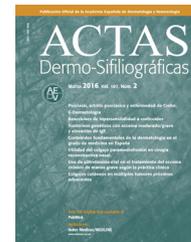




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## REVIEW

# Atypical Cutaneous Manifestations in Syphilis<sup>☆</sup>



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### PALABRAS CLAVE

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**Abstract** Although the diversity of the clinical manifestations of syphilis is well-known, atypical presentations can also occur. Such atypical presentations are associated with a high risk of transmission as a result of diagnostic confusion and treatment delays owing to the disease's ability to mimic other common skin diseases, deviate from classic clinical presentations, and adopt unique forms. Cases of atypical syphilis have been described most frequently in patients with concomitant human immunodeficiency virus (HIV) infection. Because the incidence of syphilis has been growing over recent years—particularly in patients with HIV co-infection—dermatologists need to be familiar with the less well-known clinical presentations of this venereal disease.

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### Manifestaciones cutáneas atípicas en la sífilis

**Resumen** Aunque es por todos bien conocida la heterogeneidad de manifestaciones clínicas con la que puede presentarse la sífilis, esta también puede mostrarse con patrones atípicos.

Ya sea por su capacidad de mimetizar otras dermatosis conocidas, por saltarse los patrones clínicos clásicos o por su originalidad clínica, la sífilis en sus formas atípicas puede llevar a confusiones en el diagnóstico, retrasos en el tratamiento y por tanto un alto riesgo de transmisión.

Entre pacientes coinfectados por el VIH se han descrito más frecuentemente casos de sífilis atípica. El hecho de que se trate de una infección venérea cuya incidencia está aumentando en los últimos años, especialmente en pacientes con VIH, hace necesario que los dermatólogos se familiaricen también con estas formas clínicas menos conocidas.

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## Introduction, Pathogenesis, and Epidemiology

Syphilis has been very appropriately named the *great imitator* and is of considerable clinical interest due to its wide diversity of clinical—and dermatologic—manifestations. The resurgence of syphilis in recent years has required newer generations of dermatologists to become familiar with the clinical variants of this disease, and particularly those that deviate from classical presentations.

The organism responsible for syphilis, *Treponema pallidum*, penetrates its host through intact mucous membranes and/or skin wounds and then multiplies and spreads through the body. Thirty percent of sexual partners of recently infected patients develop syphilis.

Syphilis continues to be a worldwide problem,<sup>1</sup> and in many countries, including Spain, it is a notifiable disease.

The annual incidence of syphilis has risen steadily in the United States since 2001, with data from 2013 indicating a rate of 5.3 cases of early syphilis per 100 000 inhabitants.<sup>2</sup> There has also been a notable increase in new cases in Spain, with rates doubling between 1995 and 2010.<sup>3</sup>

According to numerous reports, the greatest increase in the incidence of syphilis has occurred in men who have sex with men (MSM), largely due to their engagement in risky sexual practices (e.g., sex with unknown partners, unprotected sex, promiscuity, and use of illicit drugs, in particular, methamphetamines).<sup>4–10</sup>

Concomitant syphilis and human immunodeficiency virus (HIV) infection is very common, as the 2 conditions have the same route of infection. In addition, the presence of one infection facilitates the acquisition and transmission of the other.<sup>11,12</sup> Discharge from syphilis lesions is rich in T cells and dendritic cells. The fact that many of these cells express HIV coreceptors (CCR5 and DC-SIGN) could explain the epidemiological relationship between the 2 pathogens.

The estimated rate of concomitant primary or secondary syphilis and HIV infection in MSM in the United States is 86%.<sup>13,14</sup> The prevalence of syphilis and HIV coinfection in MSM in Spain, however, is estimated to be much lower, with data from recent years indicating a rate of around 28%.<sup>15</sup>

## Atypical Clinical Manifestations

In the absence of appropriate treatment for *T pallidum* infection, the disease progresses through different stages, each of which has characteristic clinical manifestations. Nonetheless, reports of uncharacteristic, i.e., atypical, manifestations have existed for years (Table 1). Syphilis also has other clinical manifestations that, while well-characterized and considered typical, are uncommon. In this review, we focus on atypical manifestations.

### Primary Syphilis

About 2 to 3 weeks after infection by *T pallidum*, a painless papule generally develops at the site of inoculation; this then grows and ulcerates, leaving a hard, round, ulcerative lesion known as a chancre, that is not painful. Chancres are generally solitary, and the presence of multiple sores in a patient with primary syphilis can be considered an atypical manifestation (Fig. 1).

**Table 1** Atypical Cutaneous Manifestations of Syphilis in Seronegative Patients (A) and in Patients with Human Immunodeficiency Virus Infection (B).

| A. Atypical Cutaneous Manifestations of Syphilis   |   |
|--|---|
| Stage  | Clinical Presentation   |
| Primary syphilis   | Multiple genital sores<br>Pseudotumoral oral chancre<br>Chancres in atypical locations  |
| Early secondary syphilis   | Exclusive lymph node involvement<br>Lichen planus-like lesions (possible hypertrophic forms)<br>Small papular rash<br>Follicular rash<br>Vesicular rash<br>Corymbiform rash<br>Psoriasiform rash                      |
| Late secondary syphilis  | Nodular lesions<br>Annular lesions<br>Pustular lesions<br>Frambesiform lesions<br>Photodistributed papulosquamous lesions<br>Nodular-ulcerative lesions (malignant syphilis) ± neurological involvement               |
| Tertiary syphilis  | Syphilitic gummas in an atypical location<br>Rupoid gummas in malnourished patients   |
| B. Atypical Manifestations of Syphilis in Patients With Human Immunodeficiency Virus Infection |   |
| Primary syphilis   | Overlapping of stages<br>Multiple genital chancres<br>Pseudotumoral oral chancre<br>Early-stage neurosyphilis<br>Syphilitic gummas in early infection stages  |
| Secondary syphilis   | Overlapping of stages<br>Atypical cutaneous manifestations of secondary syphilis described in Section A<br>Mycosis fungoides-like lesions<br>Early-stage neurosyphilis<br>Syphilitic gummas in early infection stages |
| Tertiary syphilis  | Overlapping of stages<br>Syphilitic gummas in an atypical location<br>Syphilitic aortitis with rapid progression<br>Asymptomatic neurosyphilis<br>Otosyphilis<br>Ocular syphilis                                      |

Other atypical variants of primary syphilis reported include pseudotumoral chancres on the dorsum of the tongue<sup>16</sup> (Fig. 2) and, more recently, a primary chancre on the hand associated with regional lymphadenopathy.<sup>17</sup>

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