

DIFFERENT LESIONS IN DIFFERENT STAGES. A CASE OF SECONDARY SYPHILIS

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Summary

Introduction: Secondary syphilis, also known as the „great imitator”, represents a great challenge for the clinician because of the polymorphism of its clinical manifestations.

Case presentation: A 44-year -old male patient, affirmatively heterosexual, presented for asymptomatic polymorphous skin and mucosal lesions. Clinical examination reveals pink macules in the abdominal region, brick-red annular plaques on the abdominal area, purple-red nodules with peripheral desquamation on the back, scaling erythematous lesions on the scrotum and penis, greasy scale covered erythematous lesions on the scalp, neck and face, purple-red lesion with central pallor in the axillar region. We do not noted any pathological changes of the hair and nails. At the general examination, we found generalized painless microadenopathies and the patient complained for diffuse muscle pain. Serological reactions were highly, Treponema Pallidum Hemagglutination Assay (TPHA) 1:10240, Venereal disease research laboratory (VDRL) 1:32. Based on the clinical and laboratory findings, the diagnosis of secondary syphilis was established and treatment with Benzatin Penicilin was performed with remission of the lesions.

Conclusion: Atypical polymorphous skin eruptions impose serological testing for syphilis.

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Introduction

Syphilis is an infectious disease caused by *Treponema Pallidum*, which can be either acquired or congenital. The acquired one has an early and a late stage, the latter being divided into three separate stages with different characteristics, the secondary stage being known as the great imitator because of the polymorphism of the lesions. The classification is based on the clinical appearance, the chancre and satellite adenopathy representing the primary syphilis (PS). Rarely, PS can present as circinate balanitis (balanitis syphilitica of Follmann). PS presenting as primary chancre associated with Follmann balanitis was also described. Secondary syphilis (SS), also known as the „great imitator“ is characterized by the the polymorphism of the skin lesions and diffuse general symptoms like headache, muscle and bone pain, nonspecific laboratory changes like pancitopenia, increased liver function tests, increased Erythrocyte Sedimentation Rate (ESR) and so on. Depending on the personal history and immunity of the patient, there may be overlapping of the stages. From 2010, a significant raise of *T. pallidum* infection rate has been observed in patients over 45 years old, especially in homosexuals and/or HIV infected patients []. In 63% of the reported cases men sex men (MSM) were involved. In this particular group, the diagnosis and staging is more difficult, from frequent unusual locations of the primary chancre (e.g. anal or oral mucosa) to completely atypical clinical picture in HIV coinfection. Also, the lack of the primary chancre in intravenous drug user (syphilis d'émblée) can raise diagnosis difficulties. In primary syphilis, the earliest lesion appears within an inoculation period of one to three weeks, as a consequence of local contact with the bacteria. Clinically, the first change is a pink papule which expands and turns into a chancre accompanied by local lymphadenopathy at the same side. Practically, the chancre represent a granulomatous reaction as a defense mechanism, the plasma cells cover the bacteria and try to stop the spreading of the infection via

blood circulation. This defense mechanism is not enough, so without antibiotic treatment, this defense reaction will decrease and from a clinical point of view we assist at the disappearance of the primary chancre with blood invasion by treponemas. In SS, we have disseminated skin lesions as a consequence of bacteremia, usually within the first year of infection, but may reappear up into the second year after the initial infection. In early secondary syphilis the primary lesions may still be present. The polymorphism of the lesions depends on the degree of the skin immunity, the level of vascular involvement and the local ischemic changes that result from these processes [].

