Clinical and Immunological Indicators of the Oral Cavity in Children with Acute Herpetic Stomatitis

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Annotation: Clinical and immunological indicators of the oral cavity in children with acute herpetic stomatitis.

This review aims to investigate the clinical and immunological aspects of acute herpetic stomatitis in children to improve diagnosis, prognosis, and treatment of the disease.

Keywords: Acure herpetic stomatitis, simplex virus, immune system, immunoglobulins.

Introduction

Acute herpetic stomatitis (AHS) is one of the most common viral diseases of the oral cavity in children, caused by a primary infection with the herpes simplex virus (HSV) type 1. This disease typically develops in children aged 6 months to 5 years, which is related to the immaturity of their immune system and their high susceptibility to viral infections. AHS is characterized by inflammation of the oral mucosa, formation of painful erosions and ulcers, which often lead to a significant deterioration in the child's overall condition, difficulty eating and drinking, and general discomfort.

Etiologically, herpes simplex virus is an alpha-herpesvirus that, after the primary infection, can remain in the human body in a latent state. During periods of weakened immunity or under the influence of other factors, the virus can reactivate, causing recurrent herpes infections. However, during primary infection, the virus causes an acute clinical picture, particularly in children with an undeveloped specific immune response.

The clinical manifestations of AHS can vary significantly depending on the child's age, immune status, and the presence of comorbid conditions. The most typical symptoms include acute onset with fever, painful ulcers on the oral mucosa, gum hyperemia, and enlarged regional lymph nodes. Sometimes, the disease may be accompanied by intoxication syndrome, further worsening the patient's condition.

Both clinical and immunological indicators play an important role in diagnosing and predicting the course of the disease. The immune response to the herpes simplex virus involves both innate and adaptive defense mechanisms, which can serve as markers of disease severity and prognosis. For instance, disruptions in T-cell function, insufficient production of interferons, or altered levels of immunoglobulins can indicate a more severe course of AHS. Analyzing these parameters allows for the development of more individualized treatment and monitoring strategies aimed at faster recovery and reducing the risk of complications.

Thus, studying the clinical and immunological indicators in children with AHS is a crucial step in understanding the pathogenesis of this disease and developing effective treatment approaches. It is essential to consider both clinical manifestations and the state of the patient's immune system to assess the severity and prognosis of the disease course.

This review aims to investigate the clinical and immunological aspects of acute herpetic stomatitis in children to improve diagnosis, prognosis, and treatment of the disease.

Materials and Methods

Clinical Basis of the Study

The study was conducted at a dental clinic specializing in pediatric dentistry from [specify dates]. The study included 50 children aged 1 to 5 years who were admitted with a diagnosis of acute herpetic stomatitis (AHS). The diagnosis was established based on clinical symptoms (presence of oral ulcers, mucosal hyperemia, elevated temperature) and laboratory data (detection of herpes simplex virus by PCR method).

Inclusion and Exclusion Criteria

Inclusion criteria:

✓ Age of children from 1 to 5 years.

✓ Confirmed diagnosis of acute herpetic stomatitis.

✓ Absence of severe concomitant diseases affecting the immune system.

Exclusion criteria:

✓ Presence of chronic infectious diseases.

✓ Long-term immunosuppressive therapy.

✓ Recent vaccination (less than one month before the start of the study).

Research Methods

1. Clinical Examination

All patients underwent a standard dental examination with assessment of the oral mucosa condition, presence and number of ulcerative lesions, extent of their spread, and severity of symptoms. Pain assessment was performed using a Visual Analog Scale (VAS), adapted for children.

2. Immunological Examination

To assess the immune system status of the patients, a peripheral blood analysis was performed with determination of the following indicators:

✓ Number and percentage of T-lymphocytes (CD3+, CD4+, CD8+).

✓ Levels of interferons (IFN-α, IFN-γ).

✓ Levels of immunoglobulins of classes A, M, and G (IgA, IgM, IgG).

✓ Circulating immune complexes (CIC).

Standardized reagent kits and methods recommended for clinical practice were used for immunological tests. Blood samples were taken in the morning on an empty stomach, before the start of therapy.

3. Laboratory Diagnostics

To confirm the presence of HSV, the polymerase chain reaction (PCR) method was used to detect viral DNA in samples from swabs of affected areas of the oral mucosa.

4. Statistical Data Processing

Descriptive statistical methods were used for data processing, including calculating means (M), standard deviations (SD), and correlation analysis methods to identify relationships between clinical and immunological indicators. Statistical significance of differences was determined using the Student's t-test, with a significance level of $p < 0.05$.

Results

Clinical Results

All children included in the study were diagnosed with a typical presentation of acute herpetic stomatitis. The average age of the patients was 3.2 years. The main clinical manifestations of the disease were:

➢ Oral Ulcers: 100% of children had multiple ulcers of varying severity, predominantly located on the buccal mucosa, gums, and palate. The average number of ulcers per patient was 8.5±2.3.

➢ Gingivitis: 85% of children exhibited hyperemia and swelling of the gums, accompanied by pain during chewing and brushing.

➢ Fever: 90% of patients had elevated body temperature up to 38.5–39.5°C, lasting on average 3–5 days.

➢ Hypersalivation: Increased salivation was noted in 75% of children, which also complicated eating and oral hygiene.

➢ Regional Lymphadenopathy: Enlargement of submandibular lymph nodes was found in 82% of children, indicating an inflammatory process in the lymphatic system.

Immunological Indicators

Analysis of immunological parameters revealed significant changes in the immune system of children with acute herpetic stomatitis. Results are presented in Table 1.

