Biochemical tests cannot differentiate between tonsillar and middle ear-derived infections

Ann Marlene Gram Christensen[1], Martin Glymer Kirkegaard[2], Thomas Skov Randrup[3] & Tejs Ehlers Klug[1]

ABSTRACT

INTRODUCTION: Infection markers are appreciated supplements in the clinical diagnosis of ear, nose and throat (ENT) infections. We aimed to examine the differential diagnostic usefulness of C-reactive protein (CRP), white blood cell count (WBC) and absolute neutrophil count (ANC) according to severity of middle ear and tonsillar infections.

MATERIAL AND METHODS: This was a retrospective study including all patients admitted to the ENT Department, Aarhus University Hospital, from January 2001 to December 2008 and diagnosed with acute otitis media, mastoidismus, acute mastoiditis, acute tonsillitis, peritonsillar abscess, parapharyngeal abscess and necrotizing fasciitis.

RESULTS: A total of 1,773 patients were included. Between the tonsil subgroups, significant differences were found in CRP ($p < 0.001$), WBC ($p < 0.001$) and ANC ($p < 0.001$) levels. However, sensitivities and specificities related to differential diagnostics were low. In the middle ear group, no differences in CRP ($p = 0.84$), WBC ($p = 0.46$), and ANC ($p = 0.72$) levels were found. The number of CRP levels above the reference value was significantly higher than the corresponding number of WBC and ANC levels. A trend (non-significant) was found towards lower parameter levels in acute tonsillitis and peritonsillar abscess patients who grew *Staphylococcus aureus* compared with patients infected with other bacteria.

CONCLUSION: CRP and ANC levels were related to severity of tonsillar-derived infections, but no such relation was found in infections with middle ear origin. None of the infection markers studied was useful for differential diagnostics.

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C-reactive protein (CRP), total white blood cell count (WBC) and absolute neutrophil count (ANC) are the most frequently used infection markers in the monitoring of head and neck infections [1, 2]. In addition, these parameters are frequently used to assess the severity of infection and whether the origin of the infection is viral or bacterial [3-5]. In the early phase of infections, symptoms and signs of complications are often unspecific [6-8]. Laboratory parameters are therefore appreciated supplements in clinical diagnostics.

CRP is an unspecific acute-phase protein produced by the liver. It is increased about six hours after an inflammatory stimulus and reaches a maximum concentration after approximately 36 hours [9]. Generally, CRP levels are higher in systemic bacterial infections than in non-bacterial infections [5, 10]. Leucocytes, especially ANC, are rapidly released from the bone marrow at the onset of fever and other physiological and metabolic changes referred to as the acute-phase response to infection.

The primary purpose of this study was to investigate the differential diagnostic usefulness of CRP, WBC and ANC according to severity of infection. Additionally, the relationship between bacterial pathogens and CRP, WBC and ANC levels was examined.

MATERIAL AND METHODS

A retrospective study was conducted including all patients admitted to the Ear, Nose and Throat (ENT) Department at Aarhus University Hospital from January 2001 to December 2008 diagnosed with acute otitis media, mastoidismus, acute mastoiditis, acute tonsillitis, peritonsillar abscess, parapharyngeal abscess and necrotizing fasciitis.

The following data were extracted from the records: age, sex, date of admission, duration of symptoms and hospitalization, type of antimicrobial therapy before, during and after admission, microbiology, swab locations, CRP, WBC and ANC. All blood samples were obtained at admission.

On the basis of the primary site of infection, patients were classified into two main groups: 1) tonsil and 2) middle ear. Each group was subdivided and categorized according to increasing severity of infection: 1)

Patient with acute tonsillitis.

ORIGINAL ARTICLE

1) Department of Otorhinolaryngology, Head and Neck Surgery, Aarhus University Hospital
2) Department of Otorhinolaryngology, Head and Neck Surgery, Vejle Hospital
3) Department of Otorhinolaryngology, Head and Neck Surgery, Holstebro Regional Hospital

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acute tonsillitis, peritonsillar abscess, parapharyngeal abscess and necrotizing fasciitis, and 2) acute otitis media, mastoidismus and acute mastoiditis.

