Diagnostic Accuracy of Clinical Symptoms and Rapid Diagnostic Test in Group A Streptococcal Perianal Infections in Children

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From 2009 to 2014, we prospectively enrolled 132 children with perianal infections. The presentation of painful defecation, anal fissures, and macroscopic blood in stools was highly suggestive of group A streptococcal perianal infection (probability 83.3%). We found a high sensitivity of a group A streptococcal rapid diagnostic testing (98%) but relatively low specificity (72.8%).

Keywords. group A streptococcal; perianal infection; children; rapid diagnostic test.

Perineal diseases caused by group A streptococci (GAS) have been reported in the pediatric literature for several decades [1, 2]. However, such diseases are probably underdiagnosed, and data on the incidence are sparse [3, 4]. Most cases are perianal, less frequently vulvovaginal disease, with occasional reports of streptococcal balanitis [4]. The classical presentation of perianal GAS infection (PASI) is a well-demarcated rash around the anus, with itching, rectal pain, and blood-streaked stools. The natural course of untreated PASI is not known, but symptoms such as discomfort, toilet avoidance, and constipation are well known to not resolve spontaneously and can persist, often for many months, until the appropriate diagnosis is made and effective treatment administered [3]. Furthermore, a high frequency of penicillin treatment failure has been observed [5, 6].

GAS rapid antigen detection tests (GAS-RADTs) have been well studied for pharyngitis in clinical practice. The main concern in the use of a GAS-RADT for sore throat is relatively low sensitivity, leading to the recommendation to perform a culture in case of negative test result [7]. Few studies have assessed GAS-RADTs in extrapharyngeal GAS infections [8, 9]. The aim of this study was to describe the clinical characteristics of PASI and assess the performance of GAS-RADT in the disease.

METHODS

From 2009 to 2014, 15 pediatricians trained to use a GAS-RADT for sore throat prospectively enrolled all patients aged 3–14 years with signs and symptoms suggestive of PASI. Children who received an antibiotic within the previous 7 days were excluded. The study protocol was approved by the Ile-de-France XI Institutional Review Board and the French administrative authority Commission Nationale Informatique et Libertés (CNIL).

Data were collected on patient age, sex, fever, constipation, pain on defecation, anal fissures, erythema (size in centimeters), blood seen in stools, itching, and duration of signs and symptoms.

After obtaining oral informed consent from parents and children (if >3 years old to understand), perianal samples were obtained by use of a double-swab collection–transportation system (Venturi Transystem Amies agar, COPAN Diagnostics, Corona, California). The RADT (StreptAtest, Dectrapharm, France), a GAS-specific immunochromatographic strip assay, was performed immediately with swab 1 collected in the pediatrician’s office. Swab 2 was held at ambient temperature and sent within 72 hours to the Robert Debré Hospital laboratory by an express messenger service. On receipt, swab 2 was rolled over one-quarter of a blood agar plate (BAP) (Columbia ANC agar + 5% sheep blood; bioMérieux, Lyon, France), and the inoculum was further distributed on the plate by streaking with use of a sterile loop. The plates were incubated anaerobically at 37°C and read after 18–24 hours. When no β-hemolytic colony was found on the BAP, one drop of a tryptone glucose

Received 29 July 2014; accepted 27 September 2014; electronically published 13 October 2014.

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Clinical Infectious Diseases® 2015:60(2):267–70
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DOI: 10.1093/cid/ciu794
yeast broth previously inoculated with the swab sample and incubated at 37°C for 24 hours was used for subsequent culture on a BAP. Microbiologists were blinded to individual clinical data and GAS-RADT results. GAS isolates were emm types as previously described [10], and emm types were analyzed according to the recently described emm clusters [11]. False-positive GAS-RADT results were defined as positive GAS-RADT results with negative GAS culture (with culture as the reference method).

Data entry used 4D 6.4 (4D) software with the database fully anonymized. GAS-RADT diagnostic accuracy (sensitivity, specificity, likelihood ratios, and predictive values and their 95% confidence intervals [CIs]) was estimated with BAP culture as the reference standard. Statistical analysis was performed using Stata/SE 13.1 (StataCorp, College Station, Texas). The association of signs or symptoms and positive GAS-RADT and/or GAS culture results was tested by multivariate logistic regression. Variables with P < .20 on univariate analysis were introduced in the model, and only variables with a significant P value (<.05) were taken into account in the final model. The Standards for Reporting of Diagnostic accuracy studies statement was followed for reporting the results of the study [12].

RESULTS

From 2009 to 2014, perianal infections (including 4 patients with associated vulvovaginal involvement) in 132 children were diagnosed by 15 pediatricians. The mean age of children was 46.6 ± 23.5 months (median, 43.1 months); 63.9% were boys. Most of the cases occurred in the autumn (peak, 21% in November), with a nadir during the summer. Calculations of GAS disease prevalence and accuracy estimates are based on the frequencies in Table 1. Overall, 51 of the 132 cultures were positive for GAS (prevalence 38.6% [95% CI, 30.0%–47.5%]). Of 51 patients with a positive culture result for GAS, 50 had a positive RADT result (sensitivity 98% [95% CI, 89.6%–100%]), and of 81 patients with a negative culture result for GAS, 59 had a negative RADT result (specificity 72.8% [95% CI, 61.8%–82.1%]). False-positive GAS-RADT results represented 16.7% of cases (n = 22).