Case presentation

We present the case of a 44 year -old-male patient, affirmatively heterosexual, presented for asymptomatic polymorphous skin and mucosal lesions. The patient interview was very difficult, he cannot describe clearly the onset and evolution of the skin lesions and avoided to discuss about his sexual life. Clinical examination reveals pink macules on the abdominal flanks, a brick-red annular plaque on the abdominal area, purple-red nodules with peripheral desquamation on the back, scaling erythematous plaques on the scrotum, annular lesions with central atrophy on the prepuce, greasy scale covered erythematous lesions on the scalp, neck and face, fair purple lesion with central pallor in the both axillary regions. On the back, in lumbar area, we noted atrophic scars and the patient does not recall any trauma history. We also noted microadenopathies and the patient complained for diffuse muscle pain. On examination of the oral mucosa, on the hard palate we observed sharply delimited ulcerations. We do not noted residual lesions of primary chancre like indurated skin or hyperpigmentation neither on the genital or anal mucosa. Also, no persistent characteristic adenopathy for primary lesions was not found after a complete examination of all the accessible lymph nodes areas. A complete urological examination does not revealed any

abnormalities. Laboratory examinations revealed TPHA 1:10240, VDRL 1:32, RPR positive on a 1:8 scale dilution, high levels of Ig M and Ig G anti-syphilis antibodies, negative anti HIV I+II antibodies, ESR-44 mm/h., increased liver function tests (GOT= 67 UI, GPT 78 UI). Based on the clinical and serological result, the diagnosis of secondary syphilis was established and treatment with Benzatin Penicilin was initiated, with remission of the lesions.

Discussion

Asymptomatic skin lesions, sometimes with strange aspect that cannot be included in common diseases, rise highly the suspicion of secondary syphilis. It is important to keep in mind the idea that the lesions can overlap in secondary syphilis [5]. In our case we observed residual roseolas, annular siphilides, psoriasiform lesions, seborrheic siphilides, ulcerations and nodules. Other lesions that are met rarely in SS are lichenoid, ectyma-like, follicular and acneiform papules, hypopigmented macules, intertriginous erythema, anetoderma [6-10]. Our patient presented also bilateral axillary erythema that cannot be included clearly in a specific type of intertrigo from a clinical point of view. More than that, this flexural lesions disappear completely after the first dose of benzatine penicillin. Based on patient diagnosis, literature reports and proper response to the antibiotic treatment, we considered the axillary lesions as a manifestation of SS. Regarding atrophic scars located on the lumbar area, even the does not recall any history of local trauma, we considered that is very difficult to include it as a stigma syphilis lesions because the patient cannot confirm the presence of previous skin lesions. Syphilis anetoderma is well described in the literature and usually result after the remission nodular lesions. In our patient we observed in the vicinity of the area a typical nodular lesion. A rare case of syphilis was reported with overlapping of primary and secondary stage, raising the possibility of a secondary superimposed infection,

this theory being confirmed by Shwetz et al in an analysis of secondary syphilis lesions. They affirm that although secondary stage lesions appear 4-10 months after the primary lesion, in rare cases of disseminated lesion an overlapping of stages may be present. Sometimes primary chancre may still be present when the roseolas arise [11]. Our patients presented an overlap between precocious SS and late SS. Annular lesions are described in SS, especially located on the genital area and usually are misdiagnosed as annular lichen planus [12-14]. Our patient presented an annular lesion on the prepuce and also extragenital lesions. Skin nodules in SS are a mimicker of lymphocytoma or cutaneous lymphoma, sarcoidosis, and Kaposi sarcoma [15-22]. Psoriasis-like lesions are found especially on the scrotal area in men, our patient presented on the scotum, prepuce and knees. Seborrheic syphilides are difficult to be suspected when they present as the only sign [23-27]. In our patient the suspicion was high because of the clinical and serological content. Oral manifestations in SS are consist usually in ulcerations, plagues or nodules [28-33]. Our patient presented unnoticed ulcerations with rapid remission after antibiotic treatment. Finally, only one case of bilateral axillary erythema as a manifestation of secondary syphilis was reported by Chantrapitak et al recently. We also consider this changes as SS lesions in our patient based on the epidemiological content, serology, proper response to the antibiotic treatment and why not based of the fact that this intertriginous axillary rash cannot be corelated with other cause, bacteriological and micological culture were negative. Anyway, more data are necessary to be reported for a clear correlation between SS and flexural erythema.

Conclusion

Atypical polymorphous skin eruptions impose serological testing for syphilis. Cases of SS must be analyzed properly according to the overlap of the stages, lesional polymorphism, different stages of different lesions.



