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The diagnostic value of serum procalcitonin, IL-10 and C-reactive protein in community acquired pneumonia and tuberculosis

W.-Y. NIU, Y.-G. WAN, M.-Y. LI, Z.-X. WU, L.-G. ZHANG, J.-X. WANG

Department of Tuberculosis, The First Affiliated Hospital of Xinxiang Medical University, Weihui, Henan Province, P.R. China

Abstract. – AIM: To explore the diagnostic value of serum procalcitonin (PCT), interleukin-10 (IL-10), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in community acquired pneumonia (CAP) and tuberculosis (PTB).

PATIENTS AND METHODS: 113 CAP cases patients and 78 PTB cases were enrolled from May 2011 to March 2012. Routine blood test, serum PCT, CRP, IL-10 and ESR of patients within 24 hours were analyzed retrospectively.

RESULTS: The serum concentrations of PCT, IL-10, CRP and ESR in CAP patients with CAP were 0.35±0.017 mg/mL, 0.095±0.004 mg/L, 59.80±5.12 mg/L and 35.00±4.81 mm/1h, respectively, significantly higher than patients with PTB ($p < 0.01$); According to the result of ROC curve analysis in CAP and PTB, the PTC area under ROC curve is 0.715 (95% CI 0.647-0.782), the sensitivity and specific degree of serum PTC were significant better than CRP and IL10 ($p < 0.05$). In tuberculosis sputum culture, the serum concentrations of IL-10 and ESR in TB positive group were 0.045±0.013 mg/L and 62.50±8.69 mm/1h, significantly higher than that of TB negative group ($p < 0.05$); whereas, the concentrations of serum PCT and CRP in TB positive and negative groups had no significant difference ($p > 0.05$).

CONCLUSIONS: The levels of serum PCT, IL-10, CRP and ESR in CAP patients are higher than that in PTB patients. Therefore, the serum PCT, IL10, CRP and ESR level is benefit to distinguish between CAP and PTB. This could provide a comprehensible evidence for both diagnosis and prognosis.

Key Words:
Serum procalcitonin, Interleukin-10, C-reactive protein, Community acquired pneumonia, Tuberculosis.

Introduction

Community acquired pneumonia (CAP) is defined as the pneumonia caused by the pathogen from community or any other place distinguished to hospital, leading to inflammatory in lung parenchyma[1]. Although the development of antibiotics make a dramatic progress of prevention and treatment, CAP is still a common public health disease spending huge medical resource. The diagnosis of CAP is according to patient's symptom, physical exam, routine blood test and many other radiologic imaging. However, it is still a difficult problem to make a precise CAP diagnosis[2]. Terms to the diagnosis of CAP, one of the critical issue is how to distinguish the CAP from tuberculosis (PTB). Simple acid fast staining and sputum tuberculomyces culture could not recognize them well, increasing the misdiagnosis rate. Procalcitonin (PCT) is a polypeptide containing 116 amino acids. Since 1993, PCT was well realized and considered to be a serum biomarker for general bacterial infections[3]. And then PCT is considered to be a one of the best probe for the severe inflammatory reaction.

IL-10 is produced from variant of cells. It has multiple biologic functions, and one of the major functions is to regulate the cell growth and cell differentiation. As a member of interleukin family, IL-10 plays an important role in immune regulation[4]. Many studies convinced that IL-10 suppresses the bacterial derived immune reaction by decreasing the secretion of TNF-α and IFN-γ, and widely prevent the spread of inflammatory.

C-reaction protein (CRP) is a major component of acute response protein. It takes part in immune reaction in many different pathologic processes of infection. Since the expression level of CRP reflects the severity of infection, it could be defined as a relative precise biomarker for the diagnosis of CAP[5].

However, it is still hard to make a distinction of the serum level of PTB, IL-10 and CRP between CAP and PTB[6]. The three biomarkers are all highly up-regulated in both of these two infection diseases. To make a clear cut conclusion for the clinical application of three biomarkers in CAP

Corresponding Author: Wenyi Niu, MD; e-mail: wenyiniu@yeah.net

Table I. The patient's general information and detection index ($\bar{x} \pm s$).