The acute tonsillitis diagnosis was based on typical symptoms (sore throat, pain on swallowing and fever) and the clinical findings of tonsillar exudate and hyperaemia. Tonsillar surface swabs for culture were obtained from most acute tonsillitis patients. In all peritonsillar abscess patients, pus was found between the tonsillar capsule and the pharyngeal constrictor muscle. Peritonsillar abscess patients underwent either acute tonsillectomy or aspiration and incision. Parapharyngeal abscess was diagnosed with the finding of pus in the parapharyngeal or retropharyngeal space and the abscess was drained through intrapharyngeal incision. Pus aspirates or swabs for culture were obtained from peritonsillar abscess and parapharyngeal abscess patients. Necrotizing fasciitis was defined as a rapidly progressing bacterial infection characterized by a quickly spreading erythema, oedema, tenderness and pain in combination with removal of necrotic tissue along the cervical fascial layers at surgical exploration. In necrotizing fasciitis, the patients' infected tissues were used for culture.

The acute otitis media diagnosis was based on the clinical finding of pus in the middle ear. Middle ear pus swabs obtained through the auditory meatus were used for culture in patients with spontaneous perforation or at the time of myringotomy. In addition to acute otitis media, patients diagnosed with mastoidismus had retroauricular erythema, swelling and pain, but no subperiostal abscess. Acute mastoiditis was diagnosed according to the same clinical symptoms as mastoidismus, but with the presence of subperiostal abscess. Acute mastoidectomy was performed in all acute mastoiditis patients and in mastoidismus patients with deterioration or no clinical response 24 hours after myringotomy and high-dose penicillin therapy. Pus specimens for culture were obtained at the time of mastoidectomy.

Standard microbiological methods were used. Pus aspirates and swab samples were performed as part of the routine diagnostic procedures. The media used were 5% blood agar, chocolate agar, anaerobic plates and thioglycolate broth. Aerobe and anaerobe cultures were incubated at 35 °C for a maximum of 72 hours. Speciation for microorganisms was performed by standard methods [11].

Statistical analyses were performed using analysis of variance (ANOVA), Student's t-test, Fisher's exact test and the Kruskal-Wallis test for non-parametric data. Normality of data was assessed using quantile quantile plots. Statistical significance was defined as $p < 0.05$.

Trial registration: not relevant.

RESULTS

During the eight-year study period, a total of 1,773 pa-

TABLE 1

Infection parameters in patients with middle ear or tonsillar infection.

	Patients, n	Age, years, median (range)	C-reactive protein, mg/l, mean (CI 95%)	White blood cell count, × 10^9/l, mean (CI 95%)	Absolute neutrophil count, × 10^9/l, mean (CI 95%)
Acute otitis media	46	11 (0-74)	80.7 (53.8-107.6)	13.7 (11.8-15.6)	9.6 (8.0-11.2)
Mastoidismus	75	1 (0-78)	83.3 (68.7-97.9)	15.3 (13.9-16.7)	9.5 (8.4-10.7)
p-value, acute otitis media vs mastoidismus	–	< 0.001	0.46	0.17	0.96
Acute mastoiditis	54	1 (0-77)	74.6 (55.5-93.6)	14.4 (12.7-16.1)	8.8 (7.4-10.2)
p-value, mastoidismus vs acute mastoiditis	–	0.27	0.54	0.42	0.41
p-value, acute otitis media vs acute mastoiditis	–	0.004	0.71	0.58	0.46
p-value, total	–	< 0.001[a]	0.84[b]	0.46[b]	0.72[b]
Acute tonsillitis	453	25 (1-89)	123.3 (115.0-131.5)	13.3 (12.9-13.7)	10.1 (9.7-10.5)
Peritonsillar abscess	1,066	21 (0-91)	113.8 (108.8-118.5)	14.3 (14.0-14.6)	11.0 (10.8-11.3)
p-value, acute tonsillitis vs peritonsillar abscess	–	< 0.001	0.10	< 0.001	< 0.001
Parapharyngeal abscess	45	47 (2-89)	195.8 (157.4-234.2)	16.2 (14.5-17.9)	13.1 (11.5-14.7)
p-value, peritonsillar abscess vs parapharyngeal abscess	–	< 0.001	< 0.001	0.01	< 0.01
Necrotizing fasciitis	34	51 (18-82)	297.6 (253.8-341.5)	15.1 (13.0-17.1)	12.8 (10.9-14.7)
p-value, parapharyngeal abscess vs necrotizing fasciitis	–	0.21	< 0.001	0.40	0.81
p-value, acute tonsillitis vs necrotizing fasciitis	–	< 0.001	< 0.001	0.08	0.02
p-value, total	–	< 0.001a	< 0.001b	< 0.001b	< 0.001b

CI = confidence interval.
a) The Kruskal-Wallis test was used for comparison.
b) ANOVA and Student's t-test were used for comparison.