Figure 1. Patients at the first examination

- a) Annular plaque on the anterior trunk; b) Red nodule on the lumbar area. Note also atrophic scars in the vicinity;*
- c) Psoriasiform plaques on the scrotum; d) Annular plaque on the prepuce; e) Red plaques on the anterior cervical area;*
- f) Oral ulceration on the hard palate*



Figure 2. Patients at the first examination

a) Atrophic scars on the lumbar area; b) Plaque covered with fine scales on the knee; c) Plaque covered with yellowish scales on the scalp; d) Discrete red macules and patches on the lateral part of the trunk; e) Arciform plaque on the upper part of the back; f) Axillary rash with central clearing



Figure 3. a,b,c,d) Skin and mucosal lesion after the first dose of benzathin penicillin

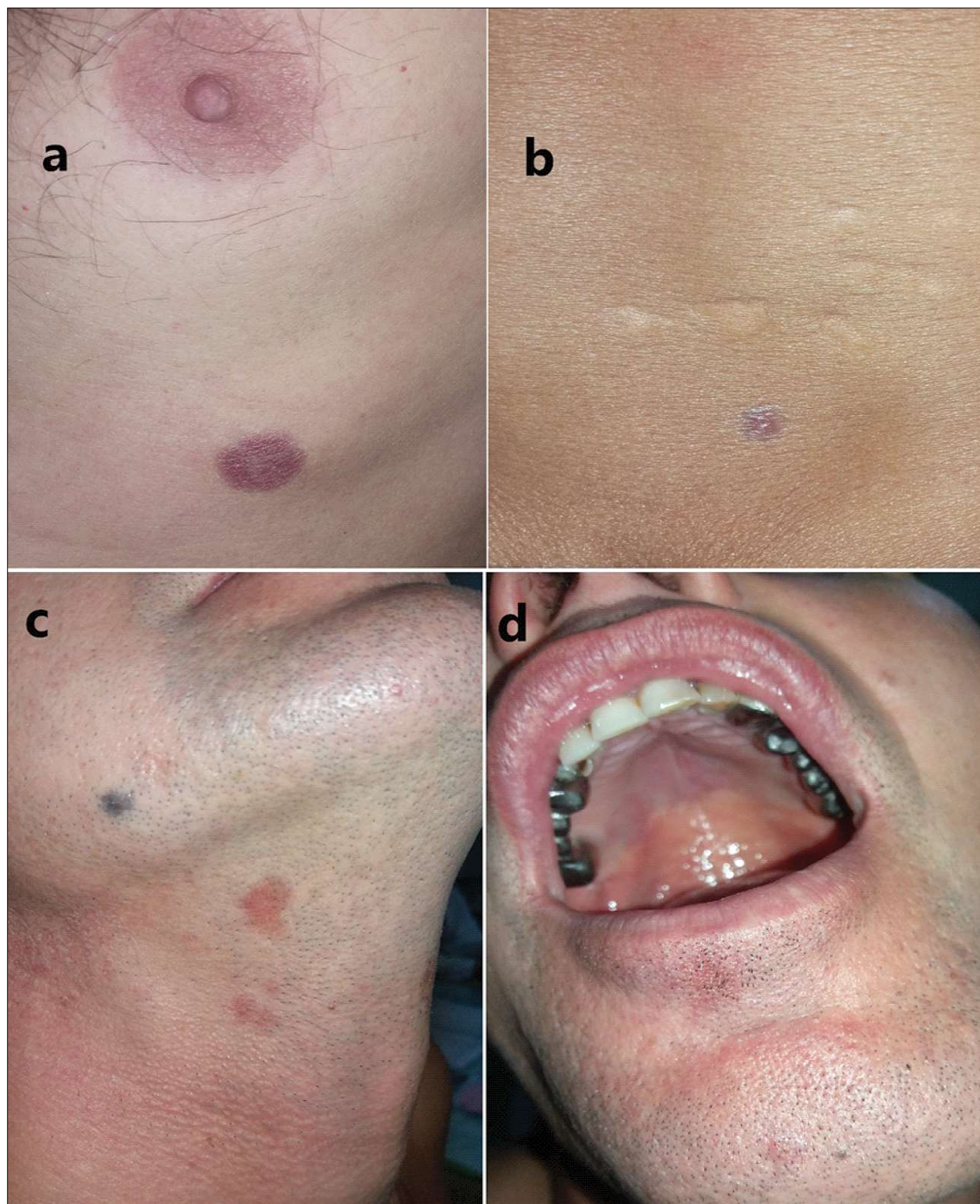


Figure 4. a,b,c,d) Skin and mucosal lesion after the second dose of benzathin penicillin

