ORIGINAL ARTICLE

Pitfalls in diagnosing septic arthritis in Hong Kong children: ten years' experience

CME

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Objectives To evaluate the initial presentation of septic arthritis in Hong Kong children with respect to clinical and laboratory findings that can aid making a prompt diagnosis.

Design Retrospective review.

Setting Five public hospitals in Hong Kong.

Patients Data concerning paediatric patients with septic arthritis were collected from January 2001 to December 2010. Patients with postoperative infections and those without enough retrievable information were excluded.

Results Of 31 patients analysed, on admission only 52% had had a fever of >38.5°C and 71% had raised white blood cell count of >12 x 10^9 /L. In 74% of these patients, Gram stains of blood culture samples yielded no positive findings. The leading causative organism was *Staphylococcus aureus* (42%), followed by group A *Streptococcus* (23%). When group A *Streptococcus* was responsible, five out of seven patients had a complicated clinical course (repeated surgeries, *Streptococcus*-related organ failure, and chronic joint stiffness). Moreover, in 19% of instances, the empirical antibiotic therapy prescribed on admission did not provide a broad enough spectrum of cover.

Conclusion Signs of sepsis such as high fever, raised white blood cell count, and positive Gram smear from blood cultures were only present in around half of these patients with septic arthritis. Furthermore, group A *Streptococcus* tended to produce many complications. Regrettably, about a quarter of the empirical antibiotic regimens started by frontline staff were deemed not have a broad enough spectrum of cover. Improvement in the initial detection and management of septic arthritis patients is warranted.

Key words
Arthralgia; Arthritis, infectious; Child; Drug therapy, combination; Staphylococcal infections

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New knowledge added by this study

- Contrary to classical teaching, in the paediatric population presenting with septic arthritis, frank clinical features of sepsis (high fever and white blood cell count, and septicaemia) are often absent, especially in infants (age <1 year).
- Septic arthritis due to group A *Streptococcus* appears to confer a high morbidity and mortality in paediatric patients, yet one fifth of those with suspected septic arthritis were not started on antibiotics that covered this organism.
- Despite increasing reports from the international literature showing that *Kingella kingae* is a significant causative organism in paediatric septic arthritis, routine culture techniques used in local public hospitals could not detect this organism.

Implications for clinical practice or policy

- When assessing paediatric patients, all frontline staff must maintain a high index of suspicion for septic arthritis and should not rely solely on the classical features of frank sepsis. Instead, they should base their judgement on the combination of clinical symptoms, physical findings, and laboratory tests to confirm their suspicions.
- Broad-spectrum antibiotics such as a third-generation cephalosporin should be given to any paediatric patient with suspected septic arthritis to ensure that the common causative organisms—including *Staphylococcus aureus*, group A *Streptococcus*, and Gram-negative organisms—are covered.
- In patients with suspected septic arthritis in whom the causative organism cannot be detected through routine microbiological tests, microbiologists should be consulted early with a view to conducting special tests for *Kingella kingae*.

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Introduction

Swift diagnosis and appropriate initial management of septic arthritis in children is imperative, so as to avoid devastating long-term complications (eg joint stiffness) and even loss of life.[1,2] In cases of suspected septic arthritis, frontline residents have long been trained to look for classical features of sepsis such as high fever, raised white blood cell (WBC) counts, and positive Gram smear findings from blood culture samples and joint aspirates. To provide a prompt diagnosis in such patients, numerous clinical management algorithms have been developed so as to differentiate between genuine septic arthritis and other benign causes such as transient synovitis.[3-7] However, these algorithms have recently been called into question, as the presenting clinical picture of septic arthritis patients is often ambiguous and signs may be subtle.[5,8,9] This review of our experience from the past 10 years was designed to look for patterns in the initial presentation of septic arthritis in children in terms of clinical features and laboratory investigations, to facilitate making a prompt diagnosis.

