Invasive Streptococcus agalactiae septic arthritis as an initial presentation of tonsillar carcinoma

Lee H C, Chong Y Y E, Cheng Y K

ABSTRACT

Invasive group B streptococcus (GBS) infection causes substantial morbidity and mortality among adults, but only in the last three decades has the role of GBS as a serious pathogen in the nonpregnant adult been better defined. It has been found that one or more serious underlying medical conditions predisposing to infection can be identified in almost all adults with invasive GBS disease. We report a 64-year-old man who had tonsillar carcinoma presenting with right knee GBS septic arthritis. In view of the rarity of invasive GBS infections in healthy non-pregnant adults, and its association with serious underlying conditions, high case fatality rates, and the need for higher doses of penicillin used in treatment, clinicians need to exercise vigilance when dealing with this disease.

Keywords: group B streptococcus, septic arthritis, Streptococcus agalactiae, tonsillar carcinoma

INTRODUCTION

Streptococci are gram-positive bacteria that can be divided into alpha-haemolytics, beta-haemolytics, or non/gamma-haemolytics, depending on their haemolytic patterns on blood agar. Beta-haemolytic streptococci can be further classified into serogroups (Lancefield system) according to the immunoprecipitation of bacterial extracts with specific antiserum. Lancefield groups A, B, C, D, and G are the more common human pathogens among beta-haemolytic streptococci.

For non-gonococcal bacterial arthritis in adults, Staphylococcus aureus ranks as the predominant organism, occurring twice as frequently as streptococcal species. Within the streptococcal species, group A streptococci are the most commonly-reported organism responsible for bacterial arthritis. Group B streptococci (GBS) are major causes of meningitis and septicemia in neonates and pregnant women, but have only been uncommonly reported to cause serious infection in adults, and even less frequently to result in septic arthritis. While a number of studies have identified associated risk factors, the importance of GBS as a cause of serious invasive disease in non-pregnant adults has not been widely appreciated. Only 75 cases of pyogenic arthritis due to GBS have been reported in a MEDLINE search over 29 years.

CASE REPORT

A 64-year-old Chinese man with a past medical history of gout, hypertension, chronic alcoholism and chronic smoking, presented with a four-day history of right knee pain and swelling. There was no history of trauma, fever, nor other joint involvement. There was no recent contact with commercial sex workers. Physical examination revealed a non-toxic man with a swollen, tender, warm right knee with limited range of motion. Other joints were normal. Cardiorespiratory, abdominal, and neurological examinations were unremarkable. Investigations revealed a white cell count 11.2 × 10^9/L (normal range 4.0–10.0) (P 84.8%, L 7.7%); haemoglobin 14.5 g/dL (13.0–17.0); platelets 281 × 10^9/L (160–390); creatinine 69 umol/L (55–100); albumin 35 g/L (40–50); total bilirubin 18 umol/L (3–24); aspartate aminotransferase 42 U/L (15–33); alanine aminotransferase 44 U/L (7–36); alkaline phosphatase 131 U/L (32–103); gamma-glutamyl transferase 750 U/L (9–41); prothrombin time 12.8 s (11.0–14.5); partial thromboplastin time 34.2 s (28.0–39.0); and uric acid level 268 umol/L (250–550).

The right knee was aspirated using an aseptic technique: 70 ml of viscous yellow fluid was withdrawn and microscopy showed > 2,250 white cells, presence of negatively birefringent crystals, with no organisms seen. He was initially treated for acute flare of gouty arthritis until the right knee aspirate cultures grew GBS (Streptococcus (S.) agalactiae). Blood and urine cultures were negative. Intra venous (IV) crystalline penicillin was started. Despite the large amount of aspirant, the effusion quickly recollected after one day. In addition, the patient continued to experience occasional chills and rigors. Knee radiographs also revealed an extensive amount of soft tissue swelling,
DISCUSSION

Any patient presenting with an acute monoarthritis should be evaluated for infectious arthritis, especially for those who have a history of underlying joint disease. Synovial fluid should be examined for crystals, but it is important to remember that the presence of crystals does not rule out a concomitant septic arthritis (as is evident in our case), since gout and infection can coexist. Synovial fluid glucose is relatively insensitive, while synovial fluid polymorphonuclear cell counts are sensitive but non-specific. Therefore, synovial fluid aspirated from an acutely inflamed joint should be sent for microbiological studies, in addition to a microscopical examination.

