J Infect Chemother xxx (2017) 1–4

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original Article

Sites of infection associated with *Streptococcus anginosus* group among children

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ARTICLE INFO

Article history:
Received 16 January 2017
Received in revised form
26 July 2017
Accepted 16 September 2017
Available online xxx

Keywords:
Streptococcus anginosus group
S. anginosus
S. intermedius
S. constellatus
Children

ABSTRACT

Streptococcus anginosus group (SAG) are parts of normal flora of the oral cavity and associated with abscess forming in various sites on the body. Although the clinical features of infections caused by each member of the SAG in adults has been reported, it has not well been known in children. The aim of this study was to clarify the site of infections associated with individual SAG species among children.

Medical records from March 2010 to July 2016 were reviewed at Tokyo Metropolitan Children's Medical Center. Any SAG species (*S. anginosus*, *S. constellatus*, or *S. intermedius*) isolated from clinical samples and recorded in the microbiological database were included for analysis.

Analysis of 52 infectious episodes found that *S. anginosus* was most frequently isolated from the genitourinary tract, and 73% of genitourinary tract infection was balanoposthitis. All genitourinary tract infections were associated with *S. anginosus*. These findings were different from those of a previous study of adults. Of all the patients, 45 patients (87%) had polymicrobial infections. More than 70% of patients infected by *S. anginosus* and *S. constellatus* were co-infected by obligate anaerobes, in comparison with only 21% of *S. intermedius* cases. Among the obligate anaerobes species, *Bacteroides* spp. was significantly accompanied with *S. anginosus*. Susceptibility to penicillin, ampicillin, cefotaxime, erythromycin, clindamycin, levofloxacin, and vancomycin was 100%, 100%, 100%, 77%, 89%, 97% and 100%, respectively.

S. anginosus was often isolated from balanoposthitis among children.

1. Introduction

Streptococcus anginosus group (SAG), which were previously called as "*Streptococcus milleri* group" up to 1996, consists of 3 distinct species, *S. anginosus*, *S. constellatus,* and *S. intermedius*. Although SAG are parts of the commensal flora of the oral cavity and genitourinary tract, they were pathogens causing abscess-forming infections in various sites on the body [1–3].

The clinical features of infections caused by each member of SAG vary in adults. *S. anginosus*, *S. intermedius*, and *S. constellatus* predominantly caused central nervous system (CNS) infections, respiratory infections, and intra-abdominal infections [4,5]. In one report on pediatric infections, *S. intermedius* was isolated from half of patients with abscesses in the head, neck and upper chest area [6]. There are some pediatric case reports or case series regarding the association between *S. intermedius* and intracerebral abscesses [7,8], but sample size was small and data on other specimens was limited. The aim of this study was to clarify the sites of infections associated with each member of SAG among children.

2. Materials and methods

2.1. Study design

Medical records from March 2010 to July 2016 were reviewed at Tokyo Metropolitan Children's Medical Center. Any SAG species (*S. anginosus, S. constellatus,* or *S. intermedius*) isolated from clinical samples and recorded in the microbiological database were included for this study. Children aged 0 month to 18 years was included and clinical charts were reviewed for data on age, sex, underlying diseases, sites of infection, and treatment. Clinical characteristics were compared among three SAG species. Same strains isolated from the same site within 1 month were excluded

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https://doi.org/10.1016/j.jiac.2017.09.011
1341-321X/

to avoid duplication, and two or more SAG species isolated from the same sample were excluded from analysis. Infection was defined as inflamed findings such as pain, redness, and/or swelling, or proved by images, which were judged by a primary physician. Isolated SAG from urine, stool and sputum without inflamed findings and from blood (1/2 set) were judged as colonization or contamination. Strains with colonization and contamination were excluded from analysis based on a review of the medical records. This study was approved by the institutional review board at Tokyo Metropolitan Children's Medical Center (ID H27b-104).

2.2. Microbiological assessment

Microbiological identification was performed by the Rapid ID32 Strep system (Bio-Merieux, France). The minimum inhibitory concentration (MIC) was measured by Microscan WalkAway-96 Plus (Siemens, Germany) with MICroFAST® Strepto panel (Beckman Coulter, USA), instead of manual microdilution method. Other bacteria were identified by Microscan WalkAway-96 Plus. The Clinical and Laboratory Standards Institute (CLSI) breakpoint (M100-S19, S22) was used.

2.3. Statistical analysis

Fisher's exact test was used for categorical data. False discovery rate correction was performed with Benjamini and Hochberg methods. $P < 0.05$ was considered statistically significant. Data were analyzed using IBM SPSS Statistics version 24 (IBM, USA).

