

Brief Communication



Diagnostic Impact of Clinical Manifestations of Group A Streptococcal Pharyngitis

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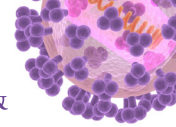
ABSTRACT

This study aims to identify the clinical characteristics for diagnosing streptococcal pharyngitis. The correlation between eighteen clinical manifestations and rapid antigen detection test results was analyzed. Among 205 patients, five clinical manifestations, pharyngeal hemorrhage (odds ratio [OR] = 11.85), palatal hemorrhage (OR = 9.32), tonsillar swelling (OR = 4.37), rash (OR = 3.02), and enlarged cervical nodes (OR = 1.91), were significantly correlated with group A Streptococcus (GAS) pharyngitis. Traditional indicators such as fever, pharyngeal redness, acute onset, headache, rhinorrhea, cough, tonsillar exudate, and cervical tenderness were not statistically related to GAS pharyngitis. Therefore, physicians should be cautious in using these traditional indicators.

Keywords: *Streptococcus pyogenes*; Group A streptococcus; Pharyngitis; Rapid test; Diagnosis

Pharyngitis is a common upper respiratory tract infection that includes tonsillitis. Group A Streptococcus (GAS) is the most common cause of bacterial pharyngitis. An accurate diagnosis of bacterial pharyngitis is important because untreated GAS pharyngitis could lead to suppurative (*e.g.*, peritonsillar abscess) or non-suppurative (*e.g.*, acute rheumatic fever or poststreptococcal glomerulonephritis) complications [1, 2]. In general, viral pharyngitis is often accompanied by common cold symptoms, such as coughing, runny nose, and sneezing. On the other hand, bacterial pharyngitis presents more severe symptoms or signs than viral pharyngitis, including high fever, enlarged and tender cervical nodes, and tonsillar exudative discharge [3-7].

The gold standard for diagnosis of GAS pharyngitis is bacterial culture. However, throat culture takes 24 - 48 hours and requires culture facilities. Therefore, culture tests are difficult to use in primary care practice. To compensate for these shortcomings, a rapid antigen detection test (RADT) was developed to detect GAS within a few minutes without need of laboratory facilities. The Korean upper respiratory tract infection guideline recommends that the RADT be performed in patients with modified Centor score of 3 or above [8, 9]. The modified Centor score helps predict the probability of streptococcal pharyngitis by



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Conflict of Interest

No conflict of interest.

Author Contributions

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taking into consideration of risk factors such as patient's age, symptoms, and physical exam. However, not all clinicians follow this diagnostic recommendation always. In this study, we analyzed the common symptoms or signs related to GAS pharyngitis diagnosed by RADT.

In total, 372 patients who showed pharyngitis symptoms were recruited for this study from August 2018 to December 2019 in five pediatric clinics. These patients were subjected to throat culture as well as a RADT. These two tests were conducted on patients with no history of taking antibiotics lately. The study was approved by the Institutional Review Board (IRB) of Gyeongsang National University Changwon Hospital (2020-02-031). The characteristics of the symptoms or signs were recorded in a prospective manner. The Sofia Strep A Fluorescent Immunoassay (Quidel, San Diego, CA, USA) was used to detect GAS antigen from throat swabs of symptomatic patients. The attending pediatricians performed the RADT according to the manufacturer's instructions. We analyzed the correlation of symptoms or signs and RADT results. Although bacterial culture was performed at the same time, we analyzed only RADT results because RADT is more available in primary care practice. We analyzed 205 patients whose symptoms or signs were recorded; 90 were men and 115 were women. The median age was 7 years old (interquartile range, 5 - 11 years old) with a range of 1 - 61 years old. Clinical manifestations, including fever (>38°C), pharyngeal redness, swallowing pain, acute onset (<2 days), tonsillar exudate, headaches, tonsillar swelling, rhinorrhea, cough, enlarged cervical nodes, tender cervical nodes, abdominal pain, pharyngeal hemorrhage, palatine hemorrhage, sore throat, rash, conjunctivitis, and diarrhea, were investigated. The correlation between clinical manifestations and RADT results was tested for significance using SPSS software version 23.0 (IBM Corp., Chicago, IL, USA). We used the chi-squared test to compare symptoms or signs between RADT-positive and RADT-negative cases. If the expected frequency was less than 5, Fisher's exact test was used. Univariate and multivariate logistic regression analyses were used to analyze the degree of influence of significantly related clinical variables on RADT results. A *P*-value of less than 0.05 was considered significant.

The overall agreement of the 372 tested throat swab specimens of the RADT with the culture showed an excellent agreement with Cohen's kappa of 0.89. The performance of the RADT based on culture was 94.1%, 95.9%, 89.6% and 97.7% for sensitivity, specificity, positive predictive value, and negative predictive value, respectively.

We analyzed the correlation between modified Centor score (0, 1, 2 *vs.* 3, 4) and RADT results. However, there was no statistical significance between high modified Centor score (3, 4) and RADT positive result (*P* = 0.067). Also, we analyzed the correlation between clinical symptoms and RADT tests in 205 patients with eighteen clinical features. As a result of examining the clinical symptoms or signs, a fever above 38°C, pharyngeal redness, swallowing pain, acute onset (<2 days), headaches, rhinorrhea, and cough were not significantly different between GAS and non-GAS pharyngitis.

