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CSF leukocyte, polykaryocyte, protein and glucose: Their cut-offs of judging whether post-neurosurgical bacterial meningitis has been cured

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ABSTRACT

Object: This paper is aimed to explore a reasonable guideline for distinguishing whether post-neurosurgical bacterial meningitis has completely been cured, so as to avoid the deficient or excessive treatment for post-neurosurgical bacterial meningitis.

Patients and methods: We conducted a retrospective analysis of 46 patients who attended General Hospital of Chinese People's Armed Police Force in Beijing, China, from January 1, 2014 to April 30, 2016. The CSF leukocyte, polykaryocyte, protein and glucose had been tested when their antibiotic treatments were empirically stopped. Between the non-relapse and relapse groups, Wilcoxon Rank Sum test was used to compare the differences of CSF leukocyte and polykaryocyte, and *t*-test was applied to contrast the distinctions of CSF protein and glucose, then, the thresholds of significant items were estimated by ROC curve.

Results: The CSF leukocyte counts in non-relapse group are 23.72 ± 14.12/mm^3, which are statistically less than the relapse group's (47.00 ± 1.00/mm^3, P = 0.014), so does the CSF polykaryocyte counts (1.74 ± 4.84/mm^3 &4.67 ± 1.15/mm^3, P = 0.012). Between the two groups, the AUCs of leucocyte and polykaryocyte are 0.926 (95% CI = 0.845–1.0, P = 0.014) and 0.884 (95%CI = 0.786–0.982, P = 0.028), respectively. Their critical values are 44/mm^3 (sensitivity = 1, specificity = 0.907) and 3/mm^3 (sensitivity = 1, specificity = 0.837). Conversely, CSF protein and glucose have no statistic differences between the two groups.

Conclusion: Both CSF leukocyte and polykaryocyte can satisfactorily indicate whether the post-neurosurgical bacterial meningitis has completely been cured, 0–44/mm^3 is recommended as the reference range of CSF leukocyte, and the CSF polykaryocyte' s is 0–3/mm^3.

1. Introduction

Post-neurosurgical bacterialmeningitis(PNBM) is a lethal complication after neurosurgery [1,2], Erdem's team reported that its fatality rate was approximate 40.8% [3]. CSF leukocyte, polykaryocyte, protein and glucose are generally used to diagnose the PNBM, and their normal reference ranges are subjectively regarded as a guideline to determine whether PNBM has already been cured. However, in clinical practice, it is true that PNBM has not recur among most patients although their CSF leukocyte, polykaryocyte, protein and glucose are still slightly abnormal when anti-infection treatment was stopped. Therefore, it is irrational to regard their normal reference values as an inflexible guideline to decide when to end anti-infection treatment for such patients.

This study is aimed to build a more scientific and reasonable criterion for judging whether PNBM has been cured. Few papers have been engaged in this work, so, it is an innovative goal for this one to explore such a guideline, which will help neurosurgeons to catch the right time to stop antibiotic treatment, so as to avoid the deficient or excessive treatment for PNBM.

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2. Patients and methods

2.1. Study location and population

The study was conducted at the General Hospital of Chinese People's Armed Police Force which is a grade iii-A hospital in Beijing. Its Department of Neurotrauma is a major neurosurgery center in Beijing and good at the treatment of PNBM. Department records of 51 patients, who were diagnosed as PNBM and successfully cured from January 1, 2014 to April 30, 2016, were reviewed, five patients were excluded because their data sheets were not complete, and 46 patients were up to inclusion criteria.

2.2. Case definition

Definition of meningitis and PNBM relapse: The definition must meet at least one of the followings: either 1) positive organism culture from CSF or 2) patient has one of the following signs or symptoms with no other recognized cause: fever (> 38.5℃),headache, meningeal signs and at least one of the followings: a. Increased white cell count(> 100/mm^3), elevated protein, and/or decreased glucose level in CSF. b. Organism was seen on Gram's stain of CSF.

2.2.1. Inclusion criteria

1) diagnosis of PNBM within one week after neurosurgery; 2) clinically healed patients whose anti-infection treatment for bacterial meningitis were empirically stopped by their doctors in charge; 3) complete data sheet; 4) age ≥16 years.

2.2.2. Exclusion criteria

1) diabetic patients who were in poor control of blood glucose;2) patients with other infectious diseases causing fever; 3) Patients with Ventriculoperitoneal drainage; 4) certain badly medical conditions, such as serious heart, lung, kidney, liver, blood or metabolic diseases, or congenital immunodeficiency syndrome.

