The Relationship between Streptococcus pyogenes emm Type and Clinical Symptoms in Balanitis Patients

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ABSTRACT

Balanitis categorized as a sexually transmitted infection is caused by the inflammation of the glans penis. Although one of the causative pathogens of balanitis is Streptococcus pyogenes, the relationship between bacterial markers in Streptococcus pyogenes and clinical symptoms has not been elucidated yet. This study analyzed the correlation between emm type and clinical symptoms of balanitis. Thirty-two samples of S. pyogenes were collected from balanitis patients in 2 medical institutes from 2009 to 2011. The emm type sequencing analysis was performed on the 32 strains and compared them to clinical symptoms. From balanitis patients, 2009 to 2011. The emm type and clinical symptoms has not been elucidated yet. This study analyzed the correlation between emm type and clinical symptoms of balanitis. Thirty-two samples of S. pyogenes were collected from balanitis patients in 2 medical institutes from 2009 to 2011. The emm type sequencing analysis was performed on the 32 strains and compared them to clinical symptoms. From balanitis patients, 2009 to 2011. The emm type showed higher penile swelling compared to the other emm type strains (p = 0.0354). All emm 58 strains caused itching. Only 3 (emm 58, emm 73, and emm 75) emm type strains caused purulent discharge from the penis. This suggests that specific emm types Streptococcus pyogenes are associated with balanitis.

KEYWORDS: balanitis, emm type, Streptococcus pyogenes

INTRODUCTION

Sexually transmitted infection is illness that has a significant probability of transmission between humans by means of human sexual behavior, including vaginal intercourse, oral sex, and anal sex (Mandell et al., 2010). Balanitis is categorized as a sexually transmitted infection, and it is defined as an inflammation of the glans penis, which often involves the prepuce (Birley et al., 1993; Edwards, 1996). Inflammation can be caused by infection with a wide variety of pathogens, including bacteria, viruses, or fungi (Mandell et al., 2010). It is a common condition that affects ~10% of male genitourinary clinic attendees; it can be a recurrent or persistent condition (Wakatsuki, 2005).

Streptococcus pyogenes (S. pyogenes) causes numerous infectious diseases such as pharyngitis, tonsillitis, nephritis, scarlet fever, necrotizing fasciitis, and streptococcal toxic shock syndrome (STSS) (Cunningham, 2000). S. pyogenes is also the causative agent of balanitis (Mandell et al., 2010). An investigator reported pyoderma of the penis followed fellatio, with S. pyogenes being isolated from the coronal sulcus (Drusin et al., 1975). There have been several short reports, including case reports, confirming the Streptococcal origin of balanitis (Deliyanni et al., 1989; Guerrero-vazquez et al., 1990; Kyriazi et al., 1991; Orden et al., 1995, 1996, 2000; Leverkus et al. 2002; Sakuma et al., 2005; Wakatsuki 2005; Nicolas et al., 2006). However, the bacterial pathophysiology and epidemiology of streptococcal balanitis has been unclear. Although the authors have reported 4 cases of streptococcal balanitis in the past, they were unable to elucidate the etiology of streptococcal balanitis owing to the limited number of cases (Minami et al., 2010).

M proteins are fibrillar coiled-coil proteins that are localized on the bacterial surface in S. pyogenes (Perez-Casal et al. 1993). M proteins are comprised of up to 4 distinct repeat regions and are anchored to the cell surface by a highly conserved C-terminal domain (Perez-Casal et al. 1993). The N-termini form highly variable extracellular fibrils. M proteins are associated with immune evasion mechanisms (Perez-Casal et al., 1993).

The classification of S. pyogenes was widely performed by comparison to the nucleotide sequence analysis of M protein—the emm type sequencing analysis. Similar to the N-terminus variability of the M proteins, the genes encoding M proteins (emm genes) also exhibit genetic variability (Beall et al., 1996). The nucleotide sequence of the variable 5’ end of the emm gene serves as the template for emm sequence typing (Beall et al., 1996).

Previous reports have showed that specific emm type S. pyogenes were frequently observed to cause severe invasive diseases, thereby suggesting that emm type could be a predictive marker of certain severe types of streptococcal diseases (Rogers et al., 2007; Steer et al., 2009; Lin et al., 2011). However, the distribution of emm type patterns in S. pyogenes from balanitis patients has not yet been reported. Hence, this study has attempted to clarify the relationship between emm type and clinical symptoms in streptococcal balanitis.