香港膿毒性關節炎小兒患者的診斷陷阱：十年經驗分享

目的 根據臨床及實驗室檢驗結果來評估香港膿毒性關節炎小兒患者初發病時的症狀，使能迅速作出診斷。

設計 回顧研究。

安排 香港五間公立醫院。

患者 收集在2001年1月至2010年12月期間因膿毒性關節炎而入院的兒童的資料。術後感染以及未有足夠資料的病人不被納入本研究範圍。

結果 共分析了31名患者的資料。入院時，只有52%患者有發燒（38.5°C以上），71%患者的白血球水平上升（>12 x 10^9/L）。血培養標本中，有74%的革蘭氏試驗結果呈陰性。主要致病的有金黃色葡萄球菌（42%），其次為甲型鏈球菌（23%）。感染甲型鏈球菌的7名患者中，5名有複雜的臨床病程（多次接受手術、出現與鏈球菌有關的器官衰竭，以及有慢性關節僵直）。19%患者入院時所接受的經驗性抗生素治療未能為患者提供廣泛的抗菌範圍。

結論 只有約一半的膿毒性關節炎患者出現如發高燒、白血球水平上升和革蘭氏試驗結果呈陽性的膿血症症狀。甲型鏈球菌往往會產生許多併發症。可惜的是，前線醫護人員在開始治療時所處方的抗生素治療往往未能為患者提供廣泛的抗菌範圍。有需要提高對膿毒性關節炎患者的初步檢測，並改善治理方法。

Methods

Data were collected from five public hospitals in Hong Kong from 1 January 2001 to 31 December 2010. The hospitals involved were: the Queen Mary Hospital, the Duchess of Kent Children's Hospital, the Tuen Mun Hospital, the Princess Margaret Hospital, and the United Christian Hospital. All the patients were eventually diagnosed with septic arthritis, and were less than 16 years old at presentation, according to the Clinical Management System (CMS) of the Hong Kong Hospital Authority. Septic arthritis was defined as (i) the isolation of bacteria from the affected joint or (ii) a clinical picture entailing fever and an irritable joint, together with numerous white cells found in aspirated fluid of the affected joint in the absence of crystal arthropathy or rheumatological disease.

Patients were excluded if they had infections of the head and neck or the spine, postoperative infections, and traumatic open wounds. One patient with paraplegia and insensate lower limbs was also excluded, as too were those without enough retrievable information from the CMS or whose past records were destroyed. Admission clinical parameters examined and logged included: concomitant co-morbidities, the joint involved and associated symptoms, duration of symptoms until admission, ability to bear weight if the lower limb was involved, and body temperature. The duration of symptoms until definitive surgical drainage of the infection was also logged. Blood parameters retrieved included WBC counts, erythrocyte sedimentation rates (ESRs), C-reactive protein (CRP) levels, blood culture results, and the causative organisms, if any. Data on all antibiotics used preoperatively and postoperatively, and all final clinical and radiological outcomes were also logged. A 'good' outcome was defined as a patient having full and pain-free range of motion of the affected joint on follow-up, without any radiological evidence of joint destruction. Risk factors including age at diagnosis, immunocompromising features, numbers of joints involved, and other available microbiological data (eg causative micro-organism, positive preoperative blood culture) were also analysed.

Results

A total of 51 patients fitted the diagnostic criteria, but 20 were excluded due to incomplete information in their records. Thus, there were 31 remaining patients (mean age, 8 years; range, 21 days to 16 years), of whom 17 were male and 14 were female. Four patients were known to be immunocompromised due to regular steroid use or chronic renal failure (Table 1). Only 52% (16/31) of children with septic arthritis had a high fever (>38.5°C) on admission; the majority had body temperatures higher than 37.5°C (Fig). The mean body temperature on admission was 38.7°C (range, 35.4-40.7°C). Among children with septic arthritis, 71% (22/31) had a raised WBC count of >12 x

10^9/L on admission, with a mean of 17.8 x 10^9/L (range, 6.0 to 32.4 x 10^9/L). Moreover, 64% of them had an ESR of >40 mm/h on admission, the mean being 66 (range, 8-131) mm/h; and 77% had a raised CRP level (>10 mg/L) on admission, the mean being 132 (range, 4-232) mg/L.

Among these patients, 74% had no positive Gram-stain smears from blood culture samples taken on admission. Notably, 22/31 patients in our series had preoperative aspiration of the affected joint. Of the 22 joint aspirates, nine were Gram-stain negative, and no causative micro-organism was isolated in six of these cases. None of the patients with multiple joint involvement had preoperative joint aspirations, as all of their blood cultures had already revealed the causative organism.

