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Original Research Article

Combined diagnostic potential of multi-slice spiral CT and serum CRP levels in children with *Mycoplasma pneumonia* after azithromycin treatment

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Abstract

Purpose: *To investigate the combined diagnostic value of multi-slice spiral computerized tomography (MSCT) and serum C-reactive protein (CRP) levels in children with mycoplasma pneumonia (MPP) after azithromycin treatment.*
Methods: *Clinical data for 60 children with MPP who were treated in The First People's Hospital of Chenzhou, Chenzhou from February 2019 to February 2020, were retrospectively analyzed. All children were treated with azithromycin. Serum CRP levels were measured using immunoturbidimetric endpoint assay, while MSCT examination was done before and after treatment. This was a self-control clinical study in which the 60 patients served as their own controls. Thus, results obtained before treatment (control group, CG) were compared with those obtained after treatment (study group, EG). Within the same period, 60 healthy subjects were selected as the healthy group (HG), and were subjected to MSCT examination and serum CRP assay. The diagnostic results of CT were analyzed, and the responsiveness, selectivity, and positive and negative predictive values of the combination of MSCT and serum CRP levels were calculated.*
Results: *Pre-treatment serum CRP level was higher in CG than in EG and HG, and CRP level was higher in EG than in HG ($p < 0.001$). The MSCT imaging features of EG were significantly different from those of CG ($p < 0.05$). The probabilities of bronchial wall thickening, hilar and mediastinal lymphadenopathy and pleural effusion were significantly higher in CG than in EG ($p < 0.05$). The responsiveness, selectivity, and positive and negative predictive values of combination of MSCT and serum CRP in MPP children after azithromycin treatment were 70.0, 66.7, 67.7 and 69.0 %, respectively.*
Conclusion: *The combination of MSCT examination and serum CRP levels resulted in high diagnostic efficiency, and it may be useful for monitoring MPP in children after azithromycin treatment. Therefore, the combined procedure may reduce the burden on families of MPP children by enhancing efficiency of diagnosis of the disease.*

Keywords: *Multi-slice spiral CT (MSCT), C-reactive protein (CRP), Azithromycin, Mycoplasma pneumonia*

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INTRODUCTION

Mycoplasma pneumonia (MPP) is caused by mycoplasma infection [1]. Since the disease is sensitive to macrolide antibiotics, azithromycin has become the most frequently used drug in the clinical treatment of MPP, and most children recover after regular treatment, indicating good prognosis [2,3]. Due to the long course of the disease, it is extremely important to systematically monitor the disease progression in children after azithromycin treatment [4].

Several studies have shown that MPP has a latent period of 14 - 21 days in children [5, 6]. After the latent period, children present with varying degrees of pneumonia symptoms. Although some children experience serious symptoms, routine X-ray examination does not usually show any obvious abnormal signs [7]. This increases the difficulty in clinical monitoring. Recently, it was reported that MSCT clearly displayed anatomical features of lung lesions, and facilitated the identification of early MPP after systematic treatment [8]. In addition, inflammatory markers are important in the diagnosis of infectious diseases. In particular, CRP is highly useful in the identification of MPP [9]. At present, not much is known about the application of MSCT and serum CRP in the diagnosis of MPP in children after azithromycin treatment. Therefore, the present study was carried out to investigate the diagnostic value of combination of MSCT examination and serum CRP levels in MPP children after azithromycin treatment.

METHODS

Research plan

The present study was a retrospective research which was carried out to investigate the diagnostic potential of combination of MSCT and serum CRP levels in MPP children after azithromycin treatment.

Enrollment of patients

The data for 60 MPP children treated at *The First People's Hospital of Chenzhou* for one year were subjected to retrospective analysis. In addition, healthy subjects matched for age and gender with the MPP children, served as the healthy group.

Inclusion criteria

Patients in the following categories were included in the study: MPP children who were positive for *Mycoplasma* antibodies and met the diagnostic criteria of *Zhu Futang Practice of Pediatrics* [10]; MPP children with complete imaging and etiological data, MPP children aged over 6 months, and those who did not take blood products, hormone drugs and immunomodulators in the previous 6 months.

Exclusion criteria

The excluded MPP children were those with hearing disorders, language disorders and unclear consciousness; children who withdrew from treatment, and those who died, changed the treatment plans or could not be followed up; MPP children without complete clinical data, those with primary immunodeficiency, liver and kidney diseases, pulmonary tuberculosis and congenital heart disease; and children whose family members were unwilling to give permission for them to participate in the study.