TABLE 2

Percentage of patients with elevated C-reactive protein levels, white blood cell counts and absolute neutrophil counts and the association between these infection parameters.

	CRP		WBC		ANC		CRP + WBC[d]		CRP + ANC[d]		WBC + ANC[d]	
	elevated	p[a]	elevated	p[b]	elevated	p[c]	both elevated	1 elevated	both elevated	1 elevated	both elevated	1 elevated
Acute tonsillitis	97	< 0.001	78	0.94	77	< 0.001	76	23	76	23	74	7
Peritonsillar abscess	98	< 0.001	85	0.53	77	< 0.001	84	15	85	14	82	7
Parapharyngeal abscess	98	0.11	86	1.00	89	0.20	86	11	89	9	86	2
Necrotizing fasciitis	100	0.11	86	1.00	86	0.05	87	13	87	13	87	0
Acute otitis media	86	< 0.01	69	0.45	71	0.08	66	23	69	20	66	9
Mastoidismus	97	< 0.01	80	0.14	67	< 0.001	78	22	70	29	69	12
Acute mastoiditis	91	0.23	80	< 0.01	52	< 0.001	78	16	50	43	49	31

ANC = absolute neutrophil count (ref. value: ≤ 7 × 10^9/l); CRP = C-reactive protein level (ref. value: ≤ 8 mg/l); WBC = white blood cell count (ref. value: ≤ 10 × 10^9/l).
a) CRP vs WBC.
b) WBC vs ANC.
c) CRP vs ANC (Fisher's exact test).
d) The combined data of the infection markers are based on patients with at least two measured parameters.

tients (919 males) were included. The median age was 22 years (range 0-91 years). At admission, infection markers were measured in 1,666 patients (94%) and microbiological specimens were collected from 1,272 patients (72%), see **Table 1**.

Infections related to the middle ear were primarily observed in infants and young children (≤ 5 years) (37%, 79% and 76% of acute otitis media, mastoidismus and acute mastoiditis patients, respectively). Most acute tonsillitis and peritonsillar abscess patients were young adults (15-29 years) (50% and 60%, respectively), whereas parapharyngeal abscess and necrotizing fasciitis patients were typically middle-aged adults (30-59 years) (67% and 57%, respectively).

The mean values of the infection parameters in relation to middle ear and tonsillar infections are summarized in Table 1.

In the tonsil group, statistically significant differences in the levels of CRP ($p < 0.001$; ANOVA), WBC ($p < 0.001$) and ANC ($p < 0.001$) were found for patients diagnosed with acute tonsillitis, peritonsillar abscess, parapharyngeal abscess and necrotizing fasciitis, respectively. With two exceptions (CRP did not distinguish acute tonsillitis from peritonsillar abscess, and ANC did not distinguish between parapharyngeal abscess and necrotizing fasciitis), CRP and ANC levels correlated with severity of infection. However, the sensitivities and specificities of CRP (sensitivity 50-80%, specificity 44-63%), WBC (sensitivity 61-80%, specificity 47-54%) and ANC (sensitivity 60-77%, specificity 44-58%) in relation to differential diagnostics were low.

In the middle ear group, no statistically significant differences in the levels of CRP ($p = 0.84$; ANOVA), WBC ($p = 0.46$) and ANC ($p = 0.72$) were found between patients diagnosed with acute otitis media, mastoidismus and acute mastoiditis. Furthermore, no association between infection markers and severity of infection was established, see Table 1.

The number of CRP levels above the reference value was significantly higher than the corresponding number of WBC and ANC levels in most middle ear and tonsil subgroups, see **Table 2**.

The microbiological findings are summarized in **Table 3**. Group A *Streptococcus* was the most frequently isolated type of bacterium among acute tonsillitis patients (57%), followed by group C/G *Streptococcus* (18%) and *Fusobacterium necrophorum* (16%). In peritonsillar abscess patients, *F. necrophorum* (48%) was the primary isolate followed by group A *Streptococcus* (32%). Parapharyngeal abscess and necrotizing fasciitis patients were commonly infected with *Streptococcus viridans* (50% and 32%, respectively) and group A *Streptococcus* (23% and 44%, respectively). Pneumococci were the most frequently isolated bacteria among patients with acute otitis media, mastoidismus and acute mastoiditis (29%, 48% and 45%, respectively) followed by group A *Streptococcus* (33%, 24% and 18%, respectively).

