all over the body with centripetal distribution. The rest of the examination was unremarkable.