Table 2 compares the demographic and clinical characteristics by GAS culture and GAS-RADT results. Anal fissures, blood seen in stool, and painful defecation were significantly more frequent for patients with positive GAS culture or GAS-RADT. On multivariate logistic regression, PASI with fissures (n = 60/129) or painful defecation (n = 72/129) was significantly associated with GAS-RADT and/or GAS culture positivity (adjusted odds ratio [AOR], 2.43 [95% CI, 1.11–5.33], P = .027 and 2.45 [95% CI, 1.20–5.22], P = .02, respectively). By contrast, the risk was not significant for blood in stools (n = 35/129; AOR, 1.98 [95% CI, 0.78–5.03], P = .148). The probability of GAS-RADT and/or GAS culture positivity was 83.3% with the presence of fissures, blood in stools, and painful defecation combined.

Ten different emm types were characterized among the 51 isolates, the main one being emm 28 (41.2%), followed by emm 89 (19.6%), emm 12 (9.8%), emm 77 (7.8%), emm 1 (5.9%), emm 4 (5.9%), emm 75 (3.9%), emm 2 (2%), emm 87 (2%), and emm 9 (2%). When emm types were analyzed by emm clusters, 36 of the 51 perianal isolates (70.6%) belonged to the same cluster, E4 (emm 2, 28, 77, and 89). The other clusters represented were A-C4 (n = 5 [9.8%], emm 12), A-C3 (n = 3 [5.9%], emm 3), E1 (n = 3 [5.9%], emm 4), E3 (n = 2 [3.9%], emm 9 and 87), and E6 (n = 2 [3.9%], emm 75).

DISCUSSION

With cases diagnosed by GAS culture, GAS-RADT, or both representing 51, 72, and 73 cases, respectively, to our knowledge, this study is the largest published on PASI. These findings confirm the relatively common diagnosis of PASI in pediatrics practice and some features previously described: male preponderance, young age (clustering in the preschool and early school-age group), seasonal distribution, absence of fever, and other systemic symptoms [3, 4]. In our study, the median duration of the symptoms before diagnosis was only 2 weeks, which is shorter than in previous reports [3, 4, 6], and could be explained by the high suspicion of PASI by pediatricians participating in the study.

Some symptoms such as painful defecation and anal fissures and, to a lesser extent, macroscopic blood in stools were highly suggestive of GAS infection: the probability of GAS-RADT and/or GAS culture positivity was 83.3% with the simultaneous presence of these 3 signs and symptoms.

We found a high sensitivity but relatively low specificity of GAS-RADT compared with GAS culture. Several hypotheses...
have been raised to explain false-positive GAS-RADT results in pharyngitis: cross-reactivity with bacteria, GAS nutritional or non-ß-hemolytic variants, or nonviable GAS. A recent study of our group explored this hypothesis in GAS pharyngitis [13]. In this study, three-quarters of the false-positive GAS-RADT results were positive on polymerase chain reaction, and most were linked with increased growth of Staphylococcus aureus. The possible inhibitory effect of other bacterial species might be explained by bacterial interference involving the production of bacteriocins and bacteriolytic substances and competition for nutrients [14]. The richness of the perianal bacterial flora argues for these explanations. However, conclusive biological evidence is needed to support this hypothesis. Nevertheless, the sensitivity of GAS-RADT in PASI seems to be high. One of the main obstacles in the use of GAS-RADT in PASI is no formal approval for sites of GAS infection other than the throat, which has medicolegal implications [15].

The very low rate of asymptomatic perineal GAS carriage has been assessed in few studies [4]. Thus, the causal relationship between perineal dermatitis and GAS-positive perianal samples is highly suggestive. Nevertheless, almost 50% of the patients of this cohort with perianal dermatitis were negative on GAS-RADT and/or GAS culture, which suggests the implication of other bacterial species in the pathogenesis. This study confirms the predominance of emm type 28 among GAS strains implicated in PASI. This characteristic is probably related to acquisition of Streptococcus agalactiae genome sequences, thus allowing emm 28 strains to have better adhesion to perineal epithelial cells [16–18]. Recently, a new emm cluster typing system was proposed to classify the many GAS emm types into clusters containing closely related M proteins that share binding and structural properties [11]. In our study, more than two-thirds of the perianal isolates belonged to the emm cluster E4, which suggests that the M protein structure itself confers a selective advantage in this ecological niche [19].

This study confirms that clinicians should be alerted to PASI, especially among preschool and young school-aged children with perineal and gastrointestinal symptoms. The presence of painful defecation, anal fissures, and macroscopic blood in stools is highly suggestive of PASI, and RADTs in this setting have high sensitivity.

**Notes**

**Acknowledgments.** We thank all the physician investigators who participated in the study: C. Batard, M. Benani, F. Corrard, P. Debert, A. Elbez, P. Martin, A. S. Michot, N. D’Ovidio, C. Romain, O. Romain, C. Schlemmer, F. Thollot. We thank E. Sobral (Department of Microbiology, Robert Debré Hospital), M. Boucherat, MD (database design), F. de La

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<th>Characteristic</th>
<th>Total (N = 132)</th>
<th>Positive GAS Culture (n = 51 [38.6%])</th>
<th>Negative GAS Culture-Positive GAS-RADT (n = 22 [16.7%])</th>
<th>Negative GAS-RADT and Negative GAS Culture (n = 59 [45.7%])</th>
<th>P Value</th>
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<td>Sex, male</td>
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<td>Duration of symptoms, wk, mean ± SD</td>
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<td>Temperature, °C, mean ± SD</td>
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Bold values indicate statistically significant results. Data are presented as No. (%) unless otherwise specified.

**Abbreviations:** GAS, group A Streptococcus; RADT, rapid antigen detection test; SD, standard deviation.

a Missing data, n = 1.

b Missing data, n = 2.
References