Patients in the middle ear group who grew *Staphylococcus aureus* had lower levels of CRP, WBC and ANC than patients infected with group A *Streptococcus* or pneumococci. This strong trend only reached statistical significance for WBC in acute otitis media patients ($p = 0.008$; ANOVA). Furthermore, there was a trend towards lower levels of CRP, WBC and ANC in acute tonsillitis and peritonsillar abscess patients in whom *S. aureus* was isolated compared with patients infected with other bacteria. However, this trend did not reach statistical significance. Necrotizing fasciitis patients infected with *S. viridans* had significantly higher levels of CRP ($p = 0.01$; Student's t-test), WBC ($p = 0.02$) and ANC ($p =$

TABLE 3

Number of microbiological findings (%) in patients with infections of middle ear or tonsillar origin.

	Acute tonsillitis	Peritonsillar abscess	Parapharyngeal abscess	Necrotizing fasciitis	Acute otitis media	Mastoidismus	Acute mastoiditis
Bacteria							
Total cultures	150	893	44	30	38	67	50
No growth	42 (28)	258 (29)	3 (7)	4 (13)	14 (37)	20 (30)	12 (24)
Normal flora	47 (31)	164 (18)	19 (43)	1 (3)	3 (8)	1 (1)	1 (2)
Positive cultures	56	471	22	25	21	46	38
Aerobic							
Streptococcus, group A	32 (57)	152 (32)	5 (23)	11 (44)	7 (33)	11 (24)	7 (18)
Streptococcus, group C/G	10 (18)	30 (6)	1 (5)	1 (4)			
Pneumococcus	–	2 (0)	–	–	6 (29)	22 (48)	17 (45)
Streptococcus viridans	–	16 (3)	11 (50)	8 (32)			1 (3)
Staphylococcus aureus	1 (2)	10 (2)	1 (5)	3 (12)	3 (14)	2 (4)	3 (8)
Haemophilus influenzae	2 (4)	6 (1)	1 (5)	–	–	2 (4)	–
Pseudomonas aeruginosa	–	1 (0)	–	–	1 (5)	6 (13)	2 (5)
Other aerobes[a]	2 (4)	10 (2)	5 (23)	2 (8)	2 (14)	3 (7)	2 (5)
Anaerobic							
Fusobacterium necrophorum	9 (16)	224 (48)	3 (14)	–	–	–	1 (3)
Fusobacterium species	–	3 (1)	1 (5)	–	–	–	–
Other anaerobes[b]	–	16 (3)	2 (9)	–	–	–	4 (11)
Yeast	2 (4)	1 (0)	1 (5)		1 (5)		

a) *Streptococcus* group B, coagulase-negative staphylococci, *Branhamella catarrhalis*, G-staphylococci, coryneform bacteria, *Klebsiella oxytoca*, *Haemophilus haemolyticus*, *Neisseria* species.
b) *Enterobacteracae*, *Escherichia coli*, *Enterococcus faecalis*, *Peptostreptococcus*, *Prevotella*, *Bacteroides fragilis*.

TABLE 4

C-reactive protein, white blood cell count, and absolute neutrophil count level according to bacterial findings in patients with infections of middle ear or tonsillar origin. The values are mean (CI 95%).

	CRP, mg/l	WBC, × 10^9/l	ANC, × 10^9/l
Acute otitis media, mastoidismus and acute mastoiditis			
Streptococcus group A	99 (68-130)	13.5 (12.0-14.9)	9.0 (7.5-10.5)
Pneumoccocus	87 (67-107)	17.5 (15.6-19.4)	9.8 (7.9-11.6)
Staphylococcus aureus	56 (6-106)	12.6 (8.4-17.4)	7.2 (5.8-13.0)
Pseudomonas aeruginosa	48 (25-70)	12.6 (8.8-16.3)	7.2 (4.8-9.5)
Acute tonsillitis			
Streptococcus group A	140 (105-174)	13.7 (12.7-14.8)	10.3 (9.3-11.4)
Streptococcus group C/G	130 (78-182)	14.4 (11.4-17.3)	11.1 (8.0-14.2)
Fusobacterium necrophorum	159 (46-272)	14.4 (12.2-16.7)	11.6 (9.7-13.6)
Peritonsillar abscess			
Streptococcus group A	110 (98-123)	15.2 (14.6-15.8)	12.0 (11.4-12.6)
Streptococcus group C/G	121 (92-149)	15.0 (13.5-16.5)	11.7 (10.1-13.4)
Streptococcus viridans	121 (85-156)	13.8 (11.8-15.7)	10.6 (8.8-12.4)
Fusobacterium necrophorum	126 (115-137)	14.9 (14.4-15.4)	11.9 (11.4-12.4)
Staphylococcus aureus	109 (65-152)	12.4 (10.7-14.1)	9.2 (6.9-11.5)
Haemophilus influenzae	91 (61-120)	12.9 (10.1-15.7)	8.4 (5.5-11.2)
Parapharyngeal abscess			
Streptococcus group A	185 (75-296)	23.8 (15.7-31.8)	19.8 (11.5-28.0)
Streptococcus viridans	203 (120-286)	15.1 (11.4-18.8)	12.4 (8.9-15.8)
Necrotizing fasciitis			
Streptococcus viridans	411 (335-488)	18.8 (15.5-22.2)	16.1 (12.6-19.6)
Staphylococcus aureus	194 (188-200)	13.1 (10.8-15.3)	11.3 (7.7-14.9)
Streptococcus group A	259 (191-327)	12.5 (9.5-15.5)	10.4 (7.6-13.2)

