CLINICAL MICROBIOLOGY

A 13-year survey of bacteraemia due to β -haemolytic streptococci in a Danish county

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Summary. During 1981–1993, 229 episodes of bacteraemia due to β -haemolytic streptococci of groups A, B, C and G were diagnosed in the County of Northern Jutland, Denmark. The annual rates for bacteraemia were quite constant during the 13-year period for each streptococcal group. Group A streptococcal (GAS) bacteraemia was the most frequent, comprising 1.4% of all bacteraemias. The incidence of GAS bacteraemia was 1.8/100 000/year in children < 5 years of age and 4.7/100 000/year in patients > 60 years old. With the notable exception of group B streptococcal (GBS) bacteraemia in neonates, β -haemolytic streptococci of groups B, C (GCS) and G (GGS) were isolated mostly from elderly patients. Except for GBS bacteraemia in neonates, approximately one-third of the bacteraemias in each group was nosocomially acquired. Predisposing factors included operative procedures in GAS and GCS bacteraemia, and diabetes mellitus in GBS bacteraemia. The skin was the most common primary focus in GAC, GCC and GGS bacteraemias, whereas the urinary tract was the commonest focus in GBS bacteraemia in adults. The mortality rates in GAS, GCS, GGS, and adult GBS bacteraemia were 23%, 16%, 17% and 19%, respectively. Of the 23 fatal cases of GAS bacteraemia, 57% died within 24 h after blood cultures had been obtained.

Introduction

β -Haemolytic streptococci continue to be significant pathogens and in the late 1980s an increase in group A streptococcal (GAS) infections in the Scandinavian countries and in the USA was reported.^{1–4} Attention has been drawn to a cluster of cases of necrotising fasciitis due to GAS in Great Britain,⁵ and there has been an increase of GAS bacteraemia again in Norway.⁶ Furthermore, reports have indicated increases of both group B streptococcal (GBS) invasive disease in adults⁷ and group G streptococcal (GGS) bacteraemias.⁸

In this study, the blood isolates in a Danish county obtained during a 13-year period (1981–1993) were reviewed retrospectively to assess any major trends in the occurrence of β -haemolytic streptococci of groups A, B, C and G in a defined study population. The aim of the study was to elucidate the epidemiology of bacteraemia with β -haemolytic streptococci of groups A, B, C and G, in association with the clinical picture and outcome.

Materials and methods

The County of Northern Jutland had a mean population of 483 000 during the observation period. There were nine local hospitals and two referral hospitals with specialised medical and surgical departments, including neurosurgery, gynaecology and paediatrics. The Department of Clinical Microbiology of Aalborg Hospital performed all the blood cultures during the study period. From 1 Jan. 1981 to 31 March 1992, a multiple-tube blood culture system was used⁹ and from 1 April 1992 to 31 Dec. 1993, a broth culture system.¹⁰ All streptococci that were β -haemolytic on horse blood 5% agar were sent to the Streptococcal Laboratory, Statens Seruminstitut, Copenhagen, for confirmation of grouping, T-typing of GAS and serotyping of GBS. The records of all patients with isolates belonging to groups A, B, C or G were reviewed retrospectively in regard to whether the bacteraemia was nosocomially or community acquired, whether there was underlying disease, the site of the primary focus and the outcome. Centers for Disease Control (CDC) define nosocomial bacteraemias as those cases in which no evidence of infection is present on admission to hospital.¹¹ Cases related either to previous admission to hospital or treatment, and infections in newborns associated with

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vaginal delivery were included.¹¹ The primary focus was assessed on the basis of clinical findings on the day of blood culture, and was considered to be verified bacteriologically if β -haemolytic streptococci of the same group were found at a relevant anatomical site. Death was considered to be related to the streptococcal bacteraemia if it occurred within 7 days after positive blood cultures were obtained. The annual incidences were calculated on the basis of the age-related population statistics for the County of Northern Jutland.

Mann-Whitney and χ^2 tests were used to assess differences between observed rates.