3. Results

3.1. Characteristics of patients

We identified 67 strains of SAG sampled from 66 patients. Among those, 13 strains isolated from urine, stool, and sputum collected from asymptomatic patient. These were excluded on the grounds of colonization or contamination. Two strains were excluded on the grounds of concurrent isolation with other SAG species. Fifty-two strains of SAG species were conclusively included for this study. The patients' median age was 7.5 years (interquartile range: 3–10 years), with male making up 73% of the total. Thirteen patients (25%) had underlying conditions, 8 of which were urological, 6 neurological, 2 malignant hematological, and 1 abdominal diseases (3 patients had multiple underlying diseases) (Table 1).

3.2. Sites of infection

The proportion of the sites of infection involving skin and soft tissue, the gastrointestinal tract, the genitourinary tract, the head and neck, and the CNS were 18 (35%), 11 (21%), 11 (21%), 10 (19%), and 1 (2%), respectively. *S. anginosus* was most frequently isolated from the genitourinary tract (11/28, 39%) and balanoposthitis was the principal form of genitourinary tract infection (8/11, 73%). Furthermore, all genitourinary tract infections were associated with *S. anginosus* (11/11).

S. constllatus (6/10, 60%) was responsible for the majority of skin and soft tissue infections. *S. intermedius* was most frequently isolated from, and the chief cause of, head and neck infections (8/14, 57%; 8/10, 80%, adjusted $p < 0.001$ in comparison with results for *S. anginosus* and adjusted $p = 0.05$ for *S. constellatus* after adjusted based on Benjamin and Hochberg methods.) (Table 2).

Bacteremia was observed in 4 patients, of whom 2 had febrile neutropenia and 2 had appendicitis. *S. constellatus* was found in the 2 patients with febrile neutropenia, and *S. constellatus* or *S. anginosus* was found in the 2 patients with appendicitis.

Samples were abscess in the body (58%), external genital discharge (15%), blood (8%), urine (4%), ascites fluid (2%) and others (13%). Forty-two percent of all samples were collected from non-sterile sites.

3.3. Polymicrobial infection

Polymicrobial infections were observed in 46 patients (88%). More than 70% of patients infected by *S. anginosus* (21/28) and *S. constellatus* (7/10) were co-infected by obligate anaerobes, in comparison with only 21% of *S. intermedius* cases (3/14). Among the obligate anaerobes species, *Bacteroides* spp. were often encountered in *S. anginosus* infections. Other gram-negative and gram-positive organisms were also isolated with SAG strains (Table 3).

3.4. Antimicrobial susceptibility

In total, 48 isolates of SAG (25 *S. anginosus*, 9 *S. constellatus,* and 14 *S. intermedius*) were subjected to an antimicrobial susceptibility test. Susceptibility to penicillin, ampicillin, cefotaxime, erythromycin, clindamycin, levofloxacin, and vancomycin was 100%, 100%, 100%, 77%, 89%, 97% and 100%, respectively (Table 4).

3.5. Treatment

Antibiotics choice and treatment duration was variable according to the site and size of the infection and accompanied organisms with SAG. The children with severe diseases (subdural abscess, maxillary sinus abscess, retropharyngeal abscess, tonsillar abscess, mediastinal abscess, and intraabdominal infection) were treated with antibiotics for median 16 days (interquartile range 13–22 days) and surgical drainage. The total number of patients with antibiotics were 11 penicillin with β-lactamase inhibitors, 3 carbapenem and vancomycin, 2 β-lactam, 2 β-lactam and metronidazole, 1 penicillin with β-lactamase inhibitors and aminoglycoside, 1 penicillin with β-lactamase inhibitors and vancomycin, and 1 quinolone. Among 17 children with skin and soft tissue infection, 14

Table 1
Characteristics of patients with *Streptococcus anginosus* group infections.

		No. of *Streptococcus anginosus* group strains (n)							
		S. anginosus		*S. constellatus*		*S. intermedius*		Total no. of strains	
		28		10		14		52	
Sex	Male	19	(68%)	7	(70%)	12	(86%)	38	(73%)
	Female	9	(32%)	3	(30%)	2	(14%)	14	(27%)
Age	Median	7 (IQR 2–10)		11.5 (IQR 8–14.75)		6 (IQR 4.25–8)		7.5 (IQR 3–10)	
Underlying disease	Yes	6	(21%)	5	(50%)	2	(14%)	13	(25%)
	No	22	(79%)	5	(50%)	12	(86%)	39	(75%)

IQR = interquartile range.

Please cite this article in press as: Furuichi M, Horikoshi Y, Sites of infection associated with *Streptococcus anginosus* group among children, J Infect Chemother (2017), https://doi.org/10.1016/j.jiac.2017.09.011