Items	CAP group	PTB group	χ^2/T	p
Case number	113	78		
Male/Female (case)	76/37	53/25	0.52	> 0.05
Age (year)	61.23 ± 18.95	59.58 ± 17.64	0.23	> 0.05
TB history [case (%)]	7(6.19)	4(5.13)	0.13	> 0.05
Antibiotic [case (%)]	46(40.71)	0(0.00)	11.56	> 0.01
PCT (ng/mL)	0.35 ± 0.017	0.06 ± 0.003	10.25	> 0.01
IL10 (ug/L)	0.095 ± 0.004	0.030 ± 0.002	15.35	> 0.01
CRP (mg/L)	59.80 ± 5.12	22.20 ± 3.23	9.84	> 0.01
ESR (mm/1h)	35.00 ± 4.81	31.50 ± 3.98	1.25	> 0.05

Note: χ^2/T represents the value of χ^2 or T.

and PTB, this retrospective study analyzes the serum samples of 113 CAP patients and 78 PTB patients. The serum level of PCT, IL-10 and CRP is deeply investigated and compared between CAP and PTB.

Patients and Methods

Clinical Data

113 CAP patients were collected for this study, including 76 male cases and 37 female cases with the average age 61.23±18.95 years. All these patients were chosen from our hospital since May 2011 to March 2012. Meanwhile, another 78 PTB patients were also collected from the same hospital, including 53 male cases and 25 female cases with the average age 59.58±17.64 years. 7 cases in CAP patients and 4 cases in PTB patients were noticed with TB history record.

Inclusion criteria: the diagnosis of CAP was followed "the Guideline of Diagnosis and Treatment for Community Acquired Pneumonia 2006 "published by National Medicine Association[7]. The diagnosis of PTB was followed "the Guideline of Diagnosis and Treatment for PTB 2011"[8].

Exclusion criteria: patients with non-infective pneumonia, HIV and highly suspected PTB; pregnant and breeding patients; and patients who is suffering severe inflammatory derived from severe trauma or surgical infection were be excluded from the CAP group. Whereas patients with HIV, non-small cell lung cancer and infection disease. There is significant difference of patient general information between the 113 CAP and 78 PTB patients, such as age, gentle, PTB history and so on (Table I). This study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of the First Affiliated Hospital of Xinxiang Medical University. Written informed consent was obtained from all participants.

Exam Protocols of Serum Samples

3-5 ml vein blood was drained from all the patients, and then blood samples were submitted to separate serum with 3200 r/min centrifuge at room temperature for 5 minutes. Serum was stored at –20°C[9]. Serum PCT test was performed by PCT *in vitro* diagnostic kits (chemiluminescent immunoassay, Beijing Huaketai Biotech Co, Beijing, China), and analyzed at Lumino portable luminometer (YZB/GEM0480-2005, Birkenfeld, Germany). The reference value was 0-0.15 ng/ml, the value over 0.15 ng/ml was defined as PCT positive[10]. IL-10 and CRP levels were tested by a two-step monoclonal competitive sandwich ELISA method and immune scatter turbidimetry (IST), respectively. The IST data was presenting to OlympusAU640 automatic biochemical analyzer, Tokyo, Japan. The reference value was 0-10 mg/l, the value over 10 mg/l was defined as CRP positive[11]. All the patients were required to take a sputum bacterial cultures. The pathogens exam of tracheal secretion was performed for the patients who were not able to collect sputum.

An automatic bacterial identification system and its drug sensitive check card were proved by VITEK® 2 Compact (BioMérieux, Marey l'Etoile France). The detail operation protocol follows the "National Guide to Clinical Laboratory Procedures".

Statistical Analysis

All the data were analyzed by SPSS16.0 software (SPSS Inc., Chicago, IL, USA). The normal distribution measurement data were present as mean ± SD (X±S), whereas the all the non-normal

distribution measurement data was present as median and quartile. All the enumeration data was present as frequency and percentage. The comparison of measurement and enumeration data was analyzed by *t*-test and chi-square test, respectively. Statistical significance was defined as $p < 0.05$.