Results

During the 13-year survey there were 6849 bacteraemias identified in the County of Northern Jutland; 249 episodes of β -haemolytic streptococcal infection were recorded in 216 patients. Thirteen patients were excluded from further investigation either because the isolate was lost on subculture (one patient), the hospital record was not available (one patient), the bacteriological diagnosis was *Streptococcus anginosus* (six patients) and group F streptococci (two patients), or a streptococcal group identification was not obtained (three patients). In seven patients with recurrent bacteraemia with β -haemolytic streptococci, only the first episode was included. This resulted in 229 bacteraemic episodes available for study. Streptococci were associated with polymicrobial bacteraemia in 21 patients; four patients had GAS, 10 GBS, three group C streptococci (GCS), and four GGS bacteraemia.

The annual number of β -haemolytic streptococcal bacteraemia, and the total number of bacteraemias, are shown in table I. GAS accounted for 43% of all β -haemolytic streptococcal bacteraemias and GBS, GGS, and GCS for 31%, 16% and 10%, respectively.

Table I. Number and distribution of β -haemolytic streptococcal bacteraemias in the County of Northern Jutland 1981–1993

Year	Number of streptococcal bacteraemias				Total number of bacteraemic episodes
	GAS	GBS	GCS	GGG	
1981	2	3	1	1	443
1982	3	4	4	1	454
1983	7	7	1	1	474
1984	7	1	2	4	503
1985	7	12	1	2	516
1986	11	6	3	1	474
1987	6	5	1	1	516
1988	10	3	2	4	521
1989	12	5	0	5	495
1990	7	6	0	4	514
1991	5	5	3	4	505
1992	11	6	2	4	676
1993	11	7	4	4	758
Total	99	70	24	36	6849

Table II. Epidemiological characteristics of patients with β -haemolytic streptococcal bacteraemia in the County of Northern Jutland 1981–1993

Parameter	GAS	GBS		GCS	GGS
		Neonatal	Adults		
Sex					
Male	49	21	20	11	25
Female	50	11	18	13	11
Age (years)					
Median	61.8	1.3*	67	57.5	65
Range	0–91	0–56*	16–91	18–89	22–85
Nosocomial cases	38	28	15	7	12
Died	23	9	6	4	7
Total	99	32	38	24	36

*Days.

Each streptococcal group comprised a reasonably constant proportion of the total numbers of bacteraemias during the observation period; there was a slight increase of GAS bacteraemias in the late 1980s. Of the GAS, 72 were T-typed: T-1 accounted for 32%, T-3,13,B3264 for 17%, and T-12 and T-28 for 14% each. During 1988–1989 nearly half the isolates were T-1, compared with a mean figure of 23% for the 13-year survey period. During a 6-month period in the beginning of 1992 nearly all GAS bacteraemias were due to T-3,13,B3264. In GBS bacteraemias in adults, of the 39% of isolates that could be serotyped, types I, II and III were represented almost equally. GBS bacteraemia in neonates occurred with a mean annual number of 3 (range 0–8); the majority (87%) were of the early onset type, i.e. occurring at the age of 5 days or less. Serotypes were identified in 87% of the isolates and serotypes I and III formed the majority of GBS bacteraemias in neonates.

The epidemiological data are shown in table II. Except for GBS bacteraemias in neonates there were no significant differences in patients with bacteraemia of the various streptococcal groups regarding sex, age, proportion of nosocomial cases, and mortality, although males predominated in GGS bacteraemias. According to our definition, 88% of GBS bacteraemias in neonates were nosocomial. The annual age-related incidences are listed in table III. The highest incidence of GBS bacteraemia (8.1/100 000/year) was in infants, and of GAS bacteraemia (4.1) in patients > 60 years old; GCS and GGS bacteraemias were not recorded in patients under 18 years old.

Cardiopulmonary diseases were the most frequent predisposing factors in patients with GAS, GCS or GGS bacteraemia, but operative procedures were also prominent in GAS bacteraemias (table IV). Diabetes mellitus was the most frequent associated disease in adult patients with GBS bacteraemia.

