Kingella kingae sternal osteomyelitis presenting as chest lump in a child

A case report and review of the literature

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We would like to thank the staff of Sydney Children’s Hospital Network and the family of the patient for the consent.

**Conflict of interest**
The authors have disclosed no conflict of interest.

**Consent**
Verbal consent was provided from the family and for the images included in the case report.

**Introduction**

*Kingella kingae* is a Gram-negative bacterium which belongs to the Neisseriaceae family. It is a facultative anaerobic, beta-haemolytic, small bacillus that appears as pairs or short chains. It frequently colonises the oropharynx of infants and children from 6-48 months. It is often responsible for musculoskeletal infections in children and it has been reported as one of the most common causes of septic arthritis and osteomyelitis in children below 4 years of age.¹

**Case Report**

A previously well 3-year-old boy, presented with a one week history of a central chest swelling which reportedly appeared suddenly. After it appeared, there was no notable change in size during the week. The swelling was associated with localised chest pain especially at night. There was a history of minor trauma in which he was hit by a book by one of his siblings. His carer did not report any documented fever but had reported decrease of appetite, 3 kg weight loss and night sweats during the prior 3 months. There was no history of overseas travel or farm animal contact.

The physical examination revealed a well-looking child with a temperature of 37.5 °C and otherwise normal vital signs. Local examination of the swelling revealed a firm, non-erythematous and non-tender swelling at the right upper border of the sternal junction/manubrium, measuring approximately 2 cm by 1.5 cm (Figure 1). There were small palpable lymph nodes in the cervical, axillary and inguinal regions. Examination was otherwise unremarkable and his weight was on the 50th centile & height on the 75th centile for age.

His peripheral white cell count was normal at 7.3x10⁹/L, C reactive protein was not raised (2 mg/L). Blood culture was negative. He also had normal lymphocyte subsets and immunoglobulins G, A and M.

Initially he was referred to the Paediatric Oncology service due to the history of a rapidly enlarging mass with night sweats, lymphadenopathy and weight loss. From an oncological perspective, the differential diagnoses included lymphoma, Langerhans cell histiocytosis (LCH), sarcoma, neuroblastoma and sternal pseudotumour of childhood. As such, further imaging of the area with a computed tomography (CT) scan and definitive tissue biopsy were
arranged. The infectious diseases team was also consulted as an infective cause was part of the differential and this included bacterial, mycobacterial & fungal infections.

His CT chest revealed a destructive bony lesion involving the manubrium and to a lesser degree the body of the sternum, centred on the manubrium sternal junction with an associated soft tissue mass with possible complex fluid components. The soft tissue mass was predominantly superficial, but contained a small deep extension in the anterior mediastinum (Figure 2).

The boy underwent a surgical tissue biopsy of the swelling. Histopathology of the tissue showed a mixed acute and chronic inflammatory infiltrate dominated by macrophages scattered eosinophils and foci of acute inflammation but no features to suggest a neoplasm nor evidence of Langerhans cell histiocytosis. Flow cytometry revealed a mixed T cell population with no abnormal population identified. Cytology of the aspirate consisted of abundant neutrophils, macrophages and vessels in a background of blood with no atypical cells identified.

On microbiological examination of the aspirated fluid, smear for acid fast bacilli (Auramine stain) and *Mycobacterium tuberculosis* polymerase chain reaction (PCR) were both negative. There were no sulphur granules on gram stain suggestive of actinomycosis. There was no growth from either bacterial (including anaerobic) or fungal cultures of aspirated fluid. However, *Kingella kingae* genomic material was detected using 16S ribosomal RNA PCR, reported two weeks later.

Once the result of the PCR was available, the boy was commenced on cephalexin 100 mg/kg/day in 3 divided doses for 6 weeks for a diagnosis of sternal osteomyelitis due to *Kingella kingae*. He tolerated the cephalexin well and the swelling had resolved completely at 6 weeks’ follow up.

**Discussion**

Bone and joint infections are the most commonly reported *Kingella kingae* infections in the paediatric population. These may be under-reported as the culture yield of *Kingella kingae* from synovial fluid and bone aspirate has been reported to be suboptimal since *Kingella kingae* is a fastidious and slow growing organism. Direct PCR for *Kingella kingae* or indirect PCR (16s RNA PCR as in our case) may identify additional cases but these are not widely available in many settings. Some recent studies using both conventional culture and PCR combinations, report *Kingella kingae* to occur in about half of osteoarticular infections in children < 4 years of age.¹

From the literature, there are studies which have looked at the significance of molecular testing in the diagnosis of *Kingella kingae* osteoarticular infections in the paediatric
Among eight studies, a total of 525 paediatric patients with osteoarticular infections were included. The joint fluid sample or bone aspirate was cultured for *Kingella kingae*, from which 38 samples were positive by culture of *Kingella kingae* and 110 samples were positive by PCR for *Kingella kingae*. From these studies, we estimate that the PCR contributes to an additional diagnosis in up to 50% of culture-negative samples of synovial fluid and for ~90-100% of culture-negative samples of bone aspirate, indicating high sensitivity of the *Kingella kingae* PCR from bone samples.

### Table 1: Studies investigating molecular diagnosis of *Kingella kingae* in culture-negative cases of synovial fluid or bone aspirate.