Objectives of the study

Our general objective is to assess the relationship between S. pyogenes emm type and clinical symptoms in balanitis patients. Furthermore, our specific objectives are to correlate the different S. pyogenes strains with the severity of balanitis, with other clinical markers, and with patients’ demographic data.
MATERIALS AND METHODS

Collection of clinical data

A prospective study was conducted in Nagoya City University Hospital, and Tawada Urological Clinic in Nagoya City, that assessed the clinical features of streptococcal balanitis that occurred between 2009 and 2011. Details of age, duration of infection, and the occurrence of clinical symptoms such as penile swelling, penile itching, and pus discharge, were collected from the medical records of both institutions. Streptococcal balanitis was defined by S. pyogenes isolates from the penis accompanied by penile reddening, which was diagnosed by urologists. The ethics committee at Nagoya City University approved of the experimental design.

Ethical statement and patient's consent

Written/verbal consent of patients was taken, after private discussion with each one of the patients, explaining the study objectives and the need for samples and clinical data collection. Patients’ confidentiality was maintained throughout the study period.

Samples

Thirty-two S. pyogenes clinical isolates were obtained from male patients with balanitis. Bacteria were identified on the basis of the growth of β-hemolytic colonies on sheep blood agar after incubation at 37°C in 5% CO₂ for 18–24 h. A confirmatory test for S. pyogenes was carried out with the Streptgram kit (Wako Chemical Inc., Tokyo, Japan). The bacterial 16S ribosomal sequencing analysis was also performed for genetic confirmation (Minami et al., 2010).

emm type sequencing analysis

Bacteria were characterized by emm type sequencing, as described previously (Beall et al., 1996). These nucleotide sequences data of emm type were further compared according to the available information from the Centers for Disease Control and Prevention surveillance studies (Available at: http://www.cdc.gov/ncidod/biotech/strep/strepindex.htm).

Statistical analysis

Chi square analysis and F-test were used to analyze the data, and p < 0.05 (95% confidence) was considered statistically significant. Analysis was performed using Statview computer software Version 4 under Mac OS 9.

RESULTS

The distribution of emm type in S. pyogenes from balanitis patients

Figure 1 shows the distribution of emm type patterns in S. pyogenes in this study. There were 5 emm 11 type strains, which were most frequently isolated. The second largest number of strains isolated was emm 75 and emm 112 (n = 4). The third largest number of strains included the emm 73, emm 77, emm 81, and emm 89 strains (n = 3). These 3 strains comprised ~70% of the total isolates. There was no significant number of specific emm type strains in this study.

Correlation between emm type and patients’ age

Table 1 shows the relationship between emm type and patient's age. The number of patients aged 20 years and 40 years was 14, and 12, respectively; these 2 age groups constituted ~88% of the total number of patients. However, the numbers of 30- and 50-year-old patients were fewer than both the 20- (n = 3) and 40-year-old patients (n = 2). No 60-year-old patients were found in this study. It was found that there was no significant relationship between emm type and age in this study.

Correlation between emm type and duration of symptoms

Table 2 shows the relationship between emm type and duration of symptoms. In ~66% of patients, the symptoms appeared within 4–14 days. The frequency of symptoms before 3 days, and after 15 days, was negligible. There was no significant relationship between emm type and duration of the symptoms in this study.

Correlation between emm type and swelling of penis

Figure 2 shows the relationship between emm type and penile swelling. While emm 11 strains caused more swelling of the penis than the other emm type strains (p = 0.0354), four (emm 50, emm 73, emm 77, and emm 89) emm type strains did not cause penile swelling.

Correlation between emm type and penile itching

Figure 3 shows the relationship between emm type and penile itching. Both all emm 50 and emm 58 strains caused penile itching, while none of the emm 112 strains did. However, there was no significant relationship between these emm types and penile itching in this study.

Correlation between emm type and secretion of pus from the penis

Out of 32 patients, 3 patients had pus secretion from the penis. The emm type patterns of S. pyogenes strains isolated from these patients were emm 58, emm 73, and emm 75, respectively.