Results

The General Information and Test Result

To distinguish the patients for CAP and PTB diagnosis, sputum bacterial culture was firstly performed. 42 cases in totally 113 CAP patients was found positive (37.17%). Meanwhile, 17 cases in totally 78 PTB patients showed positive (21.80%). The general information between these two groups had no significant difference.

To investigate the diagnosis values of PCT, IL-10 and CRP in CAP and PTB. The serum levels of these three factors were tested by individual method. The PCT, IL-10 and CRP levels in CAP patients were 0.35±0.017 ng/ml, 0.095±0.004 μg/l and 59.80±5.12 mg/l. On the other hand, the same measurements in PTB were 0.06±0.003 μg/ml, 0.030±0.002 μg/l and 22.20±3.23 mg/l. By comparing the serum levels of PCT, IL-10 and CRP, it showed that these values were significant higher in CAP patients ($p < 0.05$). Furthermore, there was little difference of the ESR values in both groups (Table I).

The Sensitivity and Specificity Exam of PCT, IL-10 and CRP in CAP and PTB Diagnosis

According to the ROC curve analysis, the area under the ROC curve of PCT was 0.715 (95% CI 0.647-0.782), the area of CRP was 0.641 (95% CI 0.636-0.771), the area of IL-10 was 0.583 (95% CI 0.507-0.812) and the area of ESR was 0.534 (95% CI 0.455-0.613). 95% CI was 95% confidence interval, 0.455-0.613 represented area under the curve.

Moreover, the sensitivity and the specificity of PCT were 76.0% and 70.1% when the truncated value of PCT was 0.090 μg/ml. And the sensitivity and the specificity of CRP were 82.0% and 60.3% when the truncated value of CRP was 15.15 mg/ml. These results showed that the sensitivity and the specificity of PCT were much better than the CRP, IL-10 and ESR. It indicated PCT was a potential biomarker in the diagnosis of CAP and PTB (Figure 1).

The serum Levels of PCT, IL-10 and CRP in the PTB Patients with Sputum Bacterial culture

According to the results of sputum bacterial culture, 17 patients was *Mycobacterium tuberculosis* positive in all the PTB patients. In TB positive group, the serum IL-10 and ESR were 0.045±0.013 μg/l and 62.50±8.69 mm/1h, respectively. Compared to the negative group (IL-10: 0.027±0.009

