

Case Report

Eosinophil rich infiltrate in secondary syphilis a rare histopathological variant

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Received: 10 May 2021

Revised: 03 June 2021

Accepted: 05 June 2021

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ABSTRACT

Secondary syphilis is a sexually transmitted infection, which is referred to as “the great imitator” and has a wide spectrum of clinical manifestations. Syphilis is classically associated with plasma cells and the presence of eosinophils usually argues against a diagnosis of syphilis. The differential diagnosis for eosinophil-rich skin lesions often includes a drug reaction, arthropod-bite reaction, allergic contact dermatitis, and a response to a helminth infestation. However, many unrelated entities, such as infections, neoplasms, and inflammatory dermatoses can have prominent eosinophilic infiltrate. We report a case of secondary syphilis which on histopathology showing psoriasiform hyperplasia with superficial perivascular infiltrate and on higher magnification these infiltrate were predominantly lymphohistiocytic along with the moderate amount of eosinophils with a paucity of plasma cells. This case report is presented to highlight the need for including secondary syphilis as one of the differential diagnoses in the presence of eosinophil-rich infiltrate when it is suspected clinically.

Keywords: Secondary syphilis, Eosinophils, Histopathology

INTRODUCTION

Syphilis is a sexually transmitted infection that can also be transmitted vertically. It is caused by the spirochete *Treponema pallidum* subspecies *pallidum* and order Spirochaetales. The World Health Organization (WHO) estimates that 11 million new cases of syphilis occur globally every year in patients between the ages of 15 and 49 years.¹ Syphilis remains an important public health problem in many low-income countries, and it has reappeared in some high-income countries, especially in high-risk groups such as men who have sex with men.¹ *T. pallidum* cannot be cultured in vitro, so diagnosis and proof of cure rely on serological examination. Skin biopsy is usually performed with serological tests to aid in the diagnosis. There is considerable histologic overlap among the various clinical form of secondary syphilis.² Skin

biopsy reveals three types of pattern such as psoriasiform hyperplasia common pattern, lichenoid and granulomatous pattern along with perivascular and periadnexal lymphohistiocytic infiltrate with a varied amount of plasma cells. Eosinophils are not usually observed.³ Silver stain and tissue immunohistochemistry are useful in detecting the organism even when dark-field examination of the patient’s lesion is negative.⁴

CASE REPORT

A 33-year-old promiscuous male presented with asymptomatic red raised lesions over palms and soles followed by involvement bilateral legs and forearm since 1 month. He had asymptomatic erosion over the hard palate which resolved spontaneously. He gave a history of

topical steroid application following which lesions over palms resolved but lesions over other sites persisted.

On examination

Multiple annular erythematous plaques over bilateral legs and palms and soles (which showed annular Biett's collarette). Deep dermal tenderness was present on the plaques.

Differential diagnoses of secondary syphilis and erythema multiforme were considered.



Figure 1: Multiple annular erythematous plaques over bilateral legs.



Figure 2: Multiple annular erythematous plaques over left leg.



Figure 3: Multiple annular erythematous plaques over right soles with Biett's collarette.

Skin biopsy from the plaque over bilateral legs shows psoriasiform hyperplasia with superficial perivascular infiltrate showing a moderate amount of lymphohistiocytic infiltrate admixed with a considerable number of eosinophils and sparse plasma cells.



Figure 4: Multiple hyperpigmented macules over bilateral palms.

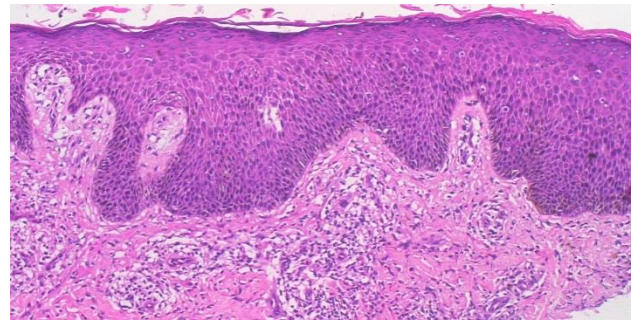


Figure 5: Psoriasiform hyperplasia with superficial perivascular infiltrates.

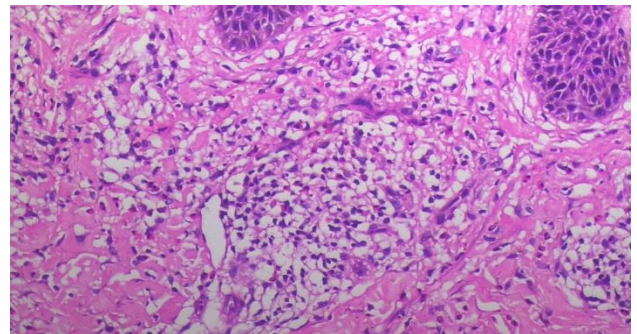


Figure 6: Lymphohistiocytic perivascular infiltrates with eosinophils.