The skin was the most frequent primary focus in GAS, GCS and GGS bacteraemia whereas urinary tract infection was most common in GBS bacteraemia

Table III. Age-related incidences of β -haemolytic streptococcal bacteraemia in the County of Northern Jutland 1981–1993

Age group (years)	Mean population (1981–1993)	GAS		GBC		GCS		GGS	
		Total	Annual incidence*	Total	Annual incidence*	Total	Annual incidence*	Total	Annual incidence*
0–4	28 275	7	1.8	32	8.1	0	0.0	0	0.0
5–9	30 128	5	1.2	0	0.0	0	0.0	0	0.0
10–19	70 330	1	0.1	1	0.1	1	0.1	0	0.0
20–60	260 754	32	0.9	15	0.4	12	0.3	15	0.4
≥ 61	94 423	54	4.1	22	1.7	11	0.8	21	1.6

*Cases/100 000 population/year.

Table IV. Predisposing factors in patients* with β -haemolytic streptococcal bacteraemia in the County of Northern Jutland 1981–1993

Predisposing factor	Number of cases of bacteraemia with				
	GAS	GBS†	GCS	GGS	Total
Diabetes mellitus	6	11	2	3	22
Cardiovascular and pulmonary diseases	17	4	8	10	39
Alcoholism	6	1	1	3	11
AIDS	0	0	0	1	1
Solid tumour	6	5	1	3	15
Haematological tumour	1	2	4	5	12
Steroid therapy	11	1	3	5	20
Operative procedures	16	5	4	2	27
Miscellaneous	21	5	3	5	34
None	32	6	3	6	47

*Some patients had more than one underlying condition.

†GBS bacteraemia in neonates not included.

Table V. Primary focus of infection in patients with β -haemolytic streptococcal bacteraemia in the County of Northern Jutland 1981–1993

Primary focus	Number of cases of bacteraemia with			
	GAS	GBS*	GCS	GGS
Wound/cellulitis	30 (12)	5 (2)	5 (3)	17 (4)
Osteomyelitis or arthritis	7 (1)	1 (0)	1 (1)	1 (0)
Pneumonia	7 (2)	1 (1)	1 (0)	2 (1)
Pharyngitis	4 (4)	0 (0)	1 (1)	3 (3)
Meningitis	1 (0)	0 (0)	3 (2)	0 (0)
Endocarditis	2 (0)	4 (0)	2 (0)	2 (2)
Genital puerperal infection	9 (9)	3 (2)	1 (0)	0 (0)
Urinary tract infection	0 (0)	6 (5)	2 (2)	0 (0)
Miscellaneous	8 (4)†	0 (0)	2 (0)‡	0 (0)
No evident focus	31	18	6	11

Numbers in parentheses indicate cases verified bacteriologically.

*GBS bacteraemia in neonates not included.

†One case each of sinusitis, abscess in gluteal muscles, necrotising fasciitis and infected haematoma; four cases of peritonitis.

‡One case each of peritonitis and salpingitis.

in adults (table V). Puerperal infection was prominent in GAS bacteraemia. This did not appear in clusters. In children with GAS bacteraemia the most common foci were osteomyelitis or arthritis. The mortality rates

of GAS, neonatal GBS, adult GBS, GCS and GGS bacteraemia were 23 %, 28 %, 16 %, 17 % and 19 %, respectively (table II). With the exception of GBS bacteraemias, the highest mortality rates were noted in patients > 60 years old (33 %, 27 % and 24 % for GAC, GCC and GGS bacteraemia, respectively). Of the 23 cases of fatal GAS bacteraemia, 57 % died sooner than 24 h after blood culture. The corresponding figures for GGS bacteraemias and neonates with GBS bacteraemia were 43 % and 78 %. However, deaths of patients with GCS bacteraemia or adults with GBS bacteraemia occurred only after 48 h. In case of skin infection, 27 % of patients with GAS bacteraemia died but none with GBS, GCS or GGS bacteraemia.

