Case Series

# Syphilis D' Emblée: A case series of the great masquerader

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## Abstract

Syphilis, a chronic infectious disease caused by Treponema pallidum subspecies pallidum, progresses through three arbitrary stages resulting in varied clinical manifestations. The aberrant presentation of syphilis in the secondary stage without any clinical evidence of the primary stage is referred to as syphilis d' emblée. Here we report a series of six cases in male patients. Five out of six patients presented with multiple, non-pruritic, macular palmar, and/or plantar lesions. One patient had typical facial and perianal lesions of condyloma lata. The diagnosis was confirmed by a reactive VDRL with titers ranging from 1:16 to 1:64 and a positive Treponema pallidum hemagglutination assay (TPHA). Syphilis being a great imitator can present in different ways without a typical history of primary chancre following sexual exposure, and can mimic many dermatological disorders in its secondary stage. Unless physicians have a high index of suspicion, the diagnosis may be missed. Early identification aids in prompt initiation of therapy and prevention of disease progression to chronic stages and systemic manifestations.

**Keywords:** Syphilis, syphilis d'emblée, VDRL

## Introduction

Syphilis is a chronic infectious disease caused by Treponema pallidum. The term "syphilis" comes from the poem "syphilis sive morbus gallicus" penned by an Italian physician named Girolamo Fracastoro. Its incidence has decreased significantly since the advent of antibiotics. However, the disease has recently reemerged.[1]

Untreated syphilitic infection has a triphasic natural history that usually progresses through three stages: primary, secondary, and tertiary, each separated by a period of time in which there is no clinical indication of infection, known as latency. The typical chancre of primary syphilis is a painless ulcer with an indurated base, commonly over the penis in males and on the labia, fourchette, or cervix, along with modest lymphadenopathy in females. Secondary syphilis exhibits varied manifestations, including mild fever, headache, sore throat, malaise, cutaneous or mucosal rash, and lymphadenopathy. Tertiary syphilis manifests itself in a variety of clinical syndromes, which can be categorized as neurosyphilis, cardiovascular syphilis, and late benign syphilis.

Because of its potentially variable clinical presentation, Sir William Osler coined the phrase "He who understands syphilis understands medicine."[2] Syphilis D' emblée is a form of early syphilis without any primary lesion. Herein we present a series of six cases of secondary syphilis with this type of presentation.

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## Case Reports

### Case 1

A 27-year-old unmarried male came with asymptomatic skin rashes over both palms and soles since 2 weeks. Dermatological examination revealed discrete bilaterally symmetrical hyperpigmented maculopapular eruptions with scaling over palms and instep of soles [Figure 1]. He had bilateral, multiple, discrete, enlarged, rubbery, non-tender, inguinal nodes of size ~1 × 1 cm. Axillary nodes were just palpable.

Serology revealed RPR to be reactive in 1:16 dilution. TPHA test was reactive in 1:32 dilution. Because the patient refused consent for inj benzathine penicillin, he was started on oral doxycycline 100 mg twice daily for 15 days.

### Case 2

A 30-year-old married male had complaints of skin rashes over both soles since 1 month. Dermatological examination showed bilateral multiple discrete symmetrical hyperpigmented maculopapular lesions with peripheral scaling over the instep of soles [Figure 2]. His wife was aymptomatic. The couple were sexually active but had a history of inability to conceive since 1.5 years.

Both had a reactive VDRL in 1:32 dilutions and TPHA was reactive in 1:64 dilutions. Both were given benzathine penicillin 2.4 million IU intramuscular single dose simultaneously. He developed fever and joint pains 4 hours after the injection. This was diagnosed as a Jarisch–Herximer reaction (JHR) and treated appropriately.

### Case 3

A 25-year-old male was admitted in the casualty for palpitation and breathlessness due to supraventricular tachycardia (SVT) and was treated with tablet Metaprolol. The patient had a history of penetrating injury to the left eye in childhood and was surgically managed with the placement of a prosthetic eye. He also had skin rashes over his feet and left shoulder.

Dermatological examination showed few, well-defined, hyperpigmented, non-tender macules (size ranging from 2 × 2 cm to 0.5 × 0.5 cm) noted over the instep region of both soles [Figure 3]. Single, well-defined, erythematous scaly plaque with raised border and central clearing of size ~2 × 2 cm was present over the posterior aspect of left shoulder. It was positive for fungal filaments on KOH mount examination.