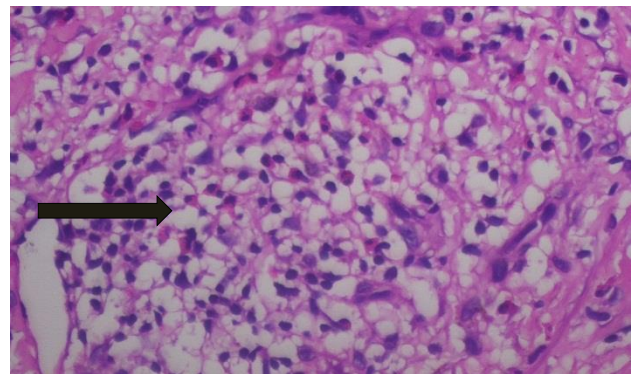


Figure 7: Multiple eosinophils along with lymphocytes and histocytes with an absence of plasma cells on higher magnification.

Diagnosis of secondary syphilis was confirmed by venereal disease research laboratory (VDRL) (1:32) and positive *T. pallidum* hemagglutination assays (TPHA).

After confirmation patient was treated with an (intramuscular (IM) injection of 2.4 MU of benzathine penicillin weekly for 3 weeks following which the patient showed improvement on 2 weeks of treatment.



Figure 8: Lesions resolving with hyperpigmentation after the first dose of benzathine penicillin (2 weeks).



Figure 9: Lesions healing by desquamation and hyperpigmentation after the first dose of injection benzathine penicillin (2 weeks).

DISCUSSION

Secondary syphilis has many histopathological variations, of which commonly seen are psoriasiform hyperplasia often with spongiosis. Parakeratosis may be present which is patchy or broad with or without intracorneal neutrophilic abscess. Although these features may mimic psoriasis, attenuation of suprapapillary thinning is uncommon.⁵ Plasma cells, irregular acanthosis, elongated rete ridges, and endothelial swelling were the most common findings overall. Plasma cells are commonly present around the vessels giving coat sleeve appearance on histopathology. Plasma cells and endothelial swelling are the main diagnostic features of secondary syphilis specimens with fewer pathological features. Irregular acanthosis and the presence of vacuolar interface dermatitis also proved to be useful in diagnosis.³ Eosinophils are not usually observed. The recruitment of eosinophils in the hypersensitivity

phenomenon is related to cytokines like IL-5 released by T-helper cells and other cytokines such as macrophages migration inhibitory factors, IL-3, IL-4, and IL-13.⁶ The study suggest eosinophil attractant cytokines play a role in these non-hypersensitivity conditions as well.^{7,8} Tissue eosinophilia has been observed in secondary syphilis but it is a rare phenomenon. Increased levels of eosinophils chemoattractant have been documented in patients with syphilis. Podwinska et al showed that blood cultures from syphilis patients in various stages of the disease showed increased levels of IL-2, interferon (IFN), tumor necrosis factor (TNF), and MIF. Patients with secondary syphilis had the greatest amount of MIF production which is an eosinophil chemoattractant.⁹ This increased production of MIF does not explain the apparent rarity of eosinophil's rich infiltrate in secondary syphilis. The possible explanation would be dysregulation of cell-mediated immunity with increased production of eosinophil chemoattracts may play a role in eosinophil rich infiltrate not associated with hypersensitivity reaction.¹⁰ The case we have reported shows psoriasiform hyperplasia with superficial perivascular infiltrate showing lymphohistiocytic and moderate amount of eosinophils with a paucity of plasma cells on histopathological section.¹¹

Silver stain and Immunofluorescence techniques are other methods to diagnose syphilis in histopathology. *T. pallidum* is usually detected at the dermal-epidermal junction by the above methods, which is probably related to the interaction between the outer membrane protein of *T. pallidum* and the extracellular matrix. The outer membrane proteins of *T. pallidum* (TP0751, TP0136, TP0483, and TP0155) can interact with extracellular matrix components such as laminin, fibronectin, collagen, and fibrinogen.

The differential diagnosis for eosinophil-rich skin lesions often includes a drug reaction, arthropod bite reaction, allergic contact dermatitis, and a response to a helminth infestation.⁸ Sharon et al showed that eosinophils are rarely observed in pityriasis lichenoides, dermatomyositis, cutaneous lupus erythematosus, and graft-versus-host disease. The presence of eosinophils in these entities will create a dilemma and can dissuade one from including them in the differential diagnosis in the histopathological study akin to secondary syphilis in our case.¹²

CONCLUSION

In the diagnosis of syphilis, histopathology can only bolster your diagnosis but they are not specific for syphilis. The classical teaching dictum in syphilis is the presence of plasma cells along with lymphohistiocytic infiltrates. The presence of eosinophils usually argues against the diagnosis of syphilis. The presence of eosinophils favors the diagnosis of drug rash, contact dermatitis, and helminth infections. The authors suggest that the presence of eosinophils in histopathology should not dissuade a clinician from suspecting syphilis. And hence syphilis

should be included in the differential diagnosis in such patients. Histopathological detections of *Treponema palladium* using silver stain or Immunohistochemistry are highly specific but have low sensitivity. Diagnosis is usually confirmed by serology. To our best of our knowledge, only four such cases have been reported to date and no case has been reported in India.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Kharkar VD, Rajendran HB. Eosinophil rich infiltrate in secondary syphilis a rare histopathological variant. Int J Res Dermatol 2021;7:605-8.