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ANALYSIS OF CORRELATIVE FACTORS OF MYCOPLASMA PNEUMONIAE PNEUMONIA COMPLICATED WITH CENTRAL NERVOUS SYSTEM DAMAGE IN CHILDREN

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Abstract:
Objective To investigate the related factors of mycoplasma pneumoniae pneumonia (MPP) associated with central nervous system(CNS) damage , and to provide evidence for its early diagnosis and treatment. Methods Children with mycoplasma pneumoniae who were hospitalized in the department of Pediatrics of our hospital from November 1, 2015 to July 31, 2019.were selected as the research objects, 113 cases in the group with no central nervous system damage of mycoplasma pneumoniae pneumonia (control group) and 24 cases in the group with central nervous system damage of mycoplasma pneumoniae pneumonia (observation group) were compared. Results There were significant differences in fever degree (℃), high MP antibody titer (≥1:160) and CRP between the two groups （P <0.05）. There were no statistically significant differences between the two groups in age, gender, delivery mode or feeding mode （P ＞0.05）.Conclusion elevated CRP may be an independent risk factor for MPP combined with central nervous system damage in children, while high MP titer may be a protective factor.
Key words: mycoplasma pneumoniae pneumonia; central nervous system damage; correlative factors; children.

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BACKGROUND:

Community-acquired upper and lower respiratory infections in school-age children are often triggered by mycoplasma pneumoniae (MP).But there is a growing recognition that younger children are also affected. Clinical manifestations range from asymptomatic to severe complex pneumonia, sometimes with extrapulmonary manifestations [1,2]。These lung exteriors are now present in 25% of MP infections and may affect almost all organs, including the skin, urogenital tract and digestive system, as well as the cardiovascular, hematopoietic, musculoskeletal and nervous systems [1,3,4]。One of the most common types of extrapulmonary diseases caused by MP is nervous system damage, which is also one of the most serious injuries.MP infection may be followed by a variety of neurological diseases, such as multiple neuronitis, aseptic meningitis, meningoencephalitis, late-onset myelitis, acute disseminated encephalomyelitis, striatal necrosis, acute cerebellar ataxia, and mycoplasma encephalitis, among which mycoplasma pneumoniae encephalitis has the highest incidence [5-7]。Its clinical manifestations are similar to viral encephalitis, lacking specificity, and the children lack the ability to express self-conscious symptoms. Their symptoms and signs are easy to be ignored by parents and doctors, resulting in the missing diagnosis of central nervous system damage. Therefore, the clinical data of 137 hospitalized children with mycoplasma pneumoniae pneumonia were retrospectively analyzed and reported as follows。

1 Data and methods

General data: Children with mycoplasma pneumoniae hospitalized in our hospital from November 1, 2015 to July 31, 2019.Were selected. There were 113 children in the MPP without central nervous system damage (control group), including 64 males and 49 females, aged from 1 month to 12 years and 9 months, with an average age of (3.28±2.778) years. There were 24 cases of MPP with central nervous system damage (observation group), including 12 males and 12 females, aged from 1 month to 6 years and 6months, with an average age of (2.91±2.122) years.

1.2 METHODS:

1.2.1 Method of case selection: MPP in both the observation group and the control group met the clinical diagnostic criteria of 《Zhu Fu Tang Textbook of Pediatrics》 [8] ,and excluding primary heart disease and other systemic diseases. Diagnostic criteria for MPP combined with CNS damage: However, there is currently no unified diagnostic criteria for damage to the CNS caused by MP infection, but diagnosis can be made according to the following diagnostic criteria: ①MP infection is associated with respiratory tract symptoms before and during the onset of MPP in children, and damages of other viscera may also occur. ②The clinical symptoms and body signs of the nervous system, such as consciousness disorder, headache, limb movement disorder, convulsion and drowsiness, were observed. ③The contents of chloride and carbohydrate in the CSF of the children were in the normal range, but the number of proteins and cells in the CSF was normal or slightly increased. ④Electroencephalogram (EEG) of the children showed symptoms of slow rhythm to different degrees. ⑤Mp-igm levels in blood or cerebrospinal fluid were positive. ⑥Infection of the central nervous system other than viral encephalitis in children. [9] ; Exclusion criteria: ① severe basic diseases (chronic leukemia, congenital heart disease, nephrotic syndrome, congenital immune deficiency, etc.); ②recent use of immunosuppressive agents or immunoglobulin; ③Repeated admissions within 3 months.

