International Journal of Infectious Diseases 17 (2013) e777–e780

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Group B streptococcal bacteremia in a major teaching hospital in Malaysia: a case series of eighteen patients

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ARTICLE INFO

Article history:
Received 10 November 2012
Received in revised form 6 January 2013
Accepted 12 January 2013

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
GBS
Bacteremia
Adult
Neonate
Malaysia

SUMMARY

Background: Group B Streptococcus (GBS) is a leading cause of infections such as meningitis and septicemia in neonates and pregnant women; however the significance of invasive GBS disease has not been clearly defined in non-pregnant adults.
Methods: We reviewed the hospital records of 18 cases with GBS bacteremia who attended the Universiti Kebangsaan Malaysia Medical Centre from June 2010 to October 2011. We analyzed the clinical findings of both bacteremic adults and neonates and compared them to previous studies of GBS bacteremia. Serotyping was done by latex agglutination test using 10 distinct antisera (Ia, Ib, and II–IX).
Results: During the period of 1 year and 4 months, there were 18 patients with GBS bacteremia. Five cases occurred in neonates, one in a parturient woman, and 12 in other adults. All neonates with bacteremia were males and two of them were premature. Septicemia was the most common clinical presentation in neonates. They were treated with intravenous (IV) penicillin G and gentamicin. The adults included nine men (69%) and four women (31%). Their mean age was 60 years and all patients had more than two underlying conditions. The most common clinical syndrome was pneumonia (n = 6, 46.5%). The others were peritonitis (n = 3, 23.1%), primary bacteremia (n = 2, 15.5%), septic arthritis (n = 2, 15.5%), skin and soft tissue infection (n = 1, 7.7%), meningitis (n = 1, 8%), urinary tract infection (n = 1, 8%), and intravascular device infection (n = 1, 7.7%). Cardiovascular diseases (n = 7, 53.8%) were the most common underlying conditions, and diabetes mellitus (n = 5, 38.5%) was second. The other co-morbid conditions were hyperlipidemia (n = 3, 23.1%), renal disease (n = 3, 23.1%), liver disease and/or alcohol abuse (n = 3, 23.1%), autoimmune disease or immunosuppressive condition (n = 2, 15.5%), malignancy (n = 2, 15.5%), respiratory disease (n = 1, 8%), and postpartum condition (n = 1, 8%), as well as miscellaneous conditions including intravenous drug abuse, HIV infection, and trauma (n = 2, 15.5%). Polymicrobial bacteremia was found in five (45.4%) cases and *Staphylococcus aureus* was the most common concurrent bacterial isolate. Of the 18 GBS isolates in both adults and neonates, serotype Ia was predominant (38.9%), followed by VI (27.8%), V (11.1%), and III (5.5%); the remaining 16.7% were non-typeable.
Conclusions: GBS bacteremia is a significant problem and is associated with serious underlying disease, which may result in a high rate of mortality, not only in neonates and pregnant women, but also in non-pregnant adults.

1. Introduction

Group B Streptococcus (GBS), also known as *Streptococcus agalactiae*, is a major cause of sepsis and meningitis in neonates, as well as a wide variety of diseases in adulthood.[1] In both pediatric and adult populations, invasive GBS infection has been associated with high mortality and morbidity.[1] GBS neonatal infection is divided into early-onset and late-onset disease. Early-onset disease occurs within the first week of life, while late-onset disease occurs between 1 week and 3 months of age.[2] The use of intrapartum antibiotic prophylaxis in the prevention of prenatal GBS infection has decreased the incidence of GBS disease by 70% during the past decade.[3] However, despite this, early-onset disease remains a leading cause of neonatal infection and death in the USA.[3–5]

GBS is also a significant cause of invasive disease among the elderly with underlying medical conditions.[6] Over the past decade, a dramatic increase in GBS infections has been seen in non-pregnant adults, and more than two-thirds of GBS disease in the USA now occurs in adults without postpartum condition.[7]

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1201-9712/$36.00 – see front matter
http://dx.doi.org/10.1016/j.ijid.2013.01.011

Table 1
Demographic and clinical data of five neonates with group B streptococcal infection

Case No.	Age at diagnosis	Maturity	Gender/race	Clinical presentation	Serotype	Treatment	Outcome
1	Day 0	34 weeks, 5 days	Male/Chinese	Septicemia, prematurity	Ia	PEN, GEN	Died
2	Day 3	38 weeks, 2 days	Male/Chinese	Septicemia, nosocomial pneumonia, respiratory distress, NNJ, GERD, TGA	Ia	PEN, GEN	Survived
3	Day 1	38 weeks, 8 days	Male/Malay	Septicemia, pneumonia, respiratory distress, NNJ	NT	PEN, GEN	Survived
4	Day 0	36 weeks, 6 days	Male/Malay	Septicemia, prematurity, pneumonia, respiratory distress, NNJ, PDA	VI	PEN, GEN	Survived
5	Day 7	39 weeks, 4 days	Male/Malay	Septicemia, hydrocele	III	PEN, GEN	Survived

GEN, gentamicin; GERD, gastro-esophageal reflux disease; NNJ, neonatal jaundice; NT, non-typeable; PDA, patent ductus arteriosus; PEN, penicillin; TGA, transposition of great arteries.