Bibliography

1. Richardson D, Fitzpatrick C, Finnerty F et al. Symptomatic secondary syphilis: empirical antimicrobial treatment or await microbiology?. *Sex Health* 2019;16(6):598-599.
2. Richardson D, Pickering A, Nichols K et al. Factors associated with testing positive for syphilis among MSM who present as sexual contacts of syphilis from a clinic-based population. *Sex Transm Infect* 2022;98(2):136-138.
3. Nieuwenburg SA, Sprenger RJ, Schim van der Loeff MF et al. Clinical outcomes of syphilis in HIV-negative and HIV-positive MSM: occurrence of repeat syphilis episodes and non-treponemal serology responses. *Sex Transm Infect* 2022;98(2):95-100.
4. Bhugra P, Maiti A. Secondary Syphilis. *N Engl J Med*. 2020;383(14):1375
5. Balagula Y, Mattei PL, Wisco OJ et al. The great imitator revisited: the spectrum of atypical cutaneous manifestations of secondary syphilis. *Int J Dermatol*. 2014 ;53(12):1434-441.
Eyer-Silva WA, Souza VPB, Silva GARD et al. Secondary syphilis presenting as a corymbiform syphilide: case report and review. *Rev Inst Med Trop, Sao Paulo*. 2018;60:e40.
6. Noviyanthi RA, Kurniadi I, Iswanti M et al. Overlap of psoriasiform and primary syphilis: an atypical manifestation of secondary syphilis (a case report). *Pan Afr Med J*, 2022;42:229.
7. Zhang J, Li X, Shi D. A case of secondary syphilis misdiagnosed as psoriasis vulgaris: Discover the real cause beyond the surface with reflection confocal microscopy and leave the great imitator nowhere to hide. *Skin Res Technol*. 2023;29(6):e13374.
8. Tambe S, Zambare U, Nayak C. Nodulo-ulcerative and erythrodermic secondary syphilis in human immunodeficiency virus-infected individuals. *Int J STD AIDS* 2019;30(5):505-508.
9. Li QF, Han K, Gurung I et al. Secondary syphilis presented with impetigo-like lesions: a rare case report. *Int J Dermatol*. 2018;57(11):e141-e142.
10. Barbosa J, João AL, João A et al. Secondary Syphilis-Induced Anetoderma. *Actas Dermosifiliogr*. 2024;115(8):838-840.
11. Quattri E, Giacalone S, Morini N et al. Secondary syphilis simulating cutaneous lymphomatous infiltration. *Ital J Dermatol Venerol*. 2023;158(3):275-276.
12. Ramoni S, Ponziani A, Boneschi V et al. Annular secondary syphilis. *G Ital Dermatol Venereol*. 2019;154(1):93-94.
13. Liu H, Goh BT, Huang T et al. Secondary syphilis presenting as erythema multiforme in a HIV-positive homosexual man: a case report and literature review. *Int J STD AIDS* 2019;30(3):304-309.
14. Chiu CY, Hasbun R. Diffused nodular secondary syphilis. *QJM*. 2023;116(1):71-73.
15. Carbone PN, Capra GG, Nelson BL. Oral Secondary Syphilis. *Head Neck Pathol*. 2016;10(2):206-208.
16. Shwetz ACA, Almeida GB, Cavalcante RS et al. Secondary syphilis concomitant with primary lesion and early neurosyphilis in a kidney transplant recipient. *An Bras Dermatol*. 2023;98(5):725-729.
17. Gupta P, Sethy M, Thakur V. Annular syphilis: atypical secondary syphilis. *QJM* 2024 ;117(5):364-365.
18. Lee YP, Lin C, Tu WT et al. Folliculotropic non-alopecic secondary syphilis presenting with rosary beads-like annular plaques. *J Eur Acad Dermatol Venereol*. 2023;37(6):e701-e703.
19. Trinh NB, Wu YH, Hieu HT. Penile annular secondary syphilis mimicking annular lichen planus. *Int J Dermatol*. 2022 Mar;61(3):e115-e116.
20. 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(12):1401-1403.
21. Sun Y, Yang TT, Huang TH et al. Secondary syphilis resembling lymphoma-like nodules in a 59-year-old woman. *J Eur Acad Dermatol Venereol*. 2022;36(12):e1027-e1029.
22. Rysgaard C, Alexander E, Swick BL. Nodular secondary syphilis with associated granulomatous inflammation: case report and literature review. *J Cutan Pathol* 2014;41(4):370-379.
23. Rosmaninho A, Sanches M, Lobo I et al. Nodular secondary syphilis. *Eur J Dermatol*. 2011;21(1):136-137.
24. Correia C, Mendes R, Sanches M et al. A unique presentation of papulonodular secondary syphilis in an elderly patient. *Int J Dermatol* 2021;60(8):e304-e306.
25. Gori A, Maio V, Grazzini M et al. Secondary syphilis mimicking Kaposi sarcoma in an HIV patient. *Eur J Dermatol* 2013;23(1):120-121.
26. Veasey JV, Lellis RF, Boin MF et al. Papulonodular secondary syphilis: a rare clinic presentation confirmed by serologic and histologic exams. *An Bras Dermatol* 2016 ;91(2):205-257.
27. Fukae S, Aozasa N, Tarumoto N et al. Secondary syphilis presenting with widespread psoriasiform lesions. *J Dermatol*. 2024;51(2):e27-e28.

