

Diagnosis and analysis of different pathogenic features of intracranial infection in children based on cerebrospinal fluid.

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Abstract

Objective: To investigate the clinical features and distribution of cerebrospinal fluid (CSF) in five kinds of typical pathogenic conditions in order to improve the early diagnosis of intracranial infectious diseases in children.

Methods: A total of 161 pediatric patients with intracranial infection in our hospital from January 2010 to December were selected, and the cerebrospinal fluid examination results were statistical treatment to get valuable diagnostic cases, and its clinical manifestations were retrospective analysis and summary.

Results: In 138 cases valuable diagnosis, 37 cases of viral meningitis in children with lymphocyte reaction and transformed lymphocyte reaction, CSF changes in the light, 27.03% of the total number of patients with tuberculosis, 50 cases of tuberculosis meningitis, 76.1% cases of tuberculosis meningitis in children, 15 showed brain pressure, 100% CSF total number of CSF white cells in acute inflammatory phase and sub-acute inflammatory reaction.

Conclusion: Children with intracranial infection early clinical manifestations are not typical, intracranial infection in children with cerebrospinal fluid cytology visible abnormal changes, changes in different periods and different characteristics of pathogens and disease of CSF examination results of different pathogens caused by intracranial infection in children with intracranial infection diagnosis, the evolution of the disease, treatment and prognosis has important reference value.

Keywords: Intracranial infection, CSF, Meningitis.

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Introduction

Intracranial Infection, which is also called Central Nervous System Infection, is a severe infectious disease, whose common clinical manifestations include Viral Meningitis, Tubercular Meningitis (TBM), Purulent Meningitis, Cryptococcal Meningitis (CM), etc. The early clinical signs and symptoms resulting from the disease are usually obscure, and children, owing to age-specific pathogens, show a rather late intracranial hypertension, which leads to hindrances to the early diagnosis of intracranial infectious disease, and may cause frequent misdiagnoses and mistreatment, resulting in a relatively high rate of fatality and disability compared to other age groups [1]. Although for adult intracranial infectious patients, the intracranial hypertension shows early and could be detected in the initial stage of the disease, there still exist some obstacles for doctors making certain the illness progression as accurate as possible. In general, infections of the central nervous system will lead to meningeal irritation and anomalous changes in the cerebrospinal fluid (CSF). With the sophistication of cytological examination in recent years, the technique of cytological examination of CSF is being extensively used in the clinical diagnosis of infections of the central nervous system, and becomes an important monitoring tool for diagnosis, treatment, and etiological analysis of the

intracranial infectious disease [2]. Therefore, studying the application of cytological examination of CSF in children cases with different pathogens has great practical significance.

Material and Methods

General data

In order to establish the application of cytological examination of CSF in diagnosing the pathogenic characteristics of children's intracranial infections, 161 pediatric patients are selected for a retrospective Analysis. The patients had been treated for intracranial infection in Tangshan Women and Children's Hospital of Hebei, P.R. China from January 2010 to December 2014. Among them, there are 110 males and 51 females with a male/female ratio of 2.2: 1. There are 49 Viral Meningitis patients, approximately accounting for 30.43%, including 33 males and 16 females, clinically characterized by pyrexia and different levels of disturbance of consciousness, with symptoms of intracranial hypertension and convulsion, 7 exhibiting meningeal irritation. There are 58 Tubercular Meningitis cases (approximately 36.02%), including 40 males and 18 females. They show pyrexia in the early phase and disturbance of consciousness, intracranial hypertension, convulsion, and meningeal irritation in the late phase. There

are 31 Purulent Meningitis patients (approximately 19.25%), including 22 males and 9 females, clinically showing pyrexia, intracranial hypertension, disturbance of consciousness, and meningeal irritation. 15 Cryptococcal Meningitis patients are researched, including 9 males and 6 females, symptoms mainly covering systematic infections like pyrexia, vomiting, and meningeal irritation. A portion of the subjects shows increased intracranial pressure and focal symptom.

Experimental equipment and method

All the subjects are subjected to a lumbar puncture for cytological examination of the CSF and blood routine examination. Specifically, the tests include routine tests, biochemical tests and pathogenic tests of the CSF.

Laboratory equipment includes Sheet Glass Centrifugal FCS-III (Made by Themo Shan don), MCDS-2011 Cell Diagnosis System, Blood Cell Counting Plate and optical microscopes, complete with Wright-Giemsa staining solution.

The first step is to extract 0.1-0.5 ml of the CSF of a subject into the specimen chamber and centrifugate it for 5 min at 1000 rpm in order to prepare the CSF smear. Next, dry the smear and dye it with the Wright-Giemsa staining solution for 10 minutes, wash it, dry it again and finally display the cells on the screen of the MCDS-2011 Cell Diagnosis System for cytological classification and to print out the report.

