

# Herpes Simplex Virus Infections of the Nipple

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**Abstract:** The usual sites of herpes simplex virus (HSV) type 1 and 2 infections are orolabial and anogenital, respectively. HSV infection of the nipple and periareolar area is exceptional but probably underrecognized. Typical features include severe pain and erosive or ulcerated erythematous confluent clusters of lesions of the nipple and periareolar area. It is usually unilateral and not recurring. HSV infection of the nipple is originating from autoinoculation, sexual transmission or breastfeeding. Diagnosis is often delayed. The Tzanck smear is the most rapid and adequate method of diagnosis. Immunohistochemistry enables viral identification. The treatment relies on topical disinfection and oral antiviral therapy, such as aciclovir, famciclovir or valaciclovir. Scarring is uncommon.

**Keywords:** Herpes simplex virus, nipple, areola, aciclovir.

## INTRODUCTION

Herpes simplex virus (HSV) type-I and -II are responsible for orolabial and anogenital herpes, respectively. HSV-I or -II infections of the pubis, the bursa, the finger or the hair follicle are more seldom [1-5]. HSV infections of the nipple and/or areola are rather exceptional.

Three patients are presented with HSV infection of the nipple, as well as a literature review.

## CASE REPORTS

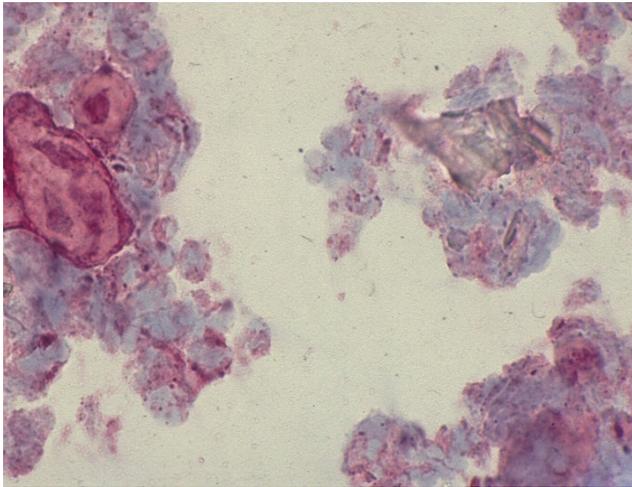
1. A 20-year-old woman presented at the emergency ward for a painful ulcerated lesion of her left nipple. There was no particular medical or surgical history other than a mild atopic dermatitis. She did not take any drugs. The lesion, affecting the entire areola and nipple (Fig. 1), was erythematous, ulcerated and extremely painful. She applied a zinc paste to alleviate the erosions. A left axillar lymphadenopathy was palpated. She presented no fever. A Tzanck smear was performed to exclude a viral infection. The immunohistochemical identification [6,7] was positive for HSV-1, whereas the HSV-2 and varicella zoster virus (VZV) stainings were negative. Serology showed a past HSV infection (IgG: +, IgM: -). The patient was not breastfeeding but had oral/hand-nipple contact with her partner who regularly experienced recurrent orolabial herpes (RHL). The patient and her partner did not suffer from genital herpes. Oral aciclovir (5 x 200 mg/d) was initiated for 7 days and about 10 days later, there was a complete resolution with no residual scarring. She never presented any recurrent herpetic lesion at this site until today.



**Fig. (1).** Erythematous and infiltrated HSV-1 infection of the nipple and areola.

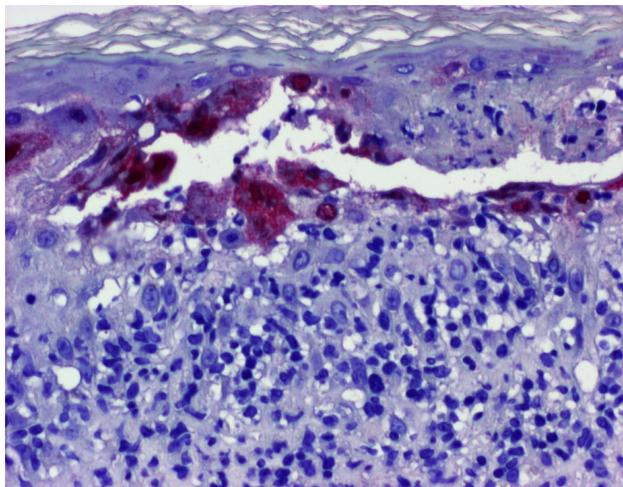
2. A 38-year-old woman was admitted at the emergency ward for very painful, eroded and soothing lesions of her left nipple. She never presented similar lesions previously. She was otherwise healthy and did not take any medication. She was non-lactating. Her partner presented RHL and the lesions presented 2 days after oral contact with the nipple. The breast was not swollen or painful and there was a unilateral axillar lymphadenopathy. The patient and her partner were not afflicted by genital herpes. Immunohistochemistry applied to a Tzanck smear revealed a positive signal for HSV-2 antigens (Fig. 2), but no signal for HSV-1 or VZV antigens. A treatment with oral aciclovir (200 mg, 5 x/d) was given for 10 days. A topical disinfection treatment was applied. After two weeks, no residual lesions were noted and the pain had disappeared completely.

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**Fig. (2).** HSV-2 positive immunostaining in multinucleated keratinocytes (Tzanck smear, Red signal, 100x).