DISCUSSION

To the authors’ best knowledge, this is the first report of the elucidation of the relationship between emm type and clinical symptoms in balanitis caused by S. pyogenes. No previous reports have investigated bacterial factors including emm type, in patients with streptococcal balanitis. From the study’s results, it can be seen that minor emm type strains cause balanitis; these are different from STSS-caused S. pyogenes which predominantly include strains emm 1, and emm 3 (Cunningham, 2000; Steer et al., 2009; Lin et al., 2011). This study has not assessed if those S. pyogenes caused STSS following balanitis. The emm type strains causing balanitis were also different from those that caused pharyngitis. The majority of emm type strains causing pharyngitis in Japan are currently emm 12, emm 4, and emm I (Wajima et al., 2008).
The study’s results suggest that a new category of emm type exist among the balanitis-causing strains, and hence, authors were interested in investigating the colonization patterns of these emm type strains.

The relationship between emm type and patients’ age implies that there are a higher number of patients in the 20- and 40-year-old groups. From this result, one speculates that young and middle-aged male patients have higher sexual activity and a higher possibility of contact with commercial sexual workers. In fact, contact with sexual workers is one of the major risk factors in sexual transmitted diseases (Wakatsuki, 2005).

Previous reports have shown that streptococcal balanitis occurs mainly in the age group of 30 years (Wakatsuki, 2005); however, the results at hand do not reiterate this finding. As the study did not find the reason the number of 30 years male patients was decreasing, further accumulation of patient’s data may resolve this question.

The relationship between emm type and duration of the symptoms also suggest that the symptoms of balanitis occur within 1–2 weeks, and not within a few days. A previous report showed that streptococcal balanitis occurred within a few days after sexual contact (Wakatsuki, 2005). There could be differences in onset time between pharyngitis and balanitis. The duration of pharyngitis is a few days (Cunningham, 2000), and this time interval coincides with that in a previously reported balanitis report (Wakatsuki, 2005).

Although these differences have not been explained clearly, the severity of balanitis, and the virulence of S. pyogenes isolates raise important questions, which need to be investigated.

When patients develop symptoms such as itching and pus secretion, most of them will consult an outpatient clinic because of the severity of the symptoms. After consultation, most patients in Japan may immediately receive antibiotics for infections caused by Neisseria or Chlamydia before the causative bacterium is identified (Wakatsuki, 2005). Antibiotics such as fluoroquinolone are also effective against S. pyogenes; this could possibly be one of the reasons that patients with streptococcal balanitis do not spread the infection, and could also explain the lack of attention paid to balanitis caused by S. pyogenes.

In the present study, the relationship between emm type and penile swelling shows that a specific emm type (emm 11) caused significant penile swelling more frequently than other strains. The authors were unaware that emm 11 S. pyogenes possessed specific high virulent factors, and hence, are currently investigating the novel putative virulent factors. The relationship between emm type and penile itching shows that emm 58 S. pyogenes had high virulence, and emm 112 had low virulence. Current results also show that ~10 % of balanitis patients had pus discharge from the penis. Specific emm type (emm 58, emm 73, and emm 75) strains were observed in this study. An earlier report showed that symptoms of pus discharge and penile itching were predominant in balanitis (Wakatsuki, 2005).

Although similar results were observed on penile itching, they were not the same for pus discharge. These differences might explain the severity of balanitis between the earlier reports and the current.

In conclusion, the study’s results suggest that a specific emm types S. pyogenes are associated with balanitis. The emm type sequencing analysis may be a useful marker for the prediction of progressive disease activity.

Recommendations for further Studies

Further accumulating patient’s data is necessarily for confirmation of the colonization patterns of specific emm type S. pyogenes in balanitis patients. The relationship between severity of balanitis and the virulence of S. pyogenes isolates also need to be clarified.

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COMPETING INTERESTS

The authors declare no competing interests.

REFERENCES


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Tables and Figures

Table 1. The relationship between emm type and patient's age.

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<th>58</th>
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Table 2. The relationship between emm type and duration of symptoms

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Fig 1. The relationship between emm type and the numbers of streptococcal isolates from balanitis patients.

Fig 2. The relationship between emm type and penile swelling.

The black and white boxes represent positive and negative for penile swelling in balanitis patients, respectively.

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Fig 3. The relationship between *emm* type and penile itching.

The black and white boxes represent positive and negative for penile itching in balanitis patients, respectively.