ANC = absolute neutrophil counts; CI = confidence interval; CRP = C-reactive protein level; WBC = white blood cell counts.

0.01) than patients infected with group A *Streptococcus*. Furthermore, necrotizing fasciitis patients infected with *S. viridans* had significantly higher levels of CRP (p = 0.03) than patients infected with *S. aureus*, see **Table 4**.

DISCUSSION

In the present study, we observed a tendency towards higher levels of infection parameters in severe and extensive infections (parapharyngeal abscess and necrotizing fasciitis) than in less extensive tonsillar infections (acute tonsillitis and peritonsillar abscess). However, the infection parameters could not stand alone in the differential diagnosis-making as the sensitivities and specificities were low.

On suspicion of abscess formation related to middle ear and tonsillar infections, CRP, WBC and ANC measurements are commonly used supplements in the diagnostic process. Interestingly, despite abscess formation in patients with peritonsillar abscess, we found (non-significant) increased CRP levels in acute tonsillitis patients compared with peritonsillar abscess patients. An important element in the explanation of this finding may be that only patients with severe acute tonsillitis were admitted, while most peritonsillar abscess patients were hospitalized for surgical treatment. A second explanation could be that *F. necrophorum* is under-detected in acute tonsillitis patients as surface swabs are less sensitive in the detection of anaerobes than aerobic patho-

gens, and patients with tonsillar infections caused by *F. necrophorum* have higher CRP and ANC levels than patients infected with other pathogens [12, 13].

No association between infection parameters and severity of infection was found in the middle ear group, but acute otitis media patients tended to have higher CRP and ANC levels than acute mastoiditis patients. As for acute tonsillitis, an explanation could be that only severe acute otitis media cases were admitted, whereas all mastoidismus and acute mastoiditis patients were hospitalized for intravenous antibiotic treatment and possibly mastoidectomy. Previous studies have reported varying results concerning the usefulness of these infection parameters as a differential diagnostic tool. Stenfeldt & Hermansson found no differences in CRP levels between patients with mild and severe acute mastoiditis [3]. However, Heslop & Ovesen reported significantly higher CRP and WBC levels in patients with acute mastoiditis than in patients with acute otitis media [4].

None of the infection parameters were more useful than others. We found that 11-23% of patients in the tonsil group had either elevated CRP and normal WBC levels or elevated WBC and normal CRP levels. Similarly, 16-23% of patients in the middle ear group had one elevated infection parameter, while the others were within the normal range. Peltola et al found discrepancies between elevated CRP and WBC levels in 14% of 6,893 children with bacterial infection. They concluded that the combination of increased CRP and WBC levels was associated with a 50% risk of bacterial infection, whereas one elevated parameter correlated with severe bacterial infection [14]. Our results do not support these findings.

In another study of children with bacterial infection, Peltola et al reported increased CRP and/or WBC levels in 96% of patients infected with pneumococci compared with only 66% in patients with *S. aureus i*nfections. Furthermore, CRP and WBC levels were increased in pneumococcal infection, whereas infections with *S. aureus* only resulted in increased CRP levels [10]. In the present study, acute otitis media, mastoidismus and acute mastoiditis patients infected with *S. aureus* tended to have lower levels of infection parameters than patients infected with group A *Streptococcus* or pneumococci. However, only the difference in WBC levels reached statistical significance. Generally, CRP, WBC and ANC levels were lower in acute tonsillitis and peritonsillar abscess patients infected with *S. aureus* than in patients infected with other bacteria. As *S. aureus* is part of the normal tonsillar flora, growth of S. aureus in cultures from acute tonsillitis and peritonsillar abscess patients might illustrate an infection that has not completely eradicated the normal flora. I.e. patients with *S. aureus* may be less infected and the levels of infection markers correspondingly less elevated. However, no difference in symptom duration was found in acute tonsillitis and peritonsillar abscess patients infected with *S. aureus* compared with patients with other pathogens.