TABLE 1. Demographics of patients

Demographics	Data
Age	
Mean	7.5 years
Range	21 days - 16 years*
Sex	
Male	17
Female	14
Co-morbidities	
Idiopathic thrombocytopaenic purpura	1†
Asthma and allergic rhinitis	1†
Systemic lupus erythematosus	1†
Nephrotic syndrome and impaired renal function	1
Affected joint	
Hips	11
Knees	5
Ankles	5
Shoulders	3
Elbows	3
Multiple joints	3
Foot (talonavicular joint)	1

* Five younger than 1 year of age
† On steroids

The leading causative organism of septic arthritis was *Staphylococcus aureus* (42%) followed by group A *Streptococcus* (23%), and group B *Streptococcus* (6%) [Table 2]. There were no cases of methicillin-resistant *S aureus*. Four out of seven of the patients with group A *Streptococcus* had complicated clinical courses (warranting repeated surgeries, limb shortening on follow-up, radiologically evident joint destruction, *Streptococcus*-related organ failure, and one mortality due to toxic shock syndrome shortly after admission). However, 4/31 patients did not receive any preoperative/pre-aspiration empirical antibiotics and 2/31 only received intravenous cloxacillin. Of the four patients who did not receive any preoperative empirical antibiotics whilst having obvious septic signs and symptoms on presentation, they all had emergency arthrotomies of the affected joint within 24 hours of admission. Among the four patients known to be immunocompromised, two were infected with *S aureus*, one with group A *Streptococcus*, and one with *Salmonella enteritidis*. The total duration of antibiotics courses ranged from 3 to 10 weeks, with a mean of 6 weeks.

Risk factors were analysed for patients who had a poor final outcome. All four patients who were chronically immunocompromised had significantly poorer final clinical and radiological outcomes