<table>
<thead>
<tr>
<th>First authors</th>
<th>Number of patients</th>
<th>Culture-positive* n (%)</th>
<th>Culture-negative n (%)</th>
<th><em>Kingella kingae</em> detected by PCR n (%)</th>
<th>Type of sample used for PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verdier (2005)²</td>
<td>171</td>
<td>64 (37.4)†</td>
<td>107(62.6)</td>
<td>15/107(14)</td>
<td>Joint fluid</td>
</tr>
<tr>
<td>Chometon (2007)³</td>
<td>131</td>
<td>60(45 ) ‡</td>
<td>61(46)</td>
<td>22/61 (36 )</td>
<td>Joint fluid</td>
</tr>
<tr>
<td>Luegmair (2008)⁴</td>
<td>6**</td>
<td>3 (50)</td>
<td>3(50)</td>
<td>3/3 (100)</td>
<td>Bone</td>
</tr>
<tr>
<td>Hertting (2008)⁵</td>
<td>2**</td>
<td>0 (0)</td>
<td>2(100)</td>
<td>2/2 (100)</td>
<td>Bone</td>
</tr>
<tr>
<td>Illharrebrode (2009)⁶</td>
<td>89</td>
<td>36(40.5)</td>
<td>53 (59.5)</td>
<td>24/53 (45 )</td>
<td>Joint fluid</td>
</tr>
<tr>
<td>Williams (2014)⁷</td>
<td>68</td>
<td>17(25) §</td>
<td>51 (75)</td>
<td>27/51 (53) §</td>
<td>Joint fluid</td>
</tr>
<tr>
<td>Slinger (2016)⁸</td>
<td>50</td>
<td>10 (20)</td>
<td>40(80)</td>
<td>7/27 (26) ¶</td>
<td>Joint fluid</td>
</tr>
<tr>
<td>Ceroni (2020)⁹</td>
<td>8**¶¶</td>
<td>0 (0)</td>
<td>7/7(100)</td>
<td>6/7 (86)</td>
<td>Bone</td>
</tr>
<tr>
<td>Olijve (2019)¹⁰</td>
<td>49</td>
<td>0 (0)</td>
<td>49(100)</td>
<td>13/49(26.5)</td>
<td>Joint/bone aspirate</td>
</tr>
<tr>
<td>Olijve (2019)¹⁰</td>
<td>16</td>
<td>0 (0)</td>
<td>16(100)</td>
<td>9/16 (56.3)</td>
<td>Tissue</td>
</tr>
</tbody>
</table>
* A pathogen causing the osteroarticular infection was isolated
  ** *Kingella kingae* osteoarticular infections of the chest wall
  †9 cases had positive culture of *Kingella kingae*
  ‡17 cases had positive culture of *Kingella kingae*
  §2 cases had positive culture of *Kingella kingae* as well as a positive PCR result
  ¶13 culture-negative samples were excluded because the residual fluid was not adequate for PCR
  ¶¶ in 1 patient, diagnosis was based on clinical grounds & positive oropharyngeal PCR for *Kingella kingae*
  ¶¶¶ (L.Olijve, unpublished data, ESPID 2019)

Additionally, from these studies, musculoskeletal infections with *Kingella kingae* are reported to present with a milder clinical picture as compared with musckuloskeletal infections due to other pathogens which present with high fever, elevated leukocyte count and inflammatory markers. We add this case to the total number reported in case series on osteoarticular infection of the chest wall as reported by Leugmair, Hertting and Ceroni. The case that we present here differs from the case series in some aspects. Firstly, our case is older than in those in the case series in which most of them were infants and toddlers aged less than 28 months. Secondly, the presentation with a chest lump with only minor features of inflammation but with other systemic symptoms of ill health drove the suspicion of malignancy initially. Thirdly, the location of the swelling being at the upper sternum compared to lower sternum in other case series.

This emphasises the importance of suspicion of *Kingella kingae* infection in children, particularly those < 48 months of age, who present with musculoskeletal lesions. Finally, molecular testing played a crucial role in the diagnosis of this culture-negative osteoarticular infection caused by *Kingella kingae*, illustrating PCR as a valuable addition to culture in determining the aetiology.

Finally, we would like to comment on the antibiotic choice in our case including the dosing and the duration. While extensive data on antimicrobial susceptibility for paediatric *Kingella kingae* isolates in Australia are lacking, amoxicillin-clavulanate or second or third generation cephalosporins have been recommended elsewhere as some *Kingella* isolates carry a beta-lactamase which hydrolyses penicillins such flucloxacillin. In Australia, however, second generation cephalosporins such as cefuroxime, commonly prescribed elsewhere, are rarely prescribed in children due to lack of suitable formulations, and the first generation cephalosporin, cephalexin, is commonly used as stepdown therapy for osteomyelitis in children, including osteomyelitis due to *Kingella kingae*. There is considerable local experience of cephalexin use for this indication despite a lack of formal efficacy and susceptibility data. Cephalexin has a palatable oral liquid formulation and often prescribed three times daily to facilitate adherence. Regarding the duration, 6 weeks’ therapy was prescribed due to the diagnosis of subacute/chronic osteomyelitis.
Learning points
Our instructive case has the following learning points: Firstly, it emphasise the importance of suspicion of *Kingella kingae* infection in young children less than 4 years of age who present with musculoskeletal infections including sternal lesions, particularly when signs of inflammation are minimal or absent. Secondly, it emphasises the importance of considering adding molecular testing in the diagnosis of culture-negative osteoarticular infections.

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   https://doi.org/10.26226/morressier.5ad774d9d462b80296ca6650
10. Olijve L. Pre-school Osteoarticular Infections (POI) – Study. European Society for Paediatric Infectious Diseases (ESPID); 6-11 May; Slovenia 2019
Figure 1: The site of the swelling
Figure 2: CT chest: The arrows showed a destructive bony lesion.
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