KOH smear from soles revealed no fungal elements. VDRL was reactive in 1:32 dilutions and TPHA reactive in 1:320 dilutions, while serology for HIV, HCV, and HBsAg was non-reactive. He had an episode of penicillin allergy in childhood and hence was started on oral doxycycline 100 mg twice daily and 1% luliconazole cream twice daily application over shoulder lesion for 15 days and was advised to review.

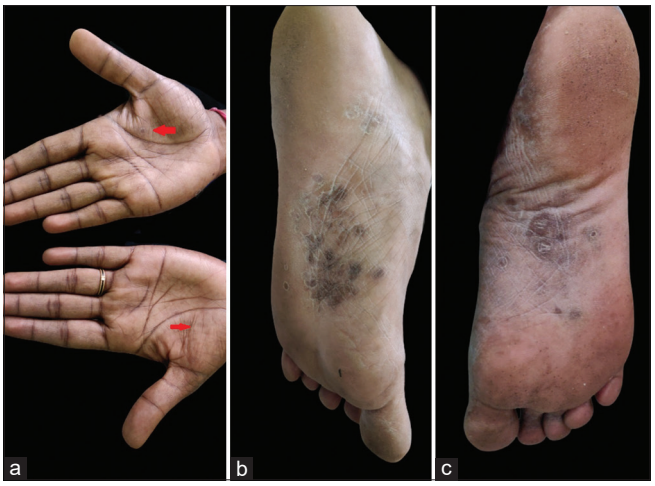


**Figure 1:** (a) Few symmetrical brownish macules over both palms. (b and c) Multiple brownish macules with scaling over the instep region of both soles

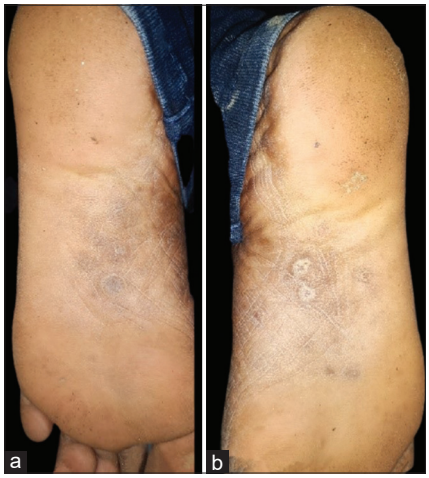


**Figure 2:** (a and b) Multiple brown macules with peripheral scaling over the instep of both soles

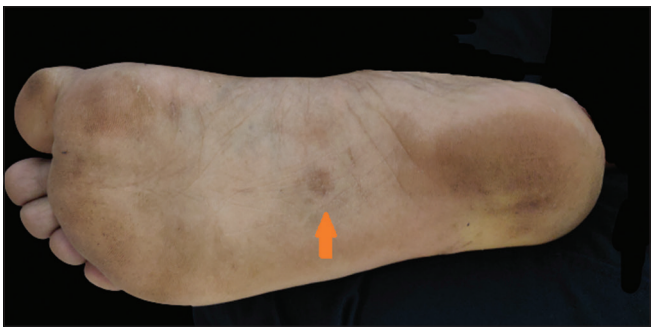

**Figure 3:** Single, brownish macule present over the instep of right sole

### Case 4

A 17-year-old boy presented with grayish plaques at angles of the mouth, genitals, and perianal region and asymptomatic papules on the forehead since 10 days. On examination, grayish moist plaques were seen at the penoscrotal angle [Figure 4c], perianal region [Figure 4b], both crura and angles of the mouth (cut

pea appearance). Generalized non-pruritic papular eruption, more prominent on the forehead [Figure 4a], just below the hairline (crown of venus), was noted. The occipital, axillary, and epitrochlear lymph nodes on both sides were enlarged, rubbery, and non-tender.

Darkground examination revealed motile organisms suggestive of spirochetes. VDRL test was reactive (1:64) and the TPHA test was also reactive (1:160). He was treated with a single intramuscular injection of benzathine penicillin 2.4 million IU.