- A 48-year-old woman without any remarkable medical history presented a painful, soothing and eroded dermatosis on the right nipple and superior part of the areola. Bisoprolol was the only medication. This lesion appeared after a slightly traumatic oral/genital-nipple contact with her partner, who suffered from recurrent genital herpes. She presented a right axillar lymphadenopathy. The couple was known to be HSV-2 serodiscordant. A 2-mm punch biopsy was performed under local anesthesia and the histologic examination revealed the presence of intraepidermal blistering with eosinophilic, sometimes swollen keratinocytes. Some keratinocytes presented intranuclear inclusions. Immunohistochemical identification revealed the presence of HSV-2 antigens (Fig. 3), but HSV-1 and VZV antigens were not detected. An initial treatment with topical antibiotics did not bring any relief. An oral treatment with aciclovir (2 x 500 mg/d, 7 days) was initiated. Complete healing without scarring occurred after 6 days. Since, she never experienced a recurrence of HSV-2 infection at this site.



**Fig. (3).** HSV-1 positive immunostaining in epidermal keratinocytes (Skin biopsy, Red signal, 100x).

## DISCUSSION

### Incidence

HSV infection of the nipple and/or areola is very rare and has an estimated frequency of about 2% of all extragenital HSV lesions [8]. However, as the diagnosis is far from easy, it is probable that this entity is underdiagnosed. Up to date, only female patients have been reported in the literature [9-12]. All the patients were adults (19-48 years) and sexually active. All the publications reports single episodes and recurrent infections of the nipple were never mentioned.

### Viral Type

The majority of infections are related to HSV-1 [11], whereas HSV-2 is more exceptional. However, viral identification is often not performed.

### Clinical Manifestations

The dermatologic manifestations include small crops of blisters on an erythematous and slightly swollen base. Erosions, excoriations and ulcerations are often observed. Either the nipple is affected alone, but frequently the areola and periareolar area are also involved. Usually, these infections are unilateral [11,13], but bilateral infections have been reported [our case, 14-16]. Infections are usually restricted to the nipple and areola [8] although cutaneous dissemination may occur [10]. Some infections are accompanied by a locoregional lymphadenopathy [13] whereas others are not. The healing time is about 7 to 10 days and does not differ from other anatomical sites. No scarring has been reported after HSV infection of the nipple. A very characteristic feature is moderate to severe pain, probably related to the high degree of nerve supply of the nipple and the neurotropic character of the virus [17].

### Risk Factors

No particular risk factors exist besides atopic dermatitis [12] and local trauma.

### Complications

HSV mastitis is a rare but feared complication [11,13]. The breast is swollen and indurated with a local painful lymphadenopathy. Another complication is the risk of infecting a newborn during breastfeeding [18]. Disseminated neonatal herpes infection can originate from HSV infection of the nipple of the mother [19]. Hence, breastfeeding is absolutely contraindicated in case of breast lesions [20,21].

### Transmission

HSV infection of the nipple can be the result of a reactivation of a previous local infection or *via* a new transmission.

At least three modes of transmission may explain HSV infection of the nipple. Transmission can occur from infant to mother, as demonstrated by the acquisition of nipple herpes, originating from a primary gingivostomatitis in a baby [14, 15, 22]. In the non-lactating woman, contamination may occur through oral sexual contact [10, 11, 16, 23], such as a partner with recurrent labial herpes. In this instance, HSV-1 is the usual culprit. The partner's hand to nipple contact is also possible [13]. Autoinoculation may

also occur from a RHL or a recurrent genital HSV infection of the patient herself [4,13].

Reactivation has been suspected of an ancient local HSV infection of the nipple by a bite on the nipple by a new male partner without RHL whereas the former partner had RHL [11].

### Diagnosis

The clinical diagnosis is very difficult as the disease is rare and is not part of the usual differential diagnoses.

The Tzanck test or cytodagnosis, combined with immunohistochemistry (IHC), is the preferential method to identify HSV 1 or 2 in a very rapid, sensitive and specific way [6,9,13,24,25].

Sometimes a punch biopsy is performed, especially as mammary Paget's disease is suspected [10,13]. The cytology reveals a ground-glass appearance of the nuclei with multinucleated syncytial cells. Subsequently, either IHC [6] or in situ hybridization (ISH) [24] using DNA probes may be used to search for HSV antigens or DNA.

PCR is another highly sensitive and specific method to identify HSV in clinical specimens [10,11].

Mammography reveals dense fibroglandular tissue with increased density of the affected breast. Skin thickening may be present. Ultrasonography shows areas of diffuse skin thickening [13]. However, mammography and ultrasonography are not diagnostic in the case of herpes of the nipple.

### Differential Diagnosis

Herpes zoster restricted to the nipple is a difficult clinical differential diagnosis, in particular as both entities are linked to pain [25]. However, extension beyond the nipple and a dermatomal distribution are favoring herpes zoster. Furthermore, bacterial infection, dermatomycosis, atopic dermatitis, Darier's disease, periareolar abscess [26] and allergic contact eczema have to be eliminated. Erosive adenomatosis and mammary Paget's disease have also to be ruled out, especially in the elderly patient.

### Treatment

As these infections are uncommon, the treatment recommendations are expert based but not evidence based. Oral aciclovir was initiated at 200 mg 5 x/d, for 5 to 7 days in the majority of the patients [10,12,13]. All patients healed after 7 to 10 days and no residual scarring was ever mentioned in the literature. Newer thymidine kinase dependant antivirals such as famciclovir and valaciclovir may also be considered as treatment alternatives. Topical disinfection is recommended.

### CONCLUSION

HSV infection of the nipple and the periareolar area are uncommon entities that may easily be misdiagnosed. Severe pain combined with an unilateral or bilateral acute erosive dermatosis should suggest the diagnosis. Sexual contact, autoinoculation and breastfeeding are recognized risk factors. Aciclovir, famciclovir and valaciclovir are the antiviral drugs of choice.

### ACKNOWLEDGEMENT

Declared none.

### CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Received: June 12, 2012

Revised: June 26, 2012

Accepted: June 26, 2012

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