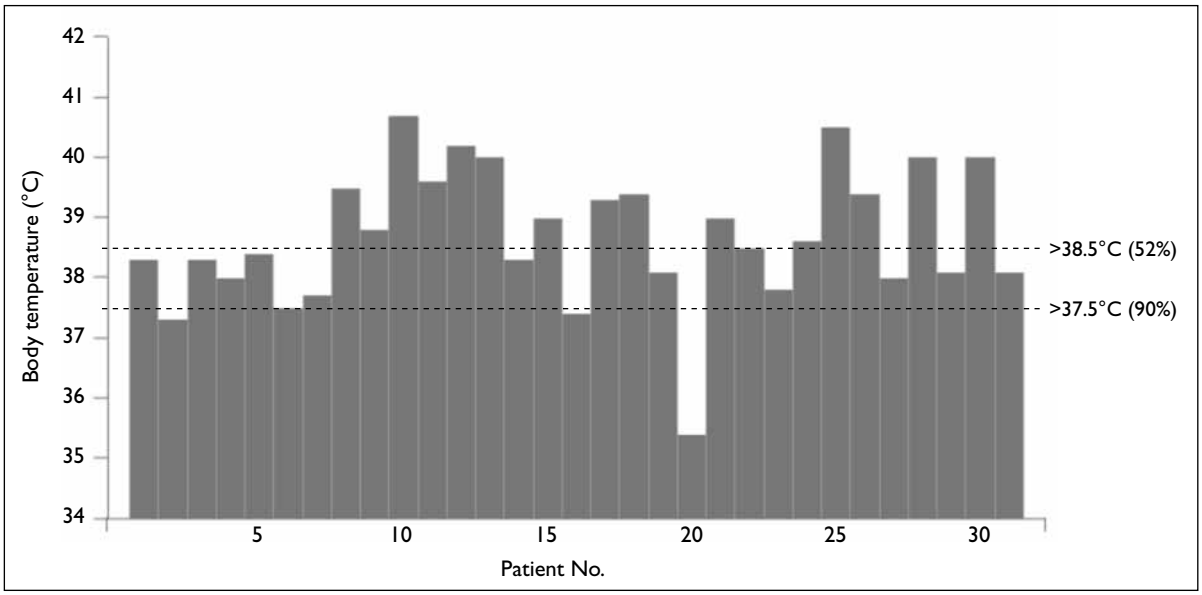

FIG. Body temperature on admission

TABLE 2. Microbiology results and final outcome

Micro-organism	Incidence	Final outcome
Staphylococcus aureus	13/31 (42%)	1 With chondrolysis and severe joint stiffness
		1 With severe joint destruction requiring surgical fusion of the ankle
		1 With mild fixed flexion contracture of the knee
		Remaining 10/13 (77%) have good outcome
Group A *Streptococcus*	7/31 (23%)	2 Developed post-*Streptococcus* glomerulonephritis requiring renal replacement therapy
		1 Developed toxic shock syndrome and died 5 hours after admission
		1 Developed radiological joint space narrowing and decreased joint space narrowing
		Remaining 3/7 (43%) have good outcome
Group B *Streptococcus*	2/31 (6%)	Both had good outcome
Streptococcus pneumoniae	1/31 (3%)	Good outcome
Haemophilus influenzae	1/31 (3%)	Good outcome
Salmonella enteritidis	1/31 (3%)	Decreased range of motion of the hip but unlimited walking
Unknown	6/31 (19%)	1 With radiological sclerosis of the talonavicular joint
		1 With ankle pain after prolonged walking
		Remaining 4/6 (67%) have good outcome

TABLE 3. Risk factors for poor outcomes

Risk factor*	Proportion with poor outcome	Relative risk and 95% confidence interval	P value†
Age ≥7 years	7/17	1.922 (0.607-6.086)	0.252
Known immunocompromise	4/4	4.5 (2.222-9.114)	0.007
Multiple joint involvement	3/3	4.5 (2.222-9.114)	0.027
Fever ≥38.5°C	6/16	1.41 (0.492-4.022)	0.252
WCC ≥20 x 10^9 /L	4/10	1.48 (0.550-3.990)	1.000
ESR ≥50 mm/h	7/16	1.97 (0.514-7.539)	0.252
CRP ≥200 mg/L	8/20	1.89 (0.736-4.835)	0.262
Symptoms for ≥5 days before surgical debridement	4/9	1.60 (0.564-4.542)	0.105
Group A *Streptococcus*	5/7	2.29 (0.889-5.877)	0.652
Positive preoperative blood culture	4/8	1.75 (0.665-4.608)	0.381

* WCC denotes white cell count, ESR erythrocyte sedimentation rate, and CRP C-reactive protein

† Fisher's exact test

(P=0.007). Similarly, those who had multiple joint involvement on presentation had statistically poorer final outcomes (P=0.027). The relative risk for poor outcomes was also increased in the presence of admission CRP levels of >200 mg/L, in those with symptoms for ≥5 days before surgical debridement, and in those with *Streptococcus* A infections (Table 3). Fisher's exact test was used for analysis. However, these differences were not statistically significant, perhaps due to the small sample size.

Regarding the five infants in this series, on admission only one had a temperature exceeding 38.5°C and their mean WBC was 24.1 x 10^9 /L (range, 14.8-31 x 10^9/L). Concerning the causative organisms of septic arthritis in this group, two were group B *Streptococcus*, and one each were *S aureus*, *Haemophilus influenzae*, *Streptococcus pneumoniae*. All of these infants had good final outcomes.

Discussion

Septic arthritis in children has devastating consequences, yet the initial clinical symptoms and signs may be subtle. According to Welkon et al,[2] initiation of appropriate medical/surgical treatment for 4 or more days after the onset of symptoms was associated with poor outcomes. In our series, a delay in surgical treatment of ≥5 days was associated a relative risk of 1.6 for the development of a poor outcome. While most orthopaedic staff are aware of this problem and are on high alert in any case of suspected paediatric septic arthritis or osteomyelitis,

in reality many patients are initially managed by non-orthopaedic specialists. Regarding the three cases in our series in which patients were initially admitted to non-orthopaedic wards, their surgical treatment was delayed by up to 15 days and they all had a poor outcome. Three of the patients attended the accident and emergency department repeatedly, before being admitted. In the latter cases, the delay in surgical treatment was up to 11 days and one of them had a poor outcome. For a period of time, five patients were treated as simple cellulitis by their primary care physicians, before being referred to hospital. While the exact details relating to these five patients including their initial clinical presentation and management are not available, notably, the delay in surgical treatment was up to 13 days, and three of them had poor outcomes. This review is therefore directed especially towards these groups of frontline staff. By contrast, of the remaining 20 patients who were promptly admitted to orthopaedic wards, only three had poor outcomes.

Assessing clinical features in a young child is often challenging. If a lower limb is affected, there may be subtle clues such as inability to bear weight. However, clues to involvement of an upper limb are less obvious. Another proposed clinical symptom is 'irritable joint', in which the child refuses to move the affected limb. In young children however, this may be very subtle and unreliable, and may be confounded by problems such as referred pain and trivial antecedent trauma.[8,9] More objective signs such as body temperature and initial laboratory findings may be more useful, especially in the very young.