## Case 5

A 30-year-old unmarried male presented with asymptomatic skin rashes over the palms of 1-month duration. On examination, discrete bilaterally symmetrical non-tender, hyperpigmented scaly maculopapular eruptions were present over both palms. [Figure 5]

He had multiple, bilateral, enlarged, rubbery, non-tender, inguinal nodes of size ~1 × 1 cm. Axillary and submandibular nodes were just palpable. RPR was reactive with 1:16 dilutions and TPHA test was reactive with 1:32 dilutions. He was treated with a single dose of intramuscular injection of benzathine penicillin 2.4 million IU.

## Case 6

A 23-year-old male came with asymptomatic skin rashes over his palms, which started 3 weeks back and gradually increased in number. Dermatological examination revealed multiple, bilaterally symmetrical, erythematous patches over both palms. [Figure 6]

Bilateral, multiple, enlarged, rubbery, non-tender, inguinal nodes were palpable. RPR was reactive with 1:16 dilutions and TPHA test was reactive with 1:32 dilutions. The patient was subsequently administered a single intramuscular dose of 2.4 million IU of benzathine penicillin.

The key features of all 6 cases are summarized in a tabular form [Table 1].

## Discussion

Secondary syphilis develops from disseminated T. pallidum infection despite high levels of anti-treponemal antibodies. Skin rash is the most common manifestation of secondary syphilis and can mimic a variety of dermatoses, including pityriasis rosea, psoriasis, erythema multiforme, and drug eruptions. Up to 60% of patients with serological evidence of syphilis have no recollection of any early syphilis symptoms or manifestations.[3] The primary stage is likely to be absent in cases of infection resulting from deep inoculation of Treponemes, as from puncture wounds with needles or blood transfusion with infected blood. This variant is called "syphilis d' emblée" and presents directly with signs and symptoms of the secondary stage.[4]

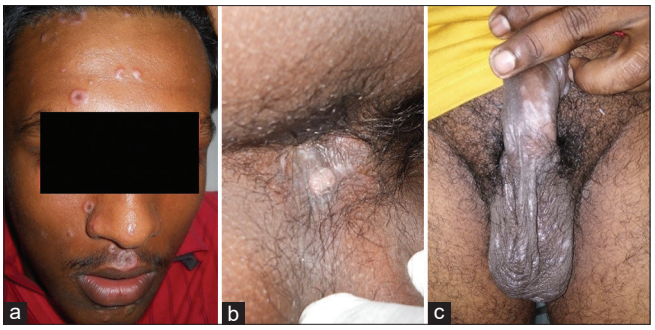


**Figure 4:** (a) Multiple non-pruritic papular eruptions prominent just below the hairline (crown of venus). (b) Single, grayish plaque in the perianal region. (c) Multiple grayish moist plaques at peno-scrotal angle