The study plan was approved by the Clinical Ethics Committee of the First Affiliated Hospital of Bengbu Medical College, and the parents or legal guardians of the children participating in the study agreed in writing and complied with all relevant ethical guidelines.

1.2.2 Laboratory testing: Fasting venous blood was extracted from the children in the next morning after admission.(Mycoplasma pneumoniae Antibody Diagnostic kit,FUJIREBIO INC):Serum MP-IgM antibody titer ≥ 1:80 passive agglutination method, and (or) (Respiratory tract nine joint detection kit, VIECELL): Mp-igm was positive by indirect immunofluorescence method; Venous blood 2ml was extracted from all the children and sent for testing, which was detected by automatic biochemical analyzer. Meanwhile, blood routine and C-reactive protein (CRP) tests were performed.

1.2.3 Statistical method: All the data were analyzed by SPSS 25.0 statistical software, and the count data were expressed as the number of cases (percentage), and χ^2 test was performed. Measurement data were represented by $x \pm s$ and tested by t or Z;$P < 0.05$ indicated that the difference was statistically significant.

2 RESULTS:

2.1 The relationship between CNS damage and age, gender, delivery mode and feeding mode: there was no statistical difference in the occurrence of CNS damage between the two groups with age, gender, delivery mode and feeding mode(P >0.05).See table 1.

2.2 Relationship between CNS damage and various factors: there were significant differences in CRP, fever degree (℃) and high MP antibody titer (≥1:160) between the two groups（P <0.05）,However, there was no significant difference in White blood cell count(WBC) , fever time (days), and poor spirit（P >0.05）.See table 2.

2.3 In the multivariate analysis, whether patients have MPP combined with CNS damage is taken as the dependent variable, while the significant variables in the univariate analysis, CRP, fever degree (℃) and high MP antibody titer (≥1:160) are taken as the independent variables. Multivariate logistic regression analysis is carried out, and stepwise regression method is adopted to screen the variables. The results showed that the variables CRP and high MP antibody titer (≥1:160)were statistically significant（P <0.05）,elevated CRP may be an independent risk factor for MPP combined with central nervous system damage in children, while high MP titer may be a protective factor. See table 3.

Table 1 Comparison of general data between control group and observation group

Group	N	Gender（Male /female）	Average age(years)	Delivery mode（Natural birth/Cesarean delivery）	Feeding mode（breastfeeding/Artificial feeding/Mixed feeding）
control group	113	64/49	3.28±2.778	60/53	64/28/21
observation group	24	12/12	2.91±2.122	17/7	13/6/5
χ2/F/Z		0.121	-0.289	2.530	0.075
P		0.728	0.773	0.112	0.963

Table 2 Comparison of related factors between control group and observation group

Factors	Observation group（n=24）	Control group（n=113）	χ^2/Z	P
fever time (days)	2.533±3.207	4.546±12.197	-0.820	-0.820
fever degree (℃)	39.15±1.134	38.46±1.077	-2.362	0.018
WBC（10^9G/L）	12.74±8.518	10.90±9.172	-1.062	0.288
CRP（mg/L）	25.91±38.031	14.84±31.171	-6.968	0.000
high MP antibody titer（≥1:160）	8	65	4.653	0.031
Poor spirit	10	26	3.557	0.059

Table 3 Multivariate Logistic regression analysis of children with MPP combined with CNS damage

Variable	B	SE	Wald	P	OR	95% CI
CRP	1.285	0.512	6.295	0.012	3.614	1.325-9.861
High MP antibody titer	-1.247	0.512	5.926	0.015	0.287	0.105-0.784
constant	-1.553	0.413	14.148	0.000		

Remark: Assignment of dependent variable:0=MPP without CNS damage 1=MPP with CNS damage
Independent variables are categorical variables fever degree：0=≤39 1=＞39, high MP antibody titer：0=≤1:80 1=＞1:80, WBC：0=≤10*10^9 1=＞10*10^9 CRP：0=≤6 1=＞6

3 DISCUSSION:

With the changes of respiratory etiology, MP has been increasing year by year in children's respiratory infections and has become one of the most common pathogens causing pneumonia in children and adolescents, causing rhinitis, bronchitis, bronchopneumonia, meningitis, myelitis and other diseases. Mycoplasma pneumoniae associated encephalitis is the most common extrapulmonary complication of Mycoplasma pneumoniae and one of the most important causes of childhood encephalitis[9].