GBS is a well-known cause of meningitis and septicemia in neonates and pregnant women. However, the importance of GBS as a cause of serious invasive infectious disease in non-pregnant adults is not widely appreciated. The annual incidence of invasive disease is estimated at 4.4/100,000 non-pregnant adults. The spectrum of infections caused by GBS includes skin/soft tissue infection, bacteremia, urosepsis, pneumonia, and osteomyelitis. Case fatality rate has been reported to be between 21% and 32%; and in 4.3% of disease survivors, recurrent infections, including endocarditis and osteomyelitis, were found. As a commensal organism, GBS has been isolated from the genital and/or lower gastrointestinal tract in asymptomatic pregnant women at a rate of 5%-40%.

It should be noted that pyogenic arthritis caused by GBS is uncommon. A MEDLINE search between the years 1972 and 2001 found that only 75 cases have been reported, of which 68% of cases were monoarticular while 32% of cases involved more than one joint. The knee was the most common joint to be affected (68%), followed by the shoulder (25%). In 31% of cases, a concomitant infectious process due to same organism was present, e.g. urinary tract infection. We reviewed the literature and noted that invasive GBS infections occurred almost exclusively in adults with serious underlying medical conditions. A number of population-based studies have found independent risk factors for invasive disease due to GBS (Table 1). These results expanded on previous case series, which showed that age > 60 years, diabetes mellitus, malignancies, chronic liver disease/alcohol abuse and HIV infection were common among adults with GBS disease.

Interestingly, not only were adults with diabetes mellitus or cancer found to be at increased risk of invasive GBS infections, this risk also increased significantly in younger patients. In addition, the types of malignancies implicated in these studies included both solid tumours and haematological cancers, as well as multiple myelomas.
Table I. Risk factors for invasive GBS infection.

<table>
<thead>
<tr>
<th>Study (Journal)</th>
<th>Design (no.)</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Population-based assessment of invasive disease due to GBS in non-pregnant adults⁶⁶ (NEJM)</td>
<td>Prospective surveillance (137)</td>
<td>Diabetes mellitus (95% CI 1.9–4.7)</td>
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<tr>
<td>Invasive GBS disease in adults⁶⁶ (JAMA)</td>
<td>Retrospective surveillance (56)</td>
<td>Diabetes mellitus (95% CI 7.8–14.4)</td>
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<tr>
<td>Risk factors for GBS disease in adults⁷⁰ (Ann Intern Med)</td>
<td>Case control study (219)</td>
<td>Diabetes mellitus (95% CI 3.5–26.9)</td>
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RR: relative risk; CI: confidence interval.

These findings suggest that adults with invasive GBS disease have underlying immune defects that predispose them to infection. This is supported by the observation that the level of maternal type-specific antibodies correlates with the risk for invasive disease.⁹ The presence of sufficient IgG antibodies to serotype-specific capsular polysaccharide has also been known to protect against systemic infection in neonates.¹¹ Since opsonophagocytic killing of GBS by human neutrophils in vitro is dependent on the complement cascade and capsule-specific antibodies, other defects such as phagocyte or complement dysfunction, and impaired macrophage Fcγ receptor function, have also been suggested to contribute to the increased susceptibility.¹³ However, the exact nature of immune alterations has yet to be defined. It is worthwhile to note that once defined, targeted preventive and therapeutic strategies can be further explored, for example, advancement in the area of vaccine development.

In an adult presenting with invasive GBS infection, such as an uncommonly-encountered S. agalactiae septic arthritis, it is not sufficient to only treat the infection symptomatically. Efforts must be made to search for possible underlying medical conditions that are known to be associated with the disease, and in a young patient, this will include the need to rule out concomitant HIV infection. In this case report, our patient had several risk factors that can lead to a state of immunosusceptibility, including old age, alcoholism (though he had no evidence of chronic liver disease), and prior articular damage caused by previous gouty attacks. In our search for underlying conditions, we discovered a metastatic left tonsillar carcinoma, which served to illustrate our point.

Finally, although GBS are usually susceptible to penicillin, it should be noted that the minimum inhibitory concentration is around 4–8 times higher than that for group A streptococci.¹⁷ Thus, high dose benzylpenicillin of at least 12 MU penicillin G a day is recommended for the treatment of serious, localised infections.¹⁸ For GBS septic arthritis, parenteral administration should be given for two weeks, followed by oral antibiotics for 1–2 weeks, given at 2–3 times the usual dose. Duration of antibiotic therapy must be guided by the clinical response.¹³ With appropriate antimicrobial therapy and repeated joint aspirations or open drainage, complete recovery occurs in one-half of the patients with GBS septic arthritis.¹⁴ Unfortunately in the other half, the disease is associated with substantial functional complications. In conclusion, in view of the rarity of invasive GBS infections in healthy, non-pregnant adults, and its association with serious underlying conditions, high case fatality rates, and the need for higher doses of
penicillin used in treatment, this paper aims to remind clinicians on the need to exercise vigilance when dealing with this disease.

REFERENCES