Discussion

An increase in GAS bacteraemia was reported in the late 1980s in Denmark, in line with other Scandinavian countries.^{1–3} T-1 temporarily became the dominant T-type in the County of Northern Jutland, conforming to the national trend.² Continuous shifts in the dominant M- and T-types among GAS are considered to contribute to changes in morbidity,^{12,13} and in the survey area a marked but transient increase of T-3,13,B3264 strains was noticed during 1992. The survey confirms previous reports that GAS most frequently cause bacteraemia whereas GCS are the least frequent.^{8,15–17} Contrary to other reports^{7,8} no increase in GBS bacteraemia in adults and GGS bacteraemia was found during 1981–1993. This may be related to differences in the study population regarding socio-economic status.

The finding that GCS and GGS bacteraemias were most frequent in elderly people, unlike GAS bacteraemia that occurred in all decades of life, agreed with previous studies.^{1,18–20} However, the incidence of 1.8/100 000/year among children < 5 years old was less than that reported elsewhere.^{1,16}

With the exception of GBS bacteraemia in neonates, the rate of nosocomially acquired bacteraemias among the β -haemolytic streptococci was similar. The finding that 38 % of GAS bacteraemias were nosocomial is in agreement with a nationwide Danish study²¹ but is higher than noted previously.^{8,16} One explanation may

be that the definition of nosocomial infection applied¹¹ is broader than in most of the above reports. Operative procedures were frequent in nosocomial GAS and GCS bacteraemia and GBS bacteraemia in adults; nearly half of the nosocomial GAS bacteraemias were related to orthopaedic, neurosurgical or gynaecological operations. The relevance of operative procedures in GAS bacteraemia has been reported previously^{8, 21} and underlines the potential for GAS to act as nosocomial pathogens. Operative procedures related to nosocomial GGS bacteraemias were not common, as noted elsewhere.⁸

As in other reports,^{7, 18–19} GCS and GGS bacteraemia, and GBS bacteraemia in adults, occurred in patients with debilitating diseases such as diabetes mellitus and cancer, whereas GAS bacteraemias were not so frequently related to serious underlying diseases.

In agreement with other reports, the skin was the most common focus in GAS, GCS and GGS bacteraemia.^{8, 15–17} An association has been reported between GGS bacteraemia and endocarditis.²² During the 13-year observation period, two cases of GGS endocarditis were recorded, one case was fatal within 72 h. Wound infection and urinary tract infection have been listed as common foci of GBS bacteraemias in adults⁷ but in this survey a primary focus could not be found in the majority of the cases, unlike other β -haemolytic streptococci.

Mortality rates of between 20% and 48% in GAS bacteraemia, that increased with age, have been reported.^{16, 17, 20} This agrees with mortality rates of 8% in children < 10 years old and 33% in patients > 60

years old in this study. The mortality rate for the other groups of β -haemolytic streptococci was at least twice as high in patients > 60 years of age than that in patients 20–60 years old. The suggestion that GGS bacteraemia is a more benign disease than GAS bacteraemia⁸ was not confirmed in this study.

The incidence of GBS bacteraemia in neonates, 0.4/1000 live births, is lower than reported elsewhere.⁷ Nine neonates with GBS bacteraemia died, all of whom had early onset disease. In the County of Northern Jutland, only one of 15 neonates with GBS bacteraemia died in the period 1988–1993, in contrast with eight of 17 who died during 1981–1987. This may indicate a more favourable prognosis of neonatal GBS bacteraemia in recent years.

In conclusion, the proportion of GAS, GCS, GGS and GBS bacteraemias was fairly constant over a 13-year period. GAS occurred in all decades of life, whereas GBS was found mainly in neonates and the elderly. GCS and GGS bacteraemias were mainly found in elderly patients. Except for GBS bacteraemia in neonates, there were no significant differences amongst the various β -haemolytic streptococci regarding age, sex, number of nosocomial isolates and mortality. Surgical intervention was an important predisposing factor in patients with GAS bacteraemia and this underlines the potential for GAS to act as nosocomial pathogens. Although there were no differences in mortality rates among the four bacterial groups, the majority of deaths of patients with GAS bacteraemia occurred within 24 h after blood cultures were obtained. This emphasises that GAS bacteraemia, although uncommon, is a serious event.

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