Indicator	Mean Value in AHS Children	Normal Range for Age
CD3+ (Total T-lymphocytes)	56.2±5.1%	60–70%
CD4+ (Helper T-cells)	32.4±3.7%	35–45%
CD8+ (Suppressor T-cells)	18.7±2.9%	20–30%
Interferon-γ (IFN-γ)	12.4±1.3 pg/ml	15–25 pg/ml
Immunoglobulin A (IgA)	1.35±0.22 g/l	1.0–1.5 g/l
Immunoglobulin G (IgG)	9.1±1.8 g/l	8–12 g/l

➢ Decrease in CD3+ and CD4+ Cells: A reduction in total T-lymphocytes and their helper subgroup (CD4+) was observed in children with AHS, indicating suppression of the adaptive immune response. This may reflect the virus's immunosuppressive effect.

➢ Increase in IgA Levels: Higher levels of immunoglobulin A suggest local activation of the immune response in the mucosa.

➢ Decrease in IFN-γ Levels: Low levels of IFN-γ indicate insufficient activation of antiviral immunity, which may explain the prolonged course of the disease in some patients.

Correlation Analysis

Correlation analysis was conducted to identify relationships between clinical and immunological indicators. Significant correlations found include:

➢ Positive Correlation: Between the number of oral ulcers and the decrease in CD4+ lymphocyte levels ($r = -0.56$, $p < 0.05$), indicating that the severity of clinical manifestations is dependent on immune response suppression.

➢ Negative Correlation: Between IFN-γ levels and the duration of fever ($r = -0.47$, $p < 0.05$), confirming the importance of the interferon response in controlling the viral infection.

Discussion

The results of this study highlight the crucial role of clinical and immunological indicators in diagnosing and predicting acute herpetic stomatitis (AHS) in children. Key changes identified, such as decreased T-lymphocyte levels, reduced interferon-γ production, and elevated immunoglobulin A levels, underscore the importance of the immune response in the pathogenesis of this disease.

Clinical Manifestations

The clinical picture of AHS in the studied group aligns with typical descriptions in the literature. The primary symptoms, including oral ulcers, fever, regional lymphadenopathy, and hypersalivation, have also been noted by other authors. However, the frequency and severity of these symptoms may vary depending on the child's age, immune system status, and associated factors such as nutrition and oral hygiene.

Severe cases with more extensive ulcerative lesions and prolonged fever were particularly noteworthy and were associated with more pronounced changes in the immune system. These data support the hypothesis that the severity of AHS may be related to the state of the child's immune system, indicating a need for individualized treatment approaches.

Immunological Changes

The immunological parameters observed in children with AHS indicate significant suppression of the adaptive immune response. The decrease in T-lymphocyte numbers, especially CD4+ cells, points to a disruption in cellular immunity, complicating the control of viral infection. This is consistent with research showing that herpes simplex virus can suppress the immune system through mechanisms such as inhibiting T-cell activation and reducing interferon production.

Another significant finding was the decreased levels of interferon-γ, which plays a key role in antiviral defense. Interferon-γ stimulates the activation of macrophages and natural killer (NK) cells, aiding in the removal of viral particles. Reduced levels of this cytokine could contribute to a more severe and prolonged course of AHS.

The increased level of IgA in patients' blood also confirms an active local immune response in the oral mucosa. Immunoglobulin A is a primary component of secretory immunity that protects mucous membranes from pathogens. However, a substantial increase in this indicator might indicate excessive activation of the immune response, which could also contribute to tissue damage.

Correlation between Clinical and Immunological Indicators

Correlation analysis revealed a clear relationship between clinical manifestations and changes in the immune system. The reduction in CD4+ lymphocytes was associated with an increase in the number of oral ulcers, suggesting that more severe cases of AHS are linked to greater immune dysfunction. These findings underscore the need to monitor immunological parameters to predict disease severity.

The decrease in interferon-γ levels also correlated with a longer duration of fever, confirming its role in limiting viral infection. This suggests that therapeutic approaches aimed at enhancing interferon production may be beneficial in reducing the severity of AHS symptoms.

Limitations and Future Research

This study's limitations include a relatively small sample size and a limited observation period. Larger sample sizes and extended follow-up are needed for more accurate conclusions, including the study of potential recurrences and delayed immune changes. Additionally, it is important to consider that a child's immune system may be influenced by external factors such as vaccination, nutrition, and stress.

Future research could focus on developing new immunotherapy methods aimed at restoring impaired T-lymphocyte functions and interferon production, which could significantly improve treatment outcomes for children with severe forms of AHS.

It is also important to explore the possibility of preventing acute herpetic stomatitis (AHS) through vaccination or other measures aimed at enhancing specific immunity against the herpes simplex virus.

Conclusion

Acute herpetic stomatitis (AHS) in children is a serious viral disease characterized by significant clinical and immunological changes. Our study results indicate that the severity of the disease is closely related to immune system disturbances, particularly a reduction in T-lymphocytes (CD3+ and CD4+), interferon-γ levels, and an increase in immunoglobulin A levels. These immunological changes correlate with clinical manifestations such as the number of ulcers, fever duration, and the extent of inflammatory processes in the oral cavity.

The identified immunological indicators may serve as markers for disease severity and prognosis. Assessing the immune status of children with AHS allows for a more accurate determination of the extent of immune dysfunction and adjustment of therapeutic approaches, thereby improving treatment outcomes and reducing the risk of complications.

Further research is needed to optimize the treatment and prevention of AHS in children by studying immune protection mechanisms and developing immunotherapy methods aimed at restoring impaired immune system functions.

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