28. Bains A, Tyagi N. Scrotal plaques as a predominant presentation in a case of secondary syphilis. *Indian J Dermatol Venereol Leprol* 2021;87(2):252-254.
29. Pisano L, Tiradritti L. Visual Dermatology: Overlapping Primary and Secondary Syphilis Mimicking Penile Carcinoma. *J Cutan Med Surg* 2020;24(6):633.
30. Mansouri S, Mai S, Senouci K et al. Secondary syphilis resembling erythema annulare centrifugum. *BMJ Case Rep* 2019;12(5):e230301.
31. Genovese G, Nazzaro G, Coggi A et al. Secondary syphilis masquerading as lupus vulgaris in an HIV-infected patient: A diagnosis suggested by histology. *Int J STD AIDS*. 2018;29(14):1454-1456.
32. Secondary syphilis mimicking tuberculoid leprosy in an HIV-positive individual: a case report. *Int J STD AIDS* 2019;30(12):1235-1238.
33. Lutz C, Ejeil AL. Oral manifestations of secondary syphilis. *Rev Prat* 2022;72(10):1109
34. Mullooly C, Higgins SP. Secondary syphilis: the classical triad of skin rash, mucosal ulceration and lymphadenopathy. *Int J STD AIDS*; 21(8):537-545.
35. Thakrar P, Aclimandos W, Goldmeier D et al. Oral ulcers as a presentation of secondary syphilis. *Lin Exp Dermatol*. 2018; 43(8): 868-875.
36. Lampros A, Seta V, Gerhardt P et al. Oral forms of secondary syphilis: An illustration of the pitfalls set by the great imitator. *J Am Acad Dermatol*. 2021;84(2):348-353.
37. de Paulo LF, Servato JP, Oliveira MT et al. Oral Manifestations of Secondary Syphilis. *Int J Infect Dis*. 2015;35:40-42.
38. Carvalho L, Hespanha B, Tinoco J. Unusual Presentation of Secondary Syphilis in the Oral Cavity. *Acta Med Port*. 2023;36(10):687-688.
39. Chantapitak J, Chuamanochan M. Intertriginous Rash in Secondary Syphilis. *N Engl J Med*. 2024;391(14):e28.

Conflict of interest
NONE DECLARED

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