

## **Nodular secondary syphilis with granulomatous inflammation**

Sir,

Rather than the usual cutaneous manifestation of maculopapular rash, some cases of secondary syphilis continue to assume diverse/atypical morphological presentations.<sup>[1]</sup> Hence, a need exists to broaden its differential diagnosis in the appropriate clinical settings. Even the classical histopathological picture may rarely be supplanted by granulomatous inflammation.<sup>[2]</sup> Herein, we report a case of nodular secondary syphilis with sarcoid-like granulomas.

A 27-year-old male, married for 12 years, presented with a diffuse, asymptomatic rash, low-grade fever, and malaise for 2 weeks, without any preceding genital or extragenital ulcer. The patient denied any history of extramarital sexual intercourse over the past 6 months. Examination revealed multiple, well-defined, symmetric papules, plaques, and nodules over the upper extremities, trunk, neck, and forehead [Figure 1a and b]. Palms, soles, mucosae, hair, and nails were uninvolved. Lymph nodes (cervical, axillary, supratrochlear, and inguinal) were enlarged, shotty, mobile, and painless. Venereal disease research laboratory (VDRL) was nonreactive.

Histopathological examination of a nodule from the upper back revealed thinned out epidermis, dense upper dermal chronic infiltrate with scanty plasma cells, mid-dermal noncaseating uniform granulomas of plump epithelioid histiocytes with abundant eosinophilic cytoplasm, and

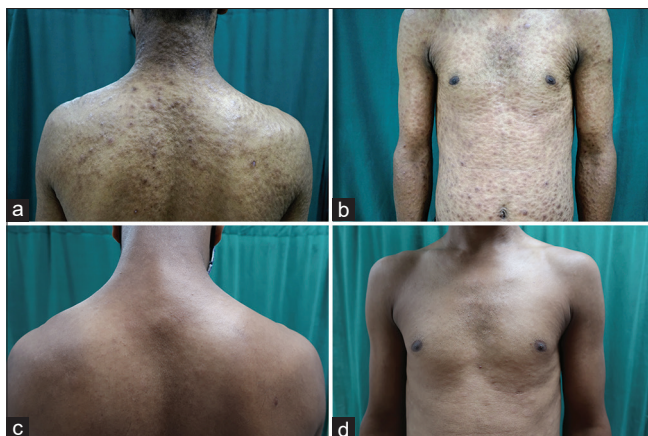


Figure 1: Pretreatment symmetric papulonodular lesions over the (a) neck and back, (b) chest, abdomen, and upper extremities; posttreatment flattening of lesions over the (c) neck and back, (d) chest, abdomen, and upper extremities

round-to-oval nuclei with small central nucleoli. The deep dermis revealed intense periadnexal and perineural inflammation [Figure 2a and b].

However, deep dermal tenderness (positive Buschke–Ollendorff sign) over some truncal lesions made us repeat VDRL quantitatively, which came back strongly reactive (1:256), as did Treponema pallidum hemagglutination assay (TPHA) (>1:640). The patient now revealed a history of unprotected sexual intercourse with a female sex worker 3 months ago. Serology for HIV, HBV, and HCV was nonreactive.

Diagnosed as having nodular secondary syphilis, the patient was administered benzathine penicillin G 1.2 million units in each buttock for 3 consecutive weeks (total 7.2 MU). All lesions flattened promptly [Figure 1c and d] and VDRL titer fell fourfold after 6 months.

Despite a steep decline, periodic outbreaks of this “great imitator” continue to be reported.<sup>[3]</sup> A papulonodular presentation sparing palms and soles with granulomatous inflammation has been described more commonly in tertiary syphilis.<sup>[4]</sup> A 2014 review of granulomatous secondary syphilis cases showed a significant correlation between the absence of palmoplantar involvement and the presence of nodular lesions; 17 out of 24 cases without palmoplantar involvement were diagnosed late and probably only with a heightened index of suspicion.<sup>[4]</sup> The duration of nodular eruptions in our patient at presentation was only 14 days, unlike the majority of previous cases, wherein it was  $\geq 4$  weeks.<sup>[4]</sup> Only three previous cases of nodular secondary syphilis with granulomatous inflammation of  $\leq 4$ -week duration have been described, with all three showing a clinical presentation akin to our patient, i.e., generalized papulonodular eruption, sparing of palms, soles, and mucosae.<sup>[4]</sup>

Histopathological analysis was not diagnostic because of the nonspecificity of sarcoid-like granulomata. The diagnosis of syphilis was therefore based on positive

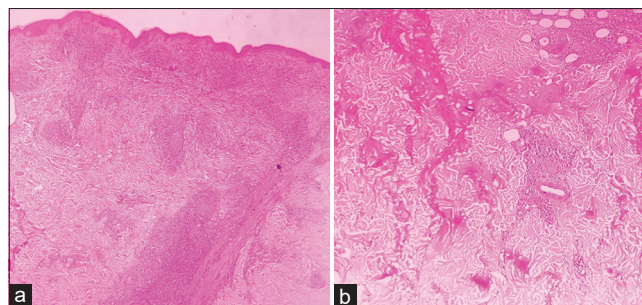


Figure 2: (a) Thinned out epidermis and dense chronic inflammation in the upper dermis and multiple granulomas in mid-dermis with periadnexal and perineural inflammation (hematoxylin & eosin,  $\times 10$ ). (b) High-power view showing perineural and periadnexal chronic inflammation (hematoxylin & eosin,  $\times 40$ )

serology corroborated by a rapid clinical and eventual serological response to penicillin.

This case demonstrating an atypical clinical as well as histopathological presentation emphasizes the need for clinicians and pathologists to be aware of the diverse manifestations of secondary syphilis in order to make an early diagnosis.

#### Acknowledgment

The patient in this manuscript has given written informed consent to publication of his case details.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

Asharbh Raman, Kirti Deo, Yugal K. Sharma, Banyameen Iqbal<sup>1</sup>, Shahzad Mirza<sup>2</sup>, Aayush Gupta  
Departments of Dermatology, <sup>1</sup>Pathology and <sup>2</sup>Microbiology, Venereology and Leprosy, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India

#### Address for correspondence:

Dr. Asharbh Raman,  
C3-1303, Mahindra Antheia, Nehru Nagar Road,  
Pimpri, Pune, Maharashtra, India.  
E-mail: asharbh@gmail.com

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<b>Quick Response Code:</b> 	<b>Website:</b> <a href="http://www.ijstd.org">www.ijstd.org</a>
	<b>DOI:</b> 10.4103/ijstd.ijstd_91_21

**How to cite this article:** Raman A, Deo K, Sharma YK, Iqbal B, Mirza S, Gupta A. Nodular secondary syphilis with granulomatous inflammation. *Indian J Sex Transm Dis* 2022;43:91-3.

**Submitted:** 27-Sep-2021  
**Accepted:** 28-Sep-2021

**Revised:** 28-Sep-2021  
**Published:** 07-Jun-2022

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