To the best of our knowledge, reports of GBS bacteremia cases in Malaysia and data from Southeast Asia are limited. Therefore, the aim of this study was to define the serotypes and review the clinical information of patients with GBS bacteremia.

2. Methods

Universiti Kebangsaan Malaysia Medical Centre (UKMMC) is a 900-bed teaching hospital in Malaysia. GBS bacteremia was diagnosed on the basis of isolation of GBS from blood culture. We reviewed the demographic and clinical information of neonates and adults who had GBS bacteremia between June 2010 and October 2011. Our study includes information on demographic variables, associated underlying conditions, clinical syndromes, treatment, and outcome. Bacteremia without a certain infection source was classified as primary bacteremia, while polymicrobial infections were defined as the isolation of bacterial species other than GBS from the same source. Pneumonia was diagnosed on the basis of clinical signs of consolidation, chest X-ray, and at least two of the following symptoms: fever, cough, purulent sputum, and chest pain. Bacteremia was considered community-acquired when the isolate was from a blood culture collected in the outpatient department or within 72 h of admission. All GBS were identified by internationally accepted and standard microbiological techniques. Serotype identification was carried out using the latex agglutination method with the Strep-B-Latex Kit (Statens Serum Institut, Denmark).

3. Results

This was a descriptive study, involving the retrospective analysis of patient records. Eighteen cases of GBS bacteremia in patients attending UKMMC were identified during the study period of 1 year and 4 months. Of these 18 patients, five were neonates and 12 were non-pregnant adults; one case occurred in a pregnant woman. Clinical features of all patients are summarized in Tables 1 and 2.

In neonates with bacteremia, three were born at full term while the other two were premature. Septicemia was the most common manifestation of the disease. Three babies presented with pneumonia, respiratory distress, and neonatal jaundice. Only one baby presented with signs of digestive disorder and was diagnosed to have gastro-esophageal reflux disease. Two babies had congenital heart defects, which included transposition of the great arteries and patent ductus arteriosus. Hydrocele was seen in one case. The babies were treated with intravenous penicillin G and gentamicin. All babies survived with the exception of one who died on the day of admission (Table 1).

The adult patients comprised nine men (69%) and four women (31%). Their mean age was 60 years, ranging from 27 to 87 years.

Table 2
Demographic and clinical data of 13 adults with group B streptococcal bacteremia

Case No.	Age (years)/gender	Race	Clinical syndrome	Underlying condition	Polymicrobial bacteremia	Serotype	Treatment	Outcome
6	54/F	Malay	Peritonitis	Hypertension, hyperlipidemia, endometrial cancer	Negative	Ia	AMC	Survived
7	70/M	Malay	Meningitis	Hyperlipidemia, CUA, trauma	Negative	Ia	ND	Survived
8	27/F	Malay	Primary bacteremia	Postpartum	Negative	VI	AMP	Survived
9	36/M	Malay	Intravascular device infection	HIV infection, IVDU, LTBI, DVT	Positive	NT	CLX, IPM	Survived
10	65/F	Malay	CAP, peritonitis	Nephritic syndrome	Negative	V	SAM, CEF, VAN	Survived
11	81/F	Malay	Septic arthritis	GIST, bowel lymphoma, colon cancer	Positive	V	TZP, MTZ	Survived
12	49/M	Chinese	UTI	DM, hypertension, liver disease, nephritic syndrome, glomerulonephritis	Negative	NT	SAM	Survived
13	65/M	Chinese	CAP, cellulitis	DM, hypertension, hyperlipidemia, IHD, LVH	Positive	Ia	VAN	Survived
14	87/M	Chinese	Pneumonia, peritonitis	DM, hypertension, IHD, stroke	Positive	VI	IPM, AMC	Died
15	65/M	Chinese	CAP, septic arthritis	DM, hypertension, gout	Positive	VI	CLX	Survived
16	65/M	Chinese	HAP	Chemotherapy	Negative	VI	CTX	Died
17	37/M	Malay	Primary bacteremia	DM, hypertension, liver disease, alcoholic, heart failure	Negative	Ia	ND	Died
18	76/M	Malay	HAP	Liver disease, alcoholic, pressure sore	Negative	Ia	ND	Died