Statistical analysis

Process the data statistically, and examine χ^2 , which is statistically significant when $P < 0.05$. The detection rate of cell number in the CSF is calculated statistically, and shows that collection of cells is successful in all 161 patients, and various numbers of well lined-up cells are visible in the cerebrospinal fluid smear. Opinions of clinical significance can be given

according to the idiocratic cytological reactions in the smear, otherwise the test results can be regarded as clinically insignificant. The total number of clinically meaningful cases of the 161 subjects is 138 and the statistical results are shown in Table 1.

Table 1. Results of the cytological examination of 161 subjects [n (%)].

Diseases	n	Significant	Insignificant	P
Viral Meningitis	49	37 (75.5%)	12 (24.5%)	<0.01
Tubercular Meningitis	58	50 (86.2%)	8 (13.8%)	<0.01
Purulent Meningitis	31	28 (90.3%)	3 (9.7%)	<0.01
Cryptococcal Meningitis	15	15 (100%)	0 (0%)	<0.01
Encephalopyosis	8	8 (100%)	0 (0%)	<0.01

In the cytological examination of the three most common children intracranial infectious pathogens, i.e. Viral Meningitis, Tubercular Meningitis, Purulent Meningitis, Purulent Meningitis accounts for the highest clinical value, followed by Tubercular Meningitis and Viral Meningitis.

Result

Tables 2 and 3 show the test results and white blood cell (WBC) count in 138 children with intracranial infections, who had been subjected to lumbar puncture for CSF checking a week after the onset of their disease. The criteria for lumbar puncture CSF white blood cells are: CSF (0-5) $\times 10^6/L$ indicates a normal level of WBC; CSF (5~50) $\times 10^6/L$ indicates a slight elevation of WBC; CSF (51~200) $\times 10^6/L$ indicates a medium level of elevation of WBC; and CSF (200~ $+\infty$) $\times 10^6/L$ indicates a drastic elevation of WBC.

Table 2. Lumbar puncture examination results of the CSF of subjects a week after the onset of the disease.

	Cases	IICP		WBC Elevation		Protein Elevation		Sugar Level		Decrease of Chloride Level	
Viral Meningitis	37	28	75.6%	10	27.03%	24	64.86%	0	0.00%	5	13.51%
Tubercular Meningitis	50	38	76.1%	50	100%	43	85.7%	30	60%	43	85%
Purulent Meningitis	28	22	80%	28	100%	22	80%	21	75%	15	54%
Cryptococcal Meningitis	15	13	86.7%	15	100%	13	86.7%	12	80%	11	73.3%
Encephalopyosis	8	0	0	3	37.5%	3	37.5%	0	0	3	37.5%

Table 3. CSF white blood cell count and constituents proportion (%).

Pathogenic Features	Cases	White Blood Cell Count ($\times 10^6/L$) (case/ratio)								White Blood Cell Constituents (case/raio)					
		0-5		5-50		51-200		>200		mono.>0.5		neutr.>0.5		normal	
Viral Meningitis	37	27	0.73	9	0.9	1	0.1	0	0	31	0.84	3	0.09	2	0.07
Tubercular Meningitis	50	0	0	3	0.06	35	0.7	12	0.24	43	0.86	5	0.10	2	0.04

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Purulent Meningitis	28	0	0	2	0.08	8	0.29	18	0.63	1	0.04	27	0.96	0	0
Cryptococcal Meningitis	15	0	0	2	0.13	11	0.74	2	0.13	12	0.8	3	0.2	0	0
Encephalopathy	8	5	0.63	2	0.67	1	0.33	0	0	2	0.25	6	0.75	0	0

In the subjects of the five types of intracranial infections, 37 have Viral Meningitis, and 75.6% of them shows increased intracranial pressure (IICP), 27.03% show elevation in the WBC with one child showing medium level elevation in WBC. In the CSF results, 8 (80%) exhibit CSF cytological reactions, mainly involving the lymphocytes, and 2 (20%) cases mainly involving monocytes. There's also some degree of decrease in the chloride level, with sugar at normal level. In the 50 cases of Tubercular Meningitis, the cerebrospinal fluid is clear in appearance, 76.1% shows IICP, 100% shows elevation in WBC, including 70% of medium level elevation. Cytological examination of CSF and WBC show that the white blood cells mainly contains neutrophil granulocytes in the early phases, and lymphocytes in the late phases, both cells coexisting in the CSF. There's a decrease of sugar and chloride level to 60% and 85% respectively. In the 28 cases of Purulent Meningitis, there is a drastic elevation of CSF white blood cells in 63% of the subjects, with 80% showing IICP, and 80% showing turbid appearance. The main content is neutrophil granulocytes, with 50% of the specimens containing 96% of the neutrophil granulocytes. Sugar and chloride decrease to 75% and 54% respectively. In the 15 cases of Cryptococcal Meningitis, 86.7% show IICP, 100% of CSF white blood cells counts elevates, with 87% showing slight and medium level increase. The main content of the CSF white blood cells is the monocytes, at a level of approximately 80%. Chloride and sugar levels decrease to 80% and 73.3% respectively. The elevation of white blood cells in the CSF is also seen in the 8 cases of Encephalopathy. The percentage is 37.5%, and the elevation level is slight and medium. The CSF white blood cells are mainly composed of the neutrophil granulocytes, with 50% of the specimens containing 75% of the neutrophil granulocytes. No decrease of sugar has been found, and the chloride level decreases to 37.5%.

