



Severe acute pharyngotonsillitis due to herpes simplex virus type 2 in an homosexual man – Report of A case and review of the literature

Michael Dan^{1,*}, Eyal Yeheskeli^{2,3}

¹Infectious Disease Clinic, Maccabi Health Services, Bat Yam, Israel and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

²Department of Otolaryngology-Head and Neck Surgery, Assaf Harofeh Medical Center, Zerifin, Israel

³Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

*Corresponding author

Abstract

A 30-year-old homosexual man developed pharyngotonsillitis the severity of which necessitated hospitalization for parenteral fluid therapy. Subsequent to unsatisfactory clinical response to antibiotic therapy and the negative tests for group A Streptococcus, together with the ulcerative aspect of tonsillar lesions, the diagnosis of herpes simplex virus, type 2 (HSV-2) was made by polymerase chain reaction (PCR) testing, and was confirmed by serology. Unlike previous concept, HSV-2 can cause infections “above the waist”, and is responsible for up to 10 percent of oral herpetic infections. Clinicians should consider HSV-2 as a potential cause of pharyngotonsillitis in sexually active individuals, especially if streptococcal culture is negative.

Keywords: herpes simplex virus, , herpes simplex virus, type 2, pharyngotonsillitis, genito-oral transmission, homosexuality

Introduction

Herpes simplex virus is a well-recognized cause of oral infection. Herpes simplex virus, type 1 (HSV-1) is very common, with an estimated seroprevalence of >90% in many populations [1]. It is frequently acquired during early childhood, primarily through oral secretions, and most often presents as herpetic gingivostomatitis. However the role of sexual transmission in severe pharyngotonsillitis caused by HSV-2 has not been widely appreciated.

Case report

A 30 year-old man presented in April 2020 with acute odynophagia, difficulty swallowing and high fever (39.7 °C). His family physician diagnosed pharyngitis and ordered some laboratory tests including streptococcal culture, respiratory viruses PCR, EBV and CMV serology, and CBC, the results of which were negative or within normal range.



Figure 1: Beefy red posterior pharynx; enlarged tonsils covered with a thick, white exudate

The patient was admitted to hospital because of worsening odynophagia and increasing difficulty swallowing. Examination on admission showed persistent fever (39.0 °C), the posterior pharynx was beefy red, and the tonsils were enlarged and covered with a thick, white exudate; multiple shallow ulcerations were seen all over the area (Figure 1); bilateral cervical lymph nodes were palpated. The remainder of the physical examination was normal. The patient had an unremarkable medical history, he denied smoking, alcohol and substance abuse. He reported monogamous homosexual relation of seven years, which included oral-genital contacts. Routine laboratory tests were repeated and showed elevated CRP of 50 mg/L while the leukocyte count was 5400/mm³ with 500/mm³ lymphocytes. COVID19 PCR test was negative as was HIV test. Intravenous amoxicillin-clavulanate treatment was initiated.

In view of the unsatisfactory clinical response to the antibiotic therapy and the negative tests for group A Streptococcus, together with the ulcerative aspect of tonsillar lesions, HSV real-time PCR (RealStar® alpha Herpesvirus PCR Kit1.0, Altona Diagnostics, Hamburg, Germany) was requested and revealed HSV-2 in tonsillar swabs.

Intravenous acyclovir led to rapid defervescence. After dissipation of pain, oral acyclovir was administered for 3 more days.

HSV-1 and HSV-2 type specific serology (Liaison, Diasorin, Saluggia, Italy) performed on serum drawn two weeks after the patient became sick was positive for HSV-2 antibodies and negative for HSV-1 antibodies, thus confirming the diagnosis of acute HSV-2 pharyngotonsillitis. His partner's serology was negative for both HSV-1 and HSV-2.

Discussion

The epidemiology of herpes simplex virus has undergone important changes in recent years. The classical concept according to which HSV-1 causes infection “above the waist” (orolabial herpes) and that HSV-2 causes infection “below the waist: (genital herpes) is no longer relevant.

In several surveys conducted mainly from industrialized countries [2-5] herpes simplex virus type 1 has clearly been the predominant HSV type isolated from genital specimens.

Acute herpetic oral infection is caused by HSV-1 in >90% of the cases. HSV-1 infections is most often transmitted via direct contact with infected oral secretions or lesions. Primary

HSV-1 infection usually occurs in childhood and mostly presents as herpetic gingivostomatitis. [1].

HSV-2 has been uncommonly associated with oropharyngeal localization of infection. Corey et al. [6] studied 209 patients with symptomatic primary HSV genital infections referred to a clinic center; they isolated HSV-2 from the pharynx from 13% of women and 7% of men, most of whom had pharyngitis symptoms. In a study from 1993 [7], HSV was isolated from 35 cases of pharyngitis in a cohort of college students. All but two isolates were typed as HSV-1 by immunofluorescence; the remaining two (5%) were therefore presumed to be HSV-2. A paper published in 2010 described 215 patients in a university health settings with symptomatic culture-positive HSV infections. Out of 81 oral infections, 6 cases (7%) were caused by HSV-2, all of whom were <24 years of age [4]. In a report from 2013, a cohort of 183 cases of primary HSV infection in young immune competent women was investigated; although the number of oral cases was small (9) they were all exclusively linked to HSV-1 [5]. In a report from Germany [8], 3 out of 18 (16.6%) persons with a positive HSV PCR result from specimen taken at the orolabial site were found to shed HSV-2. Hence, according to most studies HSV-2 was responsible for up to 10% of herpetic pharyngitis case, mainly in younger adults

In addition to these study derived findings, HSV-2 isolation from oral lesion was documented in a number of case descriptions. We have identified in the medical literature 10 case reports of HSV-2 pharyngotonsillitis (11 cases together with our patient) [9-17]. The mean age of the patients was 25.0 years, range 18-42 years. Seven patients (63.6%) declared practicing oral sex, 2 denied and in one case it was not mentioned (Table 1).