At present, the pathogenesis of mycoplasma pneumoniae associated with CNS damage in children is still unclear. Through clinical research, the mechanism of CNS damage includes the following aspects:(1)Systemic spread of MP leads to direct infection and local tissue damage: MP infected with respiratory tract can be transferred to the central nervous system through the space between respiratory cells in the epithelium, causing direct structural and functional damage.(2) Immune-mediated injury:①Humoral immunity: the mechanism that multiple viscera organs such as heart, brain, lung, kidney, smooth muscle, etc is the same as the MP immune antigen, some MP ingredients with the host molecular mimicry between myelin is considered to be the pathological mechanism of immune mediated process, especially the adhesion and reduces glycolipids galactose brain glycosides C sample structures. ②Cellular immunity: the dynamic balance of CD4 and CD8 cells was broken, which aggravated the disease. Cytokines: The latest study found that il-6 and IL-8 were significantly increased in MP children, which confirmed the influence of MP on the immune function of the body.(3)Vascular damage and hypercoagulability: Immune-mediated vascular endothelial injury leads to vasculitis, followed by endovascular clotting and cerebral vascular thromboembolism, resulting in ischemic injury of the nervous system.(4)Neurotoxin effects: Although in vitro studies have confirmed that MP releases neurotoxin, this toxin has not been detected in children with MP infection [4, 10, 11] .

This study found that the central nervous system damage caused by MP infection was correlated with CRP and MP antibody titers. These results suggest that mp-infected children are prone to central nervous system damage when the above conditions occur. The two related factors (CRP and MP antibody titer) found in this study tend to the immune injury hypothesis, which provides a certain reference for the treatment of the central nervous system injury caused by MP infection. It also suggests that early diagnosis and treatment of MP infection is very important. Domestic studies have reported that CRP is significantly increased in MPP children with systemic inflammatory response. The higher the CRP level is, the more serious the disease is [12].The increased CRP level suggests an increased likelihood of extrapulmonary complications. The reason may be that CRP gradually increases in the body when the body is infected, which further leads to the accumulation of neutrophils in blood, and finally the body presents with complications [13].

MPP complicated with central nervous system damage, respiratory symptoms, with the exception of children with mild symptoms, often overlooked, some typical tend to lead to the difficulty of diagnosis, and condition with the onset of heavy, fast progress and clinical symptom complex and nonspecific characteristics, with other encephalopathy is more difficult to identify, should cause the pediatrician.

The prognosis of this disease is related to the age of onset, characteristics of onset, clinical manifestations and treatment. The younger the age, the earlier the onset, the more severe the performance and the later the treatment, the worse the prognosis. The prognosis of neurologic damage caused by MP infection is related to many factors. The main factors of poor prognosis include:(1)Onset of neurological

symptoms(2)Involving the brain stem, or accompanied by cerebral infarction, cerebral hemorrhage;(3)Chronic uncontrollable frequent convulsions and disturbance of consciousness;(4)Abnormal EEG performance over 4 weeks;(5)Head CT or MRI with significant changes [14] .

This study has some limitations. First, it has a limited number of patients, especially among infants and school-age people. In addition, the study included only children from Bengbu, China. Although extrapulmonary complications associated with mycoplasma pneumoniae infection have been reported in other parts of the world, these current findings may not necessarily be extrapolated to other countries without further research.

CONCLUSION:

This study suggests that when MPP infected children have low MP antibody titer, increased CRP and other factors, head MRI and EEG should be performed in a timely manner, so as to facilitate early treatment and minimize the occurrence of central nervous system damage.

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