Discussion

The basic principle of cytological examination is, through the dynamic observation of the CSF cells in the cell harvester, to study changes in inflammatory cells and immunologically competent cells in relation to each other, judge the effects of clinical treatment and provide references for monitoring and evaluation. Compared with the routine examination of CSF, the cytological examination may contribute to the early conformation of the pathogens of infectious diseases in that, through more detailed classification and morphological observation, the cytological examination can more easily present the pathological changes caused by immunologically competent cells and phagocytes.

As the infection of the Central Nervous System, Children's intracranial infection may have many pathogenic

manifestations, such as intracranial hypertension, meningeal irritation, intracranial nerve damages which lead to various levels of disturbance of consciousness. Classification and recognition of normal and abnormal cells in the cerebrospinal fluid can be done through the analysis of the cytological reactions in the CSF smears, and judgment of the pathogens of intracranial infections can be made according to the result. Though causes of the intracranial infection vary, the development of cytological reactions can be divided into three stages, namely the Acute Exudative Inflammation Period, the Subacute Proliferation Period and the Convalescent Period. Intracranial infections caused by different pathogens shows different durations and characteristics in different stages [3].

Cytological reactions in the CSF of Children afflicted with viral meningitis features lymphocyte reaction and transformed lymphocyte reaction, and a special form of activated lymphocytes-encephaloid lymphocytes appear during the Acute Exudative Inflammation Period. Although a certain number of neutrophil granulocytes appear, they won't last long. The lymphocytes exhibit encephaloid, petaloid, distortion, and folding on the smears due to damages on the nuclei by the virus [4-6]. Some monocytes or activated monocytes will appear in the Convalescent Period.

Tubercular Meningitis is characterized by the coexistence of transformed lymphocyte reaction and lymphocyte reaction, and in the Subacute Proliferation Period, the neutrophil granulocytes, monocytes, and lymphoid cells coexist and are of similar proportion. In the smear, the lymphocytes are of different sizes and forms, coupled with phlogocytes at in the same period. It is difficult to distinguish Tubercular Meningitis and Purulent Meningitis in the Acute Exudative Inflammation Period and the Subacute Proliferation Period. However, the elevation of intracranial pressure and white blood cell count in Purulent Meningitis are both higher than that in Tubercular Meningitis. Take white blood cell count for example, the number of white blood cells account for over $1000 \times 10^6/L$ in Purulent Meningitis [7].

In its acute exudative inflammation period, Purulent Meningitis is characterized by neutrophil reactions, with the neutrophil granulocytes amounting to 90% of the white blood cells, and clinically 50% of the afflicted children can be diagnosed of the pathogenic bacteria. In the Subacute Proliferation Period, the inflammation may flare up or enter the chronic stage to be further traced and observed through the cytological examinations of the CSF. The aggressiveness and destructiveness of the bacteria gives the Purulent Meningitis its specificity in that the white blood cells may count as much as thousand or even tens of thousands [8-13]. With the development of the disease, the number of the neutrophil granulocytes drastically decreases, and meanwhile the

mononuclear phagocytes gradually increase, which is particularly evident in the cytological examination of the CSF of new-born babies who have the intracranial infections.

Cryptococcal Meningitis is clinically similar to Tubercular Meningitis so that misdiagnoses often occur in practice. At present, the most common clinical diagnosis uses the cerebrospinal fluid or the etiological examination of the brain tissue for the cryptococci, by means of, for instance, Indian ink staining [14,15]. The main constituent of the cerebrospinal fluid of most Cryptococcal Meningitis patients is monocytes. The decrease of the chloride is relatively indistinct. The first cytological examination of afflicted children shows mixed reactions, with 71% spotting cryptococci through cytoscopy. Compared with Non-Cryptococcal Meningitis patients, the first routine examination and cytological examination of the cerebrospinal fluid of Cryptococcal Meningitis patients show some degree of specificity.

In conclusion, the clinical manifestations of children's intracranial infections which are caused by different pathogens are atypical in the early phase of infection, but different pathogens show different features in the different phases of infection and reaction, and cause each indicator to be somewhat abnormal. The cytological examination of CSF provides a clinical reference for the pathogenic diagnosis of children's intracranial infections and elaboration of the time of onset and the mechanism of immune reactions.

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