Treponema Pallidum Epidermotropism in Nodular Secondary Syphilis

Jorge Magdaleno-Tapia, Cristian Valenzuela-Øñate, José Maria Ortiz-Salvador, Pablo Hernández-Bel, Victor Alegre-De Miquel

Abstract

Nodular secondary syphilis results from the hematogenous and lymphatic dissemination of spirochetes. Clinically, the lesions appear as partially infiltrated plaques or red-violaceous nodules, which can be solitary or multiple. Several hypotheses have been put forward to explain the formation of these infiltrated or granulomatous lesions. Among the most accepted are the specific hypersensitivity reactions to Treponema pallidum or the lengthy duration of the disease. We present a case of nodular syphilis where immunohistochemistry revealed the presence of multiple spirochetes invading the epidermis.

Key Words: Epidermotropism, granulomatous lesion, nodular syphilis, treponema pallidum

Introduction

The secondary stage of syphilis results from the hematogenous and lymphatic dissemination of spirochetes. The most commonly observed clinical presentation is a generalized, nonpruritic papulosquamous eruption. However, more infiltrated lesions, often copper-colored or corymbose arrangements, have been reported. Several hypotheses have been put forward to explain the formation of these infiltrated or granulomatous lesions. Among the most accepted are the specific hypersensitivity reactions to Treponema pallidum or the lengthy duration of the disease. Clinically, the lesions appear as partially infiltrated red-violet plaques or nodules, sometimes simulating a pseudolymphoma or panniculitis. We present the case of a patient with nodular syphilis mimicking Sweet syndrome with epidermotropism of Treponema pallidum as demonstrated in histopathology.

Case Report

A 55-year-old male attended our department with a 30-day history of multiple nodules on his face and upper arms and trunk. Mucous membranes, palms, and soles were not affected, and there was no regional lymphadenopathy. He experienced no fever, headache, sore throat, cough, or weight loss. The patient was not taking any medication. He informed us that he had suffered from gonorrhea and syphilis 20 years before, which had been adequately treated. The patient was a homosexual man, with a stable partner for the last 6 months, and he denied any sexual activity outside this relationship.

On physical examination, we observed multiple erythematous infiltrated plaques of annular morphology, located on his forehead, thorax, nape of the neck, and upper part of the back and arms. Some of these lesions presented a central flattening with a raised border [Figure 1a]. One infiltrated annular lesion was observed on his upper lip [Figure 1b]. In addition, there were two desquamating ring lesions on the back of both hands [Figure 2a], with none on palms and soles. The occipital area of the scalp showed mild moth-eaten alopecia [Figure 2b].

Our initial clinical impression was that this was a case of Sweet syndrome; however, he had no fever, and routine blood test results were normal. Screening for sexually transmitted infections revealed the following results: rapid plasma reagin 1:128 and fluorescent treponemal antibody absorption (FTA-ABS) were positive, while the test for HIV was negative. We
continued to consider the possibilities of secondary syphilis or Sweet syndrome associated with late latent syphilis. We decided to perform a biopsy and to administer the first dose of 2.4 MU of benzathine penicillin.

The histological study showed psoriasiform hyperplasia of the epidermis with a dense granulomatous infiltrate in the papillary and reticular dermis. These granulomas were formed by epithelioid histiocytes and numerous multinucleated Langhans giant cells, surrounded by a dense lymphoplasmacytic infiltrate [Figure 3]. In addition, numerous capillaries with edematous walls and prominent endothelial cells were observed.

Immunohistochemical staining for *T. pallidum* was positive, especially in the epidermis and the epidermal ridges, which was evidence of the prominent epidermotropism of this spirochete [Figure 4].

The patient was diagnosed as a syphilitic reinfection in the form of granulomatous nodules and plaques. The skin lesions healed 1 month after the first dose of penicillin.

Figure 1: (a) Multiple erythematous nodules of annular morphology located in the upper part of the back. (b) Infiltrated annular plaque on the upper lip

Figure 2: (a) Two desquamating ring lesions on the dorsal right and left hand. (b) “Moth-eaten” hair loss observed in the occipital area (circles)

Figure 3: Tuberculoid granulomas formed by epithelioid histiocytes, numerous multinucleated Langhans giant cells and surrounded by a dense lymphoplasmocytic infiltrate (H and E, ×200)

Figure 4: Immunohistochemical staining (×1000) for *Treponema pallidum* was positive especially within the epidermis (a) and the epidermal ridges (b)
Discussion
The incidence of sexually transmitted infections is currently on the rise. Typically known as the “great imitator,” secondary syphilis often mimics other diseases.\[3\] Nodular secondary syphilis was first described some 30 years ago, and very few cases are described in the literature.\[4\] Clinically, the lesions appear as partially infiltrated plaques or red-violaceous nodules, which can be solitary or multiple, and they may occasionally simulate a pseudolymphoma or neutrophilic dermatosis.\[5\]

Several pathogenic hypotheses have been postulated to explain the formation of secondary syphilitic nodular granulomatous lesions. Some authors suggest that this kind of lesion is a specific hypersensitivity reaction to a treponemal infection, while others believe that the formation of dermal granulomata should be correlated with the duration of the disease and that they are eruptions that occur during the transition to the tertiary phase.\[2\] In the present case, we did not know the duration of the infection, and the detection of spirochetes in the lesional skin did not justify the hypersensitivity reaction hypothesis. We believed that the prominent treponemal epidermotropism observed in this case might have influenced the unusual clinicopathological aspects. Frequently, \textit{T. pallidum} has a predilection for the dermal-epidermal junction zone or dermis (mesodermotropism), compared, for example, with the subspecies \textit{T. pertenue} in yaws specimens, which shows remarkable epidermotropism.\[6\] Other authors, however, have described an epitheliotropic pattern for \textit{T. pallidum} in 81% of secondary syphilis cases.\[7\]

In conclusion, we present a case of nodular syphilis in a homosexual male. Immunohistochemistry revealed the presence of multiple spirochetes invading the epidermis, which could be the cause of the infiltrated skin lesions.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Rysgaard C, Alexander E, Swick BL. Nodular secondary syphilis with associated granulomatous inflammation: Case report and literature review. J Cutan Pathol 2014;41:370-9.
2. Hernández-Bel P, López J, Sánchez JL, Alegre V. Nodular secondary syphilis. Actas Dermosifiliogr 2009;100:520-2.
3. Li F, Wang T, Wang L. Secondary syphilis primarily presenting with multiple nodules on the scalp: Case report and published work review. J Dermatol 2017;44:1401-3.
4. Glatz M, Achermann Y, Kerl K, Bosshard PP, Cozzio A. Nodular secondary syphilis in a woman. BMJ Case Rep 2013; 2013: bcr2013009130.
5. Liu J, Ma D. Disseminated nodular and granulomatous secondary syphilis. J Dermatol 2014;41:650-1.
6. Engelkens HJ, ten Kate FJ, Judanarso J, Vuzevski VD, van Lier JB, Godschalk JC, \textit{et al}. The localisation of treponemes and characterisation of the inflammatory infiltrate in skin biopsies from patients with primary or secondary syphilis, or early infectious yaws. Genitourin Med 1993;69:102-7.
7. Martín-Ezquerra G, Fernandez-Casado A, Barco D, Jucglà A, Juanpere-Rodero N, Manresa JM, \textit{et al}. Treponema pallidum distribution patterns in mucocutaneous lesions of primary and secondary syphilis: An immunohistochemical and ultrastructural study. Hum Pathol 2009;40:624-30.