AMC, amoxicillin–clavulanic acid; AMP, ampicillin; CAP, community-acquired pneumonia; CLX, cloxacillin; CTX, cotrimoxazole; CUA, calcific uremic arteriopathy; DM, diabetes mellitus; DVT, deep vein thrombosis; F, Female; CEF, cefepime; GIST, gastrointestinal stromal tumor; HAP, hospital- acquired pneumonia; IHD, ischemic heart disease; IPM, imipenem; IVDU, intravenous drug user; LTBI, latent tuberculosis infection; LVH, left ventricular hypertrophy; M, Male; MTZ, metronidazole; ND, no data; NT, non-typeable; SAM, ampicillin–sulbactam; TZP, piperacillin–tazobactam; UTI, urinary tract infection; VAN, vancomycin.

Table 3
Clinical syndromes of 13 adults with group B streptococcal bacteremia

Clinical syndrome	No. (%) of patients
Pneumonia	6 (46.5)
Primary bacteremia	2 (15.5)
Peritonitis	3 (23.1)
Septic arthritis	2 (15.5)
Urinary tract infection	1 (7.7)
Skin and soft tissue infection	1 (7.7)
Meningitis	1 (7.7)
Intravascular device infection	1 (7.7)

Eight patients (61.5%) were ≥65 years old. All patients had more than two underlying conditions, as listed in Table 2. The clinical syndromes are shown in Table 3 and were as follows: pneumonia (n = 6, 46.5%), peritonitis (n = 3, 23.1%), arthritis (n = 2, 15.5%), skin and soft tissue infection (n = 2, 15.5%), meningitis (n = 1, 7.7%), urinary tract infection (n = 1, 7.7%), and intravascular device infection (n = 1, 7.7%). There were only two cases (15.5%) of primary bacteremia. The most common clinical syndrome was pneumonia. All six patients with pneumonia were elderly, aged ≥ 65 years, and three of them had diabetes mellitus as well as hypertension. Of the six cases of pneumonia, three were community-acquired and three were hospital-acquired.

The underlying medical conditions of the 13 adults with GBS bacteremia are presented in Table 4. In the current series, cardiovascular diseases (n = 7, 53.8%) were the most common underlying condition among adults, whereas respiratory disease was the least (n = 1, 7.7%). Diabetes mellitus, which was present in five cases (38.5%), was the second most prominent underlying condition and associated with hypertension in all five patients. The other co-morbid conditions were hyperlipidemia (n = 3, 23.1%), renal disease (n = 3, 23.1%), liver disease and/or alcohol abuse (n = 3, 23.1%), autoimmune disease or immunosuppressive condition (n = 2, 15.5%), and malignancy (n = 2, 15.5%). One patient was in the postpartum period. Other underlying conditions included intravenous drug abuse, HIV infection, and trauma. In cases of polymicrobial bacteremia, the concordant isolates included *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, coagulase-negative staphylococci, and Gram-negative cocci (unspecified). All of the patients received antibiotic therapy and all except four survived. No data are available for treatment of two adults who died (Table 2).

Table 4
Underlying medical conditions of 13 adults with group B streptococcal bacteremia

Condition	No. (%) of patients with condition
Cardiovascular disease[a]	7 (53.8)
Diabetes mellitus	5 (38.5)
Hyperlipidemia	3 (23.1)
Liver disease and/or alcohol abuse	3 (23.1)
Renal disease[b]	3 (23.1)
Autoimmune disease or immunosuppressive condition[c]	2 (15.5)
Malignancy[d]	2 (15.5)
Postpartum	1 (7.7)
Respiratory disease[e]	1 (7.7)
Miscellaneous[f]	2 (15.5)

[a] Includes hypertension, deep venous thrombosis, ischemic heart disease, left ventricular hypertrophy, and stroke.
[b] Includes calcific uremic arteriopathy, nephritic syndrome, and glomerulonephritis.
[c] Includes chemotherapy and gout.
[d] Includes endometrial cancer, gastrointestinal stromal tumor, bowel lymphoma, and colon cancer.
[e] Includes latent tuberculosis infection.
[f] Includes intravenous drug user, HIV infection, and trauma.

The serotypes of the GBS strains are presented in Tables 1 and 2. Serotype Ia was the most prevalent capsular polysaccharide type, accounting for 38.9% of cases, followed by serotypes VI (27.8%), V (11.1%), III (5.5%), and non-typeable (16.7%). Serotypes II, IV, and VII –IX were not found.