In conclusion, CRP and ANC levels were correlated with severity of tonsillar infection, whereas middle ear infections were not. However, these parameters had a low sensitivity and an even lower specificity why levels were not useful as differential diagnostic markers. Especially, it should be noted that CRP levels tended to be higher in acute tonsillitis patients than in peritonsillar abscess patients. Procalcitonin is a relatively new marker of bacterial infection, which has the advantage of a more rapid and specific induction [15-17]. Future studies of procalcitonin's potential as a differential diagnostic maker are warranted.

CORRESPONDENCE: *Ann Marlene Gram Christensen*, Øre-næse-halsafdelingen, Kirurgisk Afsnit, Aarhus Universitetshospital, Bygning 10, Nørrebrogade 44, 8000 Aarhus C, Denmark. E-mail: ann.mgc@hotmail.com.

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LITERATURE

1. Rusan M, Klug TE, Ovesen T. An overview of the microbiology of acute ear, nose and throat infections requiring hospitalisation. Eur J Clin Microbiol Infect Dis 2009;28:243-51.
2. Kaplan EL, Wannamaker LW. C-reactive protein in streptococcal pharyngitis. Pediatrics 1977;60:28-32.
3. Stenfeldt K, Hermansson A. Acute mastoiditis in southern Sweden: a study of occurrence and clinical course of acute mastoiditis before and after introduction of new treatment recommendations for AOM. Eur Arch Otorhinolaryngol 2010;267:1855-61.
4. Heslop A, Ovesen T. Severe acute middle ear infections: microbiology and treatment. Int J Pediatr Otorhinolaryngol 2006;70:1811-6.
5. Elsammak M, Hanna H, Ghazal A et al. Diagnostic value of serum procalcitonin and C-reactive protein in Egyptian children with streptococcal tonsillopharyngitis. Pediatric Infect Dis J 2006;25:174-5.
6. Wolf H, Ovesen T. Necrotizing fasciitis in the head and neck region. Ugeskr Læger 2008;170:2563-6.
7. Page C, Biet A, Zaatar R et al. Parapharyngeal abscess: diagnosis and treatment. Eur Arch Otorhinolaryngol 2008;265:681-6.
8. Brook I. Microbiology and management of peritonsillar, retropharyngeal, and parapharyngeal abscesses. J Oral Maxillofac Surg 2004;62:1545-50.
9. Kofteridis DP, Samonis G, Karatzanis AD et al. C-reactive protein and serum procalcitonin levels as markers of bacterial upper respiratory tract infections. Am Journal Infect Dis 2009;5:282-7.
10. Peltola V, Mertsola J, Ruuskanen O. Comparison of total white blood cell count and serum C-reactive protein levels in confirmed bacterial and viral infections. J Pediatr 2006;149:721-4.
11. Murray P, Baron E, Jorgensen J. Manual of clinical microbiology. Washington DC: ASM Press, 2007.
12. Klug TE, Henriksen JJ, Fuursted K et al. Significant pathogens in peritonsillar abscesses. Eur J Clin Microbiol Infect Dis 2011;30:619-27.
13. Ehlers Klug T, Rusan M, Fuursted K et al. Fusobacterium necrophorum: most prevalent pathogen in peritonsillar abscess in Denmark. Clin Infect Dis 2009;49:1467-72.
14. Peltola V, Toikka P, Irjala K et al. Discrepancy between total white blood cell counts and serum C-reactive protein levels in febrile children. Scand J Infect Dis 2007;39:560-5.
15. Carrol ED, Newland P, Riordan FA et al. Procalcitonin as a diagnostic marker of meningococcal disease in children presenting with fever and a rash. Arch Dis Child 2002;86:282-5.
16. Brunkhorst FM, Wegscheider K, Forycki ZF et al. Procalcitonin for early diagnosis and differentiation of SIRS, sepsis, severe sepsis, and septic shock. Intensive Care Med 2000;26 Suppl 2: S148-52.
17. Luzzani A, Polati E, Dorizzi R et al. Comparison of procalcitonin and C-reactive protein as markers of sepsis. Crit Care Med 2003;31:1737-41.