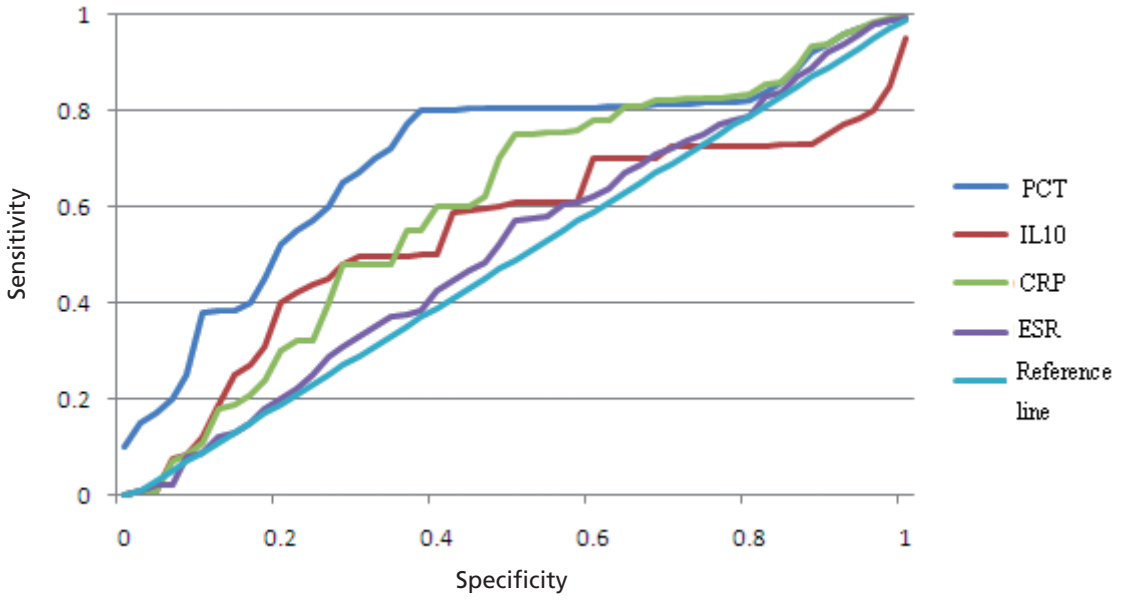

Figure 1. ROC curve of PCT, IL10, CRP and ESR in the diagnosis of CAP and PTB.

Table I. The serum level of PCT, IL-10 and CRP in the PTB patients with sputum bacterial culture [M (Q)].

Groups	Cases	PCT (ng/mL)	IL10 (ug/L)	CRP (mg/L)	ESR (mm/1h)
Positive group	17	0.06 ± 0.003	0.045 ± 0.013	22.50 ± 3.85	62.50 ± 8.69
Negative group	51	0.06 ± 0.003	0.027 ± 0.009	20.50 ± 2.85	30.00 ± 4.78
t		0.01	7.85	1.23	10.54
p		> 0.05	< 0.01	> 0.05	< 0.01

μg/l and ESR: 30.00 ± 4.78 mm/1h), the IL-10 and ESR were significant higher in positive groups ($p < 0.05$). However, the PCT and CRP level showed no difference ($p > 0.05$) (Table II).

Discussion

Low serum concentration of PCT is thought to be a good indicator in the antidiastole of CAP and PTB. However, its poor sensitivity and specificity impede the clinical application in the CAP diagnosis[12,13]. In this study we also show the similar evidence that PCT is not sufficient precise biomarker to distinguish these two diseases. The serum level of PCT, IL-10 and CRP in CAP patients were significant higher than the PTB patients, but unlike IL-10 and CRP, the PCT could not distinct the CAP and PTB.

The area under ROC curve may reflect the sensitivity and specificity of each factor. The result indicates that among the four factors we investigated, PCT showed its conspicuous advance in sensitivity and specificity. Ugajin et al[14] reported that the sensitivity (86.3%) and the specificity (60.3%) was noticed when the truncated value of PCT was 10 mg/l. There could some reasons leading the different result: (1) PCT has a short half-life time. The patients in this study has a local pneumonia but not widely infection, so the serum PCT did not show a dramatic high level[3,15]. (2) most of the patients in this study have received the antibiotic treatment, which might affect the test result. (3) the method we used for testing serum PCT is chemiluminescent immunoassay, which is different to the ELISA methods used in previous work[16].

Interestingly, the IL-10 and ESR levels in TB positive groups show noticeable higher than in TB negative groups. However, the PCT and CRP show no difference between the groups. It might due to the biologic activity mechanism of IL-10 and ESR. IL-10 regulates the inflammatory reactions via T cells and presents anti-inflammatory effect by inhibiting the overexpression of proinflammatory factor[17,18]. Moreover, ESR is linked to the activity of *Mycobacterium tuberculosis*[19]. All these findings imply that during the diagnosis of CAP, physicians may take a blood sample to test serum PCT, IL-10 and CRP to estimate the patient is CAP or not; and then IL-10 and ESR might help distinct the non-CAP patients is either PTB disease or non-PTB disease.

It still needs more detail research to find the golden standard for the diagnosis of CAP and PTB.

Conclusions

The serum levels of PCT, IL-10 and CRP in CAP patients are significant higher than the ones in PTB. PCT has limit value in PTB patients. To improve the precision of diagnosis and treatment, serum PCT, IL-10 and CRP are helpful factors that could be carefully examined and analyzed.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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