2.3. Clinical procedures

Lumbar punctures were performed as soon as postoperative patients had a fever(> 38.5 ℃) and meningeal irritation. CSF samples were collected into sterile polystyrene tubes and submitted for analyses including CSF leukocyte, polykaryocyte, protein, glucose, bacterial culture and smear. And we corrected Hemorrhagic CSF by RBC to WBC ratio of 400 to 1. Initially, patients, conforming to the definition of meningitis, received an empirical regimen of vancomycin. Subsequently, their antibiotic agents were adjusted according to the results of drug sensitive tests or treatment effect. The CSF leukocyte, polykaryocyte, protein and glucose were routinely reviewed every 1–3 days, and were also tested when their antibiotic treatments were empirically stopped. Then, their doctors carried out telephone follow-up and recorded the results one month later.

2.4. Statistical methods

Statistical analyses were performed with SPSS18.0 for Windows. The Single Sample Kolmogorov Smirnov test was used to verify whether all measurement data conformed to normal distribution. Measurement data with normal distribution was analyzed by *t*-test, others with abnormal distribution was compared by Wilcoxon Rank Sum test, and categorical variables were evaluated by Chi-square test. The Receiver Operating Characteristic (ROC) curve was used to evaluate the clinical usefulness of items with statistical significance between relapse and non-relapse groups and determine their cutoffs. Two-sided tests were used and P values ≤ 0.05 were considered statistically significant.

3. Results

Among the 46 patients who were up to inclusion criteria, 29 patients were male and 17 were female. Their ages ranged from 17 to 68 years (average = 46.12 ± 14.17 years). Cultures of CSF were carried among this set of patients, the results were positive in 11 (23.9%) cases including 3 cases with the pathogen of gram-positive bacterium and 8 cases with the pathogen of gram-negative bacterium (acinetobacter baumannii in 4 cases). When antibiotic treatments were stopped, all patients' temperature keeps normal and their meningeal irritation is negative, but CSF leukocyte counts > 10/mm^3 was observed in 39 cases, and CSF polykaryocyte counts > 5/mm^3 was observed in 5 cases. At the same time, CSF protein concentration > 0.45 g/L was observed in 32 cases, and CSF glucose < 2.80 mmol/L was observed in 23 cases.

Of these 46 cases, 3 (6.5%) had a relapse of PNBM and 43 (93.5%) had not. The CSF leukocyte counts are 23.72 ± 14.12/mm^3 in the non-relapse group and 47.00 ± 1.00/mm^3 in the relapse group. The CSF polykaryocyte counts are 1.74 ± 4.84/mm^3 in the non-relapse group and 4.67 ± 1.15/mm^3 in the relapse group. The concentration of CSF protein is 0.95 ± 0.80 g/L in the non-relapse group and 0.48 ± 0.39 g/L in the relapse group. The concentration of CSF glucose is 2.82 ± 0.52 mmol/L in the non-relapse group and 3.44 ± 0.60 mmol/L in the relapse group. Comparison between the two groups showed that there was no significant differences in the CSF protein and glucose concentrations (P = 0.320, 0.054 respectively). However, the counts of CSF leukocyte and polykaryocyte in non-relapse group were less than the relapse group's (P = 0.014, 0.012 respectively) (Fig. 1). Between the two groups, the AUC of leucocyte is 0.926 (95% CI = 0.845–1.0, P = 0.014) with a critical value of 44/mm^3 (sensitivity = 1, specificity = 0.907), and the AUC of polykaryocyte is 0.884 (95% CI = 0.786–0.982, P = 0.028) with a critical values of 3/mm^3 (sensitivity = 1, specificity = 0.837) (Fig. 2). The differences of age and sex were not statistically significant (P = 0.545, 0.331 respectively).

4. Discussion

PNBM often happens from the third day to the seventh day after neurosurgery, with the incidence of 0.3%–8.9% [4]. There is a hallmark event that the Blood-Brain Barrier (BBB) is broken down because of pathogen derived toxins and host over-expressed inflammatory factors [4–7]. BBB is the structure foundation for the central nervous system to maintain its internal environment stable [8]. It can prevent almost all kinds of cells permeating from the blood into subarachnoid space [9,10], and block almost all other materials out of brain except for the small molecules and lipophilic materials [9,11]. But, in the process of PNBM, there are two related but distinct types of BBB dysfunction [12]: (1) massive cellular infiltration across the BBB and (2) increased permeability.

4.1. The CSF leukocyte count

In the early stage of PNBM, there is a rapid influx of leukocytes from the blood into the subarachnoid space to form the defense line against pathogenic bacteria [13]. At the same time, leukocyte apoptosis, the primary removal method of leukocytes, is delayed in order that leukocytes can keep efficient at combating bacteria in the inflammatory environment for long enough [8,14]. So, CSF leukocytes massively increase in this stage. Some papers have reported that both LPS and inflammatory cytokines can enhance leukocyte `infiltration by a likely way of facilitating leukocytes adherence to vascular endothelial cells [9–11]. And leukocyte lifespan can be prolonged because of increased stability of Mcl-1 and XIAP proteins [15,16] and low oxygen tension in the infection site [17,18].

In the recovery phase, on account of the elimination of these factors, CSF leukocytes decrease. However, it does not reach the normal