4. Discussion

GBS is a Gram-positive coccus associated mainly with infection in newborns.[4] Antibiotic prophylaxis during the intrapartum period for GBS carrier patients has reduced the rate of neonatal GBS infection.[5] However, GBS can cause infection in pregnant and non-pregnant adults.[4] A recent study from a teaching hospital in Malaysia reported the vaginal carriage rate of GBS in pregnant women to be 9.7% and the annual incidence of GBS septicemia in babies to be 0.4/1000 live-births.[8]

In the present study, we reported 18 cases of GBS bacteremia occurring in five neonates and 13 adults. Although the current investigation involved a small number of GBS bacteremia in neonates, the data were compared with prior data for potential similar patterns. All five cases were male, which supports the findings of other studies on gender distribution.[9,10] The reason for male dominance is unclear, but perhaps it is related to sex-linked factors in host susceptibility.[9]

In Malaysia it is not standard policy to screen each pregnant woman for GBS carriage during antenatal checks. Therefore, if they are GBS carriers, they can transfer this to their newborn, which explains our neonate cases who presented within the first 7 days of life.

In our series, GBS bacteremia occurred in adults with varied underlying diseases, including diabetes mellitus, cardiovascular failure, renal disorders, liver disease, skin and soft tissue infection, and malignancy, as well as autoimmune diseases or immunosuppressive conditions. Cardiovascular diseases were observed to be the most frequently associated underlying medical condition in this study. However, since our study is not population-based and our estimate is based on a single institution with a small sample size, the explanation of the results may include some regional or institutional bias. Thus, a larger study should be performed to determine whether cardiovascular disease is the most common underlying medical condition or not in this local geographical region.

In other studies, diabetes mellitus was the most prevalent risk factor in populations from Europe, the USA,[4,11–14] and Southeast Asian countries including Malaysia.[1,15] Malignancy was less predominant, which is parallel to previous findings in Malaysia[15] and France,[13] but is different from Western countries,[4,11] as well as Taiwan.[7]

In this study, the most frequent clinical syndrome was pneumonia, which is different from prior studies in Malaysia, Taiwan, and Western countries; these have shown the skin and soft tissues to be the most common sites of infection.[7,11,15,16] Only one patient had a skin and soft tissue infection, which was cellulitis. Polymicrobial bacteremia was found in five (45.4%) cases and *S. aureus* was the most common concurrent bacterial isolate in GBS bacteremic patients, similar to previous reports.[11,12,15]

In the USA and Europe, serotypes Ia, II, III, and V predominate, and in Japan, serotypes Ib and III were determined to be the most common GBS strains among neonatal and adult cases.[1,6,14,17] Serotypes III and Ia have become increasingly frequent among pregnant women in Korea.[5] In Malaysia, a recent study from a teaching hospital revealed that serotypes Ia and VI were predominant among pregnant women, similar to the findings of our investigation in neonates and adults.[15] Interestingly, these two common serotypes are related to mortality. Of five patients who died, three demonstrated serotype Ia and two demonstrated

serotype VI. Therefore, these two serotypes seem to be more virulent in humans.

In the present study, the overall mortality rate was 5/18 (28%), which comprised 1/5 infant cases (20%) and 4/13 adult cases (31%). We found that the case fatality rate in adults was slightly higher than those of previous reports, which have ranged from 9.5% to 20.2%.[1,7,11,12,16] Mortality among patients aged ≥67 years was 75% (3/4), three times that of those younger than 67 years (25%, 1/4); this is concordant with previous findings in the USA and Taiwan.[7,12]

Of the four adult patients who died, only one had polymicrobial bacteremia and the other three had GBS bacteremia alone. Thus, in support of previous findings in Japan,[1] there was no significant association between polymicrobial infection and fatality. Mortality seems to be highly dependent on the presence of pneumonia, and the reported mortality from pneumonia with GBS bacteremia has been considered high.[12]

In conclusion, GBS infection in non-pregnant adults is increasing and usually affects the elderly and those with underlying medical conditions, particularly cardiovascular diseases and diabetes mellitus. Preventive strategies, such as a GBS vaccine are likely to be important in both infant and adult groups.

Acknowledgements

The authors acknowledge the Universiti Putra Malaysia for providing funding (04-04-10-1002RU/F1) to conduct the present research. The authors also acknowledge the authorities and staff of Universiti Kebangsaan Medical Centre, Malaysia for their cordial assistance during the study. Thanks also to Farida Jamal, Professor of Medical Microbiology at the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia for her thoughtful comments on the discussion.

Conflict of interest: No conflict of interest to declare.

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