According to classical teaching, frank signs of sepsis such as high fever are usually present if there is septic arthritis. Indeed, many clinical algorithms to differentiate septic arthritis from more benign causes such as transient synovitis of the hip are based on these signs.[1,3-7] Most such algorithms use a body temperature of ≥38.5°C as a cut-off temperature suggestive of septic arthritis. In our series however, only half the patients had such a high fever on presentation, in which case half of the cases would have been missed. If the threshold for body temperature was lowered to 37.5°C, then 90% of the patients would have been diagnosed. When it comes to body temperature in these patients, we therefore suggest a high index of suspicion. Notably, patients who were initially managed by primary care physicians or in the accident and emergency department (and were frequently given paracetamol), only four out of eight had a temperature of ≥38.5°C.

Many studies have shown that objective tests such as WBC count and inflammatory markers were helpful in diagnosing children with septic arthritis.[1,10] Thus, blood tests were routinely performed for all of our patients with suspected septic arthritis. Indeed, initial blood tests (WBC, ESR, and CRP levels) showed abnormalities in three quarters of our confirmed cases. In general, we also noted that the higher the initial levels of these inflammatory markers, the poorer the eventual patient outcomes (Table 3).

Contrary to classical teaching, septicaemia was not detected in most of our patients with septic arthritis. In three quarters of the patients, blood cultures taken at presentation grew no organisms. Furthermore, nine (41%) out of 22 Gram stains on smears of joint aspirates obtained prior to surgical debridement of the affected joint yielded no bacteria. Thus, the bacterial load in the systemic circulation and in infected joints may not always be as high as commonly believed. Regarding the three patients initially admitted to non-orthopaedic wards, none were given antibiotics prior to obtaining blood cultures. One of the three patients who was seen repeatedly in the accident and emergency department before admission was given Augmentin (GlaxoSmithKline, London, UK) for presumed cellulitis, but there was no growth in the preceding blood culture. In any case, caution must be exercised and initial microbiological results must be closely correlated with clinical findings when it comes to the diagnosis of septic arthritis. Such is the lack of consensus about the clinical findings that standardised diagnostic protocols were not available in any of the centres that we reviewed. However, orthopaedic units should create their own diagnostic protocols for suspected paediatric musculoskeletal infection, taking account of symptoms, signs, imaging, as well as blood test and joint aspiration findings.

Consistent with worldwide experience, *Staphylococcus* was the most common cause of septic arthritis in our series. The final outcome of our patients with such arthritis was also consistent with that reported in the literature,[1,10] with good outcomes in 77% of our patients. Group A *Streptococcus* was the second leading causative organism, but tended to produce many local and systemic complications in our patients. Similar devastating consequences due to group A *Streptococcus* infection have also been described by others.[9,11] Regrettably, one fifth of our patients received no broad-spectrum empirical antibiotics or only a single narrow-spectrum agent. Frontline staff managing suspected septic arthritis patients should be vigilant about the choice of empirical antibiotics and ensure a broad enough spectrum to adequately treat group A *Streptococcus* and Gram-negative organisms. A third-generation cephalosporin (such as ceftriaxone) is generally recommended for empirical treatment of these patients.

There is increasing evidence that patients with septic arthritis in which the causative organism is

not quickly apparent may be due to a Gram-negative coccobacillus known as *Kingella kingae*.[1,10,12] This organism was not identified in any of our patients. However, special techniques/tests are required for its detection (injecting joint fluid directly into a BACTEC bottle blood culture or by polymerase-chain-reaction tests for *Kingella*), which are not routinely performed in our locality.[12,13] It seems that the final outcomes of these patients are similar to those of patients with *Staphylococcus* infections, but other reports suggest that *K kingae* may produce a milder septic arthritis.[10]

Based on our series, we suggest an especially high index of suspicion when encountering infants. On admission, a high fever was found only in an abysmal 20% of infants with septic arthritis. Moreover, group B *Streptococcus* is the most common causative organisms in this age-group, which is significantly different from the rest of the paediatric population, and must be borne in mind when prescribing antibiotics. In our experience, all infants with group B *Streptococcus* infections had good final clinical and radiological outcomes.

These findings and recommendations are directed at increasing the vigilance of frontline staff, and hopefully they will help to better prepare such staff for the initial assessment and management of suspected septic arthritis in paediatric patients.

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