The exclusion conditions for healthy children comprised hearing disorders, language disorders, unconsciousness, and low compliance or refusal to participate in the study.

General information

Sixty MPP patients were included in the present research. All subjects were treated with azithromycin, and serum levels of CRP were determined using immunoturbidimetric endpoint assay [Beckman original kits; NMPA (I) 20082401894], and MSCT examination was done before and after treatment. The results obtained before treatment were considered as data for control group (CG, n = 60), while those obtained after treatment were considered as data for study group (EG, n = 60). At the same period, 60 healthy subjects were selected as the healthy group (HG). Clinical and socio-demographic data were comparable amongst the groups ($p > 0.05$). The MPP children comprised 35 boys and 25 girls aged 0.5 - 7 years, with a mean age of 3.56 ± 0.89 years. There were 18 cases of severe lung injury and 42 cases of mild lung injury amongst the patients. The healthy subjects comprised 34 boys and 26 girls aged 0.5-8 years (mean age = 3.60 ± 0.80 years).

Ethical compliance

Approval for this research was received from the ethical authority of *The First People's Hospital of Chenzhou* (approval no. 20181222), and the study was executed in line with the guidelines of Declaration of Helsinki [11]. Signed written informed consents were obtained from the patients and/or guardians who were provided

information regarding the aim, importance and scope of the investigation, with a firm commitment not to disclose their identities.

Conditions for exiting from the research

Patients whose medical data were not subjected to analysis were MPP children who had severe and undesirable side reactions, those whose conditions became worse during the study, children with serious comorbidities or aggravated conditions, and children whose families opted to withdraw them from the study.

Treatments

The MPP children were treated with azithromycin (Suzhou Pharmaceutical Factory of Jiangsu Wuzhong Pharmaceutical Group Co.; NMPA approval no. H20010606) at a dose of 10 mg/kg body weight/day via intravenous infusion in 5 % glucose injection solution (Anqiu Lu'An Pharmaceutical Co. Ltd; NMPA approval no. H20123065). The concentration was 1g/L, and the intravenous infusion time was not less than 1 h. A 5-day treatment constituted one course. Two courses of treatment were used.

MSCT examination

Before and after treatment, the MPP children were examined using MSCT (Philips Brilliance 16-slice spiral CT instrument, NMPA (I) 20093300931). The patients were examined in the supine position, and were scanned from the tip to the bottom of the lungs, with tube voltage of the MSCT scanner set at 120 KV, tube current of 160 mA, scanning pitch of 0.875:1, and thickness and spacing of 5 mm. Thin-slice scanning was performed if necessary. If the children had special conditions, scanning was performed after oral administration of 3 % chloral hydrate (Shaanxi Panlong Pharmaceutical and Logistics Co. Ltd; NMPA approval No. H37022673). The images resulting from examination of the MPP children were reviewed by two senior radiologists and one senior respiratory physician who were not aware of the laboratory test results of the children. The radiologists and physician used three-dimensional reconstruction technology to evaluate the lesion sites and edge morphology, and independently analyzed the imaging features of the lesions.

Determination of serum CRP levels

Fasting venous blood (5 ml) was collected from each patient in the morning. The blood samples were centrifuged at 3000 rpm for 10 min to obtain sera. Immunoturbidimetric endpoint assay (Beckman original kits; NMPA (I) 20082401894) was used to determine serum CRP levels before and after treatment. The reference range in the kits was 0 – 8 mg/L.

Evaluation of parameters

Serum CRP levels

The serum CRP levels were compared amongst the groups.

MSCT diagnostic results for MPP children

The MSCT imaging features (large area of patchy shadow, mottling, increased lung markings, strip shadow and ground glass opacity) and other lung manifestations (bronchial wall thickening, hilar and mediastinal lymphadenopathy, cavity sign and pleural effusion) were compared before and after treatment.

