Primary herpetic oropharyngitis in adults: Differences in clinical features between Herpes simplex virus type 1 and type 2. A retrospective study.

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Abstract

Key points 1. This is the first report of adult primary herpetic oropharyngitis in the view point of the differences between the two types of herpes simplex virus (HSV). 2. 41 (25 type 1 and 16 type 2) HSV specific antigen positive cases among 68 immunoserologically confirmed adult HSV primary infection cases were investigated. 3. Significantly low incidence of oral lesions and high incidence of nausea were seen in HSV type 2 oropharyngitis cases, that might mean particular correlation vagus nerve and HSV type 2. 4. Significantly increased white blood cell count and high C-reacative protein value were seen in oropharyngitis by HSV type 2. 5. HSV type 2 possibly cause more severe symptoms and higher inflammatory reactions than type 1, without oral lesions.

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Significantly low incidence of oral lesions and high incidence of nausea were seen in HSV type 2 oropharyngitis cases, that might mean particular correlation vagus nerve and HSV type 2.

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Key Words: Herpes simplex virus, oropharyngitis, primary infection

Objectives

Although primary infection with herpes simplex virus (HSV) type 1 usually occurs in children, it is sometimes seen in adults. Primary herpetic oropharyngitis, which is oral and pharyngolaryngeal infection caused by HSV, in adults is known to cause more severe symptoms than that seen in children[1], and hospitalization is

often recommended[2]. HSV type 2, which is well known as a cause of genital herpes, is also known to cause oropharyngitis, as one of the sexually transmitted diseases[3]. There have been no studies on the differences between herpetic oropharyngitis caused by HSV type 1 and 2.

Nakagawa et al. have already reported the first case series of primary herpetic oropharyngitis in adults with immuneserological diagnostic criteria, and suggested the possibility that there might be some differences of the clinical symptoms between HSV type 1 and 2[4]. In this study, we tried to investigate the differences between HSV type 1 and 2 in more details.

Participants

All adult patients of acute-onset throat pain with white exudates or stomatitis-like lesions in the oropharyngeal mucous membrane, who had visited the Department of Otolaryngology at XXXX Hospital within the 16-year period from April, 2004 to March, 2020.

Design

We reviewed the clinical files of participants and selected cases that met immune serological diagnostic criteria of Nakagawa et al[4], retrospectively. The immune serological diagnostic criteria is shown in Table 1.

<Table 1 should be placed here>

In all selected cases, HSV-specific antigen was tested at the firs visit, by direct immunofluorescence staining using fluorescein isocyanate-labelled monoclonal antibody for glycoprotein (Denka Seiken, Tokyo, Japan) on samples obtained from oropharyngeal mucosal white lesion with a cotton swab.

Settings

Ethical considerations

Data gathering for this investigation was performed in the patients who were already prescribed an otorhinolaryngologic evaluation; therefore, it did not have need of additional diagnostic or therapeutic procedure. All patient data were anonymized prior to data analysis. This study was approved by the ethical organization of XXXX Hospital No. 20-4.

Statistical analyses

All P-values were two sided and P-values of 0.05 or less were considered statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a modified version of R (The R Foundation for Statistical Computing, Vienna, Austria) commander designed to add statistical functions frequently used in biostatistics[5].

The authors have been following CARE guidelines.

Main outcome measures

The types, number, sex, age, clinical findings including laryngofiberscopic examination, laboratory datas, and treatments of the HSV-specific antigen-positive cases were reviewed.

Results

Fourty-one patients were positive for HSV-specific antigen (15 male, 26 female; age range, 17-65 years; (mean ± standard deviation) 26.7 ± 9.1years), among sixty-eight patients who met the criteria as primary HSV oropharyngitis (27 male, 41 female; age range, 16-65 years; mean 27.2±8.8 years). Type 1 positive cases were 25 and type 2 were 16.

The difference in clinical features between type 1 and type 2 is shown in Table 2.

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Although white slightly raised mucosal lesions spreading widely in pharynx were seen in all patients regardless of types, oral herpetic lesions, like gingivitis, labialis, buccal mucosal lesion, glossitis, were seen in 11 of 25 type 1 patients and 0 of 16 type 2 patients ($p<0.01$). Nausea was complained by 6 patients in type 1 and 11 in type 2 ($p<0.01$). Increased white blood cell counts and higher C-reactive protein(CRP) values were significantly seen in type 2 patients ($p<0.05$, $p<0.01$, respectively).

Female, older patients, higher admission rate, and longer inpatient period were likely to be seen in type 2, there were no statistically significant differences.

Conclusions

Oral lesions and digestive tract symptoms

A significant low incidence of oral lesions were seen in HSV type 2 infection. During primary HSV infection, the main site of viral replication is not the local mucous membrane. HSV is transported intra-axonally to the nerve-cell bodies in ganglia, where the majority of viral replication occurs, after invasion to the endplate of sensory nerve endings. Then HSV spread widely to other mucous membranes through centrifugal migration by way of peripheral sensory nerves[6]. If HSV enters the sensory nerves of pharyngeal wall, viral replication should occur in the ganglia of glossopharyngeal or vagus nerve, then causes pharyngitis. The fact that significant less number of patients with HSV type 2 showed oral lesions suggests that HSV type 2 possibly have the tendency to enter the endplate of the glossopharyngeal or vagus nerve endings, not the trigeminal nerve, which is well known as major affected nerve by HSV type 1. The result that significant larger number of patients complained nausea, which is considered as one of typical symptom of vagal neuritis[7], in type 2 infected patients reinforce this supposition.

Moreover, HSV type 2 infection may have a potential to be misdiagnosed as a bacterial pharyngitis/tonsillitis, because of its low incidence of causing oral stomatitis, which is well known as a typical finding of HSV infection.

Inflammatory reactions

HSV type 2 infection showed more severe inflammatory reactions, increased white blood cell counts and higher CRP, than type 1. Higher CRP in HSV type 2 may be related to the result that HSV type 2 viremia is more likely seen than type 1 during primary infections[8,9]. McMillan et al. reported that 33 type 1 and 2 type 2 HSV patients were seen among 613 pharyngitis in university students at an university health cernter[10]. The fact that a higher rate of type 2 seen in this study possibly indicate the severity of type 2, because this study was based on an outpatient clinic of an acute general hospital which treats more severe patients.

Increased white blood cell counts may also make type 2 HSV infection mimic bacterial pharyngitis.

Clinical applicability

Severity of HSV infection has the great variation from asymptomatic infection to severe oropharyngitis causing poor oral uptake. Inpatient care with hydration and intravenous injection of antiviral agents should be considered for the patients who cannot ingest food, water, or take medicine orally, and who show poor general states[2].

The results of this study showed the difference in the clinical symptoms of HSV oropharyngitis by its types. If type 2 infection is suspected, poor oral uptake, caused not only by throat pain related to severe inflammatory reaction, but also by nausea, should be predicted, and inpatient care will be considered. Moreover, suspicious of type 2 infection forces us to investigate their potentially infected partners.

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