Significance was found in the univariate logistic regression analysis for pharyngeal hemorrhage (odds ratio [OR] = 11.85), palatal hemorrhage (OR = 9.32), tonsillar swelling (OR = 4.37), rash (OR = 3.02), and enlarged cervical nodes (OR = 1.91) influencing RADT positivity (**Table 1**). On the other hand, tonsillar exudate (OR = 0.52) was negatively related to the RADT. In the multivariate logistic regression analysis, pharyngeal hemorrhage (OR = 3.90) and tonsillar exudate (OR = 0.45) were significantly related with RADT (**Table 2**).

Table 1. Comparison of clinical characteristics and RADT results for the diagnosis of group A streptococcal pharyngitis

Variable	RADT (+), N (%) (n = 60)	RADT (-), N (%) (n = 145)	Total, N (%) (n = 205)	P-value ^a
Fever	54 (90.0)	135 (93.1)	189 (92.2)	0.640
Pharyngeal redness	53 (88.3)	114 (78.6)	167 (81.5)	0.153
Swallowing pain	50 (83.3)	108 (74.5)	158 (77.1)	0.338
Acute onset (<2 days)	46 (76.7)	105 (72.4)	151 (73.7)	0.649
Tonsillar exudate	29 (48.3)	93 (64.1)	122 (59.5)	0.052
Headache	28 (46.7)	74 (51.0)	102 (49.8)	0.645
Tonsillar swelling	37 (61.7)	39 (26.9)	76 (37.1)	<0.01
Rhinorrhea	19 (31.7)	52 (35.9)	71 (34.6)	0.680
Cough	20 (33.3)	49 (33.8)	69 (33.7)	1.000
Enlarged cervical nodes	25 (41.7)	39 (26.9)	64 (31.2)	0.065
Tender cervical nodes	19 (31.7)	39 (26.9)	58 (28.3)	0.665
Abdominal pain	17 (28.3)	35 (24.1)	52 (25.4)	0.671
Pharyngeal hemorrhage	31 (51.7)	12 (8.3)	43 (21.0)	<0.01
Palatal hemorrhage	26 (43.3)	11 (7.6)	37 (18.0)	<0.01
Sore throat	5 (8.3)	17 (11.7)	22 (10.7)	0.641
Rash	9 (15.0)	8 (5.5)	17 (8.3)	0.047
Conjunctivitis	0 (0.0)	7 (4.8)	7 (3.4)	0.109
Diarrhea	0 (0.0)	6 (4.1)	6 (2.9)	0.185

Either by the chi-squared test or by the Fisher's exact test.

RADT, rapid antigen detection test; N, number.

Table 2. Results of univariate and multivariate logistic regression analyses of clinical predictors of group A streptococcal pharyngitis

Variable	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Pharyngeal hemorrhage	11.85 (5.44 - 25.79)	<0.001	3.90 (1.00 - 15.10)	0.049
Palatal hemorrhage	9.32 (4.18 - 20.71)	<0.001	2.18 (0.54 - 8.77)	0.274
Tonsillar swelling	4.37 (2.31 - 8.26)	<0.001	1.69 (0.71 - 4.03)	0.234
Rash	3.02 (1.10 - 8.25)	0.031	2.08 (0.63 - 6.83)	0.226
Enlarged cervical nodes	1.91 (1.01 - 3.58)	0.046	1.58 (0.65 - 3.79)	0.309
Tonsillar exudate	0.52 (0.28 - 0.96)	0.037	0.45 (0.20 - 0.98)	0.046

OR, odds ratio; CI, confidence interval.

This is a rare clinical study in Korea to analyze the correlation between the clinical manifestations of GAS pharyngitis and the results of RADT. According to the acute sore throat monitoring project conducted by Korean Centers for Disease Control and Prevention in 2009 - 2011, etiologic bacteria or viruses were detected in only 54.7% of the cases [10]. Most of the cases (84%) were caused by virus. The cases of GAS pharyngitis were only 7.9%, whereas the antibiotic prescription rate was 43.1%, suggesting that there were many unnecessary antibiotic prescriptions [10]. In this study, we investigated eighteen clinical symptoms or signs for patients with suspected acute pharyngitis who visited small- to medium-sized pediatric clinics in Changwon during 2018 - 2019. The five clinical symptoms or signs, pharyngeal and palatal hemorrhage, tonsillar swelling, enlarged cervical nodes and rash, were significantly correlated with GAS pharyngitis diagnosed by a RADT. These results are partly in line with a previous study in 2016 in Korea, in which palatal hemorrhage and rash were significantly correlated with bacterial pharyngitis [11].

In the multivariate logistic regression analysis, tonsillar exudate was negatively correlated with the diagnosis of GAS pharyngitis. This result may be driven by vague expression of 'tonsillar exudate'. The terminology 'tonsillar exudate' seems rather subjective; therefore, 'tonsillar pus-like discharge' would be better for a clearer description. In addition, there was no significant difference in fever, pharyngeal redness, acute onset, headache, rhinorrhea, cough, or tender cervical nodes between GAS and non-GAS pharyngitis on the contrary to the previous knowledge [3-7]. Therefore, physicians should be cautious using the traditional

scoring system, such as modified Centor score. Considering the degree and type of each clinical symptoms or signs with pharyngitis vary for each patient, consistency with the clinical judgments of different physicians on the symptoms or signs might be difficult to achieve in this study.

In conclusion, clinical manifestations of pharyngitis are of low diagnostic value by themselves, and our study of clinical manifestations of GAS pharyngitis demonstrated far different from the previous knowledge. Therefore, the diagnosis of GAS pharyngitis based on clinical manifestations should be further evaluated in Korea. In particular, the use of the RADT, which is easy to use when diagnosing patients with sore throat, can increase the accuracy of the diagnosis of bacterial pharyngitis in primary care clinics.

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