Combined diagnostic efficacy of MSCT and serum CRP levels

These were computed as in Eqs 1 – 4.

$$SE = \frac{TP}{(TP+FN)} \times 100 \quad \ldots\ldots\ldots (1)$$

$$SP = \frac{TN}{(TN+FP)} \times 100 \quad \ldots\ldots\ldots (2)$$

$$PPV = \frac{TP}{TP+FP} \quad \ldots\ldots\ldots\ldots (3)$$

$$NPV = \frac{TN}{TN+FN} \quad \ldots\ldots\ldots\ldots (4)$$

where *SE* = sensitivity; *TP* = number of true positives; *FN* = number of false negatives; *SP* = specificity; *TN* = number of true negatives; *FP* = number of false positives; PPV = positive predictive value; NPV = negative predictive value.

Statistics

Data processing was done using SPSS 20.0, while graphics were done with GraphPad Prism 7. Counting and measured data were compared using χ^2 and Student's *t*-test. Statistical significance was assumed at $p < 0.05$.

RESULTS

Serum CRP levels

Serum CRP level was higher in CG than in EG and HG, with a higher CRP level in EG than in HG ($p < 0.001$), as presented in Figure 1.

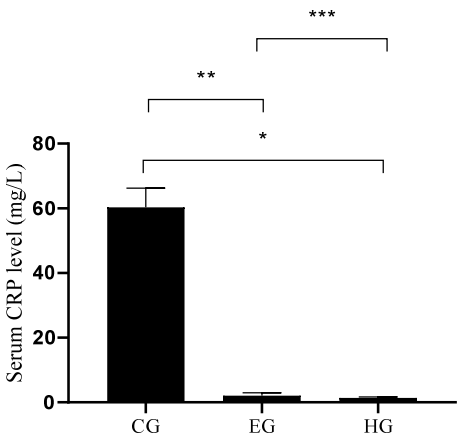

Figure 1: Serum CRP concentrations (mg/L). *P < 0.001, CRP level of CG vs CRP level of HG; **p < 0.001, CRP level of CG vs CRP level of EG; ***p < 0.001, CRP level of EG vs CRP level of HG

MSCT diagnostic results for MPP children

The MSCT imaging features of EG were markedly different from those of CG (p < 0.05). The probabilities of bronchial wall thickening, hilar and mediastinal lymphadenopathy and pleural effusion were markedly higher in CG than in EG (p < 0.05). These results are shown in Table 1 and Table 2.

Diagnostic efficiency of combined determination of MSCT and serum CRP levels

The responsiveness, selectivity, and positive and negative predictive values of combination of MSCT and serum CRP levels in MPP children after azithromycin treatment were 70.0, 66.7, 67.7 and 69.0 % respectively (Table 3 and Table 4).

Table 1: Analysis of MSCT imaging features of MPP children [n (%)]

Group	CG (n = 60)	EG (n = 60)	χ^2	*P*-value
Large area of patchy shadow	48 (80.0)	24 (40.0)	20.000	0.000
Mottling	35 (58.3)	20 (33.3)	7.552	0.006
Increased lung markings	18 (30.0)	8 (13.3)	4.910	0.027
Strip shadow	13 (21.7)	4 (6.7)	5.551	0.018
Ground glass opacity	12 (20.0)	4 (6.7)	4.615	0.032

Table 2: Analysis of other pulmonary manifestations in MPP children [n (%)]

Group	CG (n = 60)	EG (n = 60)	χ^2	*P*-value
Bronchial wall thickening	46 (76.7)	20 (33.3)	22.761	0.000
Hilar and mediastinal lymphadenopathy	10 (16.7)	2 (3.3)	5.926	0.015
Cavity sign	2 (3.3)	0 (0)	2.034	0.154
Pleural effusion	6 (10.0)	0 (0)	6.316	0.012

Table 3: Diagnostic results of combination of MSCT and serum CRP levels

Parameter		Pathology +	Pathology -	Total
MSCT	+	40	15	55
(before treatment)	-	20	45	65
CRP	+	45	18	63
(before treatment)	-	15	42	57
MSCT combined with CRP	+	58	4	62
(before treatment)	-	2	56	58
MSCT	+	24	24	48
(after treatment)	-	36	36	36
CRP	+	30	26	56
(after treatment)	-	30	34	64
MSCT combined with CRP	+	42	20	62
(after treatment)	-	18	40	58
Total	+	***60***	***60***	***120***