Table 1. Summary of reported cases in the literature

Ref; Yr	Age	Gender	Risk factor	Diagnosis	Treatment	Orogenital sex	HSV-1
9; 1975	20	F	-	Culture	None	+	N.R.
9; 1975	21	F	-	Culture	None	+	N.R.
10; 1978	25	M	bisexual	Culture	Penicillin*	-	N.R.
11; 1979	21	M	-	Serology	Penicillin*	+	+
12; 2012	24	F	HIV+	Culture	Valacyclovir	-	-
13; 2013	23	F	-	Serology	Acyclovir	+	N.R.
14; 2013	42	F	-	PCR	Acyclovir	+	N.R.

15; 2014	18	F	-	Real-time PCR	Valacyclovir	+	-
16; 2014	32	M	-	Serology	Acyclovir	?	-
17; 2015	20	M	-	IHC	Acyclovir	?	N.R.
P.C.;2020	30	M	Homosexual	Real-time PCR	Acyclovir	+	-

Ref. –reference; Yr – Year of publication; IHC - Immunohisto-chemistry;

* - Before acyclovir was marketed; N.R. – Not reported; P.C. –Present Case

Clinical signs of HSV-2 pharyngitis range from mild pharyngeal erythema to severe diffuse ulcerative or exudative pharyngitis. The primary illness most often begins with fever, malaise, myalgia, headache, and sore throat. Small vesicles and ulcerations appear on the pharyngeal wall, tonsils, and soft palate. In severe cases, acute exudative pharyngitis can progress to obstructive pharyngitis requiring airway protection. Usually, there are no lesions present in the anterior mouth or lips. Enlarged and tender anterior cervical lymph nodes are usually present. The general course of the infection lasts 10- 14 days [13].

In conclusion, this case illustrates an uncommon aspect of HSV-2 Infection in atypical localization which may occur in sexually active individuals. Whether the rarity of this entity is due to epidemiological factors or to HSV type-specific biology is unknown. Clinicians should consider HSV-2 as a potential cause of pharyngotonsillitis in sexually active individuals.

Authors' contribution

Both authors have contributed the workup of the case. M. dan has contributed to the writing of the manuscript.

References

- [1] Johnston C and Wald A. Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection. <https://www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-of-herpes-simplex-virus-type-1-infection>
- [2] Samra Z, Scherf E and Dan M. Herpes Simplex Virus Type 1 Is the Prevailing Cause of Genital Herpes in the Tel Aviv Area, Israel. *Sex Transm Dis* 2003; 30: 794-796.
- [3] Wald A. Genital HSV-1 infections. *Sex Transm Infect.* 2006; 82(3):189-190.

- [4] Horowitz R, Aierstuck S, Williams EA, et al. Herpes simplex virus infection in a university health population: clinical manifestations, epidemiology, and implications. *J Am Coll Health*. 2010; 59: 69-74.
- [5] Bernstein DI, Bellamy AR, Hook III EW, et al. Epidemiology: clinical presentation, and antibody response to primary infection with herpes simplex virus type 1 and type 2 in young women, *Clin Infect Dis* 2013; 56: 344–351.
- [6] Corey L, Adams HG, Brown ZA, et al. Genital herpes simplex virus infections: clinical manifestations, course, and complications, *Ann Intern Med* 1983; 98: 958–972.
- [7] McMillan JA, Weiner LB, Higgins AM, et al. Pharyngitis Associated With Herpes Simplex Virus in College Students. *Pediatr Infect Dis J* 1993;12: 280-284.
- [8] Wolff MH, Schmitt J, Rahaus M, et al. Clinical and subclinical reactivations of genital herpes virus. *Intervirology* 2002; 45: 20–23.
- [9] Chang TW. herpetic angina following orogenital exposure. *J Am Vener Dis Assoc* 1975;1:165-164.
- [10] Young EJ, Vsinrub B, Musher DM, et al. Acute Pharyngotonsillitis Caused by Herpesvirus Type 2. *JAMA* 1978; 239:1885–1886.
- [11] Tustin AW and Kaiser AB. Life-threatening pharyngitis caused by herpes simplex virus, type 2. *Sex Transm Dis* 1979; 6: 23-24.
- [12] Lee L, Agwu A and Hutton N. Severe Primary HSV-2 in a Perinatal HIV-Infected Woman with Advanced Immunosuppression. *Case Rep Med* 2012; 2012: 346039.
- [13] Azimi S. Herpes Pharyngitis.
<http://www.med.ucla.edu/modules/xfsection/print.php?articleid=42>
- [14] Barazzutti H, Savini H, Zandotti C, et al. An unusual disseminated viral primary infection: rash, hepatitis and polyserositis. *J Clin Virol* 2013; 58: 601-604.
- [15] Rosain J, Froissart A, Estrangin E et al. Severe acute pharyngotonsillitis due to herpes simplex virus type 2 in a young woman. *J Clin Virol* 2015; 63: 63-65.
- [16] George AK and Anil S. Acute herpetic gingivostomatitis associated with herpes simplex virus 2: Report of a case. *J Int Oral Health* 2014; 6: 99- 102.
- [17] Abe K, Aoyagi H, Okada N, et al. Severe oropharyngitis due to herpes simplex virus type 2 infection in an immunocompetent adult. *Am J Gastroenterol* 2015;110:1140; doi:10.1038/ajg.2014.419.