Table 4: Diagnostic efficacy of combination of MSCT and serum CRP levels

Group	**Sensitivity** (%)	**Specificity** (%)	**Positive predictive value** (%)	**Negative predictive value** (%)
Before treatment				
MSCT	66.7 (40/60)	75.0 (45/60)	72.7 (40/55)	69.2 (45/65)
CRP	75.0 (45/60)	70.0 (42/60)	71.4 (45/63)	73.7 (42/57)
CT combined with CRP	96.7 (58/60)	93.3 (56/60)	93.5 (58/62)	96.6 (56/58)
After treatment				
MSCT	40.0 (24/60)	60.0 (36/60)	50.0 (24/48)	50.0 (36/72)
CRP	50.0 (30/60)	56.7 (34/60)	53.6 (30/56)	53.1 (34/64)
CT combined with CRP	70.0 (42/60)	66.7 (40/60)	67.7 (42/62)	69.0 (40/58)

DISCUSSION

Mycoplasma pneumonia (MPP), a bacterium that causes pulmonary inflammatory disease in children, is sensitive to macrolide antibiotics. Clinical studies have shown that azithromycin, a second generation of macrolide antibiotics, is associated with high safety and effectiveness, and it has mild impacts on liver and kidney function [12]. In recent years, with continuous progress in the application of antibiotics in children, it has been found that azithromycin involves a relatively long course of treatment, thereby increasing the possibility of organ damage in children and delaying treatment [13].

Close examination of changes in disease condition in MPP children after azithromycin treatment, and enhancement of efficacy of diagnosis are key to ensuring good prognosis for the patients. At present, the major clinical disease monitoring methods involve serum marker assay and imaging examination [14]. Studies have shown that CRP is highly sensitive to infectious diseases [15]. Therefore, it was selected in this study as a serological indicator. During infectious diseases in children, the CRP level increases sharply and peaks within 1 - 2 days, with the peak value about 10 folds higher than the normal level. The present study showed that the serum CRP level of CG was increased, indicating that the children were in the mycoplasma infection period.

After systematic treatment with azithromycin, there was reduced infection in the children, and serum CRP concentrations in children whose infection was eliminated were reduced to normal levels within 7 days. Moreover, serum CRP levels of children whose infection was not completely eliminated were decreased by more than 50 %. Therefore, the CRP level in EG was significantly decreased, but it was still higher than that in HG because the children did not fully recover. This suggests that CRP may be useful in monitoring the dynamics of the disease in children, and it may provide an important basis for clinical judgment of presence of organ injury. In the study by Kutty *et al*, the sensitivity of CRP in the diagnosis of MPP was 72.9 %, but in the diagnosis of MPP after antibiotic treatment, the sensitivity was 66.7 % [16]. These values are close to the data obtained in this study. These results demonstrate that CRP has high diagnostic value in MPP children treated with antibiotics, and it is a cheap and convenient diagnostic method for pediatric patients.

With improvements in imaging technology, MSCT is of high advantage in the diagnosis of MPP with mild signs [17]. Research has revealed that this method is very effective for determination of pathological conditions such as bronchus inflammation and interstitial pneumonia, and it is highly sensitive to small pulmonary lesions associated with diagnosis of early MPP [18]. In the present study, MSCT examination of the lungs before treatment showed large areas of patchy shadow, mottling, ground glass opacity and thickened bronchial wall. After treatment, the density of lesion sites was decreased, with narrowed lesion range and decreased patch absorption. The CG group had bronchial wall thickening, hilar and mediastinal lymphadenopathy, and pleural effusion.

The diagnosis of MPP was enhanced by the combined use of MSCT examination and CRP levels. Following treatment, the sensitivity, specificity and positive and negative predictive values of combination of MSCT and serum CRP levels were 70.0, 66.7, 67.7 and 69.0 %, respectively, indicating that the combination of the two diagnostic methods may be effectively used to monitor the prognosis of children and provide a reliable basis for judging changes in progression of the disease.

Limitations of the study

It is important to note that this study did not classify the MPP children on the basis of prognosis. Assessment of diagnostic efficacy of the combination of MSCT and serum CRP in

MPP children treated with azithromycin on the basis of prognosis may increase its clinical reference value.

CONCLUSION

The combination of MSCT and serum CRP levels in monitoring MPP in children after azithromycin treatment results in high diagnostic efficiency. Therefore, the procedure may reduce the burden on families of MPP children by improving the efficiency of diagnosis of the disease.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. You Li and Ye Zhang conceived and designed the study, and drafted the manuscript. You Li, Hui Lou, Yang Cao and Xing Huang collected, analyzed and interpreted the experimental data. Hui Lou and Ye Zhang revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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