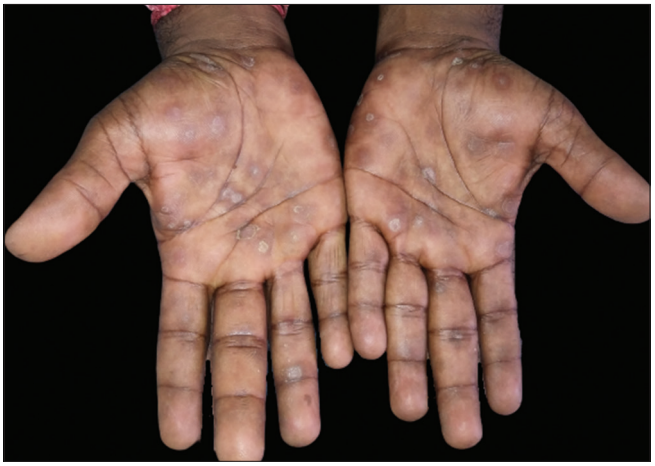

**Figure 5:** Multiple, brownish scaly macules over both palms

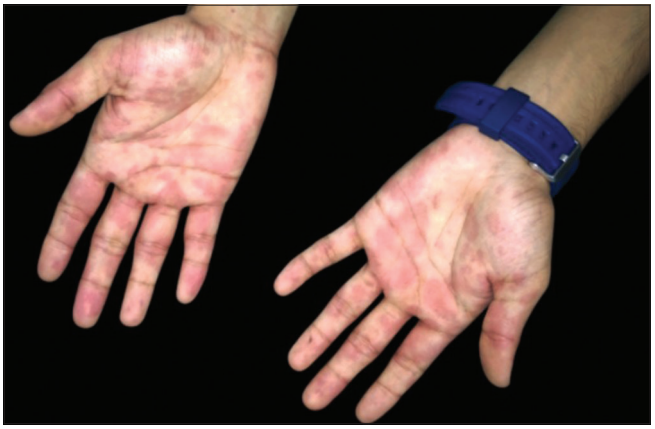

**Figure 6:** Multiple, erythematous non-scaly patches over both palms

In our case series, five out of six (83%) patients had involvement of palms and/or soles. Differential diagnoses of secondary syphilis, palmoplantar psoriasis, and contact dermatitis were considered for these lesions on palms and soles. The palmoplantar rash in secondary syphilis is usually well-demarcated, discrete, and sometimes minimal, consisting of just one or two lesions that go unnoticed.[3,5] It is therefore important to always consider secondary syphilis as a possibility when dealing with asymptomatic, atypical, papulosquamous skin lesions, especially those affecting palms and soles.

**Table 1: Clinical summary of cases**

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 |
|---|---|---|---|---|---|---|
| Age (in years) | 27 | 30 | 27 | 17 | 30 | 23 |
| Sex | M | M | M | M | M | M |
| Marital status | Unmarried | Married | Unmarried | Unmarried | Unmarried | Unmarried |
| Duration | 2 weeks | 1 month | 1 month | 10 days | 1 month | 3 weeks |
| H/o sexual exposure | Denies | Present<br>LMC - 1 week back<br>EMC - Denies | Denies | Denies | Denies | Denies |
| H/o blood transfusion/ drug abuse | Absent | Absent | Absent | Absent | Absent | Absent |
| H/o Genital ulcer | Absent | Absent | Absent | Absent | Absent | Absent |
| H/o constitutional systemic symptoms | Nil | Nil | H/o palpitation and breathlessness present | Nil | Nil | Nil |
| Examination | | | | | | |
| 1. Skin rash | Scaly hyperpigmented macules over palms and soles | Scaly hyperpigmented macules on soles | Hyperpigmented macules on both soles, scaly plaque on left shoulder | Paupular eruption on face, neck<br>Scaly plaques on scalp | Scaly hyperpigmented maculopapular eruptions on palms | Erythematous patches and macules on palms |
| 2. Mucus membrane lesions | Nil | Nil | Nil | Grayish moist plaques over angles of mouth, genitals and perianal region | Nil | Nil |
| 3. Lymphadenopathy | Rubbery non-tender Inguinal; just palpable axillary nodes | Non-enlarged, just palpable inguinal nodes | No enlarged, just palpable inguinal nodes | Enlarged, rubbery, non-tender occipital, axillary & epitrochlear nodes | Enlarged, rubbery, non-tender inguinal; just palpable axillary, submandibular nodes | Enlarged, rubbery, non-tender Inguinal nodes |
| 4. Ocular examination | Normal | Normal | Prosthetic left eye | Normal | Normal | Normal |
| 5. Systemic examination | No abnormalities noted | No abnormalities noted | SVT | No abnormalities noted | No abnormalities noted | No abnormalities noted |
| 6. Comorbidities | Nil | Nil | SVT | Nil | Nil | Nil |
| 7. Routine lab investigations | Within acceptable range | Within acceptable range | Within acceptable range | Within acceptable range | Within acceptable range | Within acceptable range |
| 8. Serology | VDRL (1:16), TPHA (1:32)- Reactive | VDRL (1:32), TPHA (1:64) - Reactive | VDRL (1:32), TPHA (1:320) - Reactive | VDRL (1:64), TPHA (1:160)- Reactive | VDRL (1:16), TPHA (1:32) - Reactive | VDRL (1:16), TPHA (1:32) - Reactive |
| Treatment given | C. Doxycycline 100 mg BD * 15 days | Benzathine penicillin 2.4 million IU IM single dose | C. Doxycycline 100 mg BD * 15 days | Benzathine penicillin 2.4 million IM single dose | Benzathine penicillin 2.4 million IM single dose | Benzathine penicillin 2.4 million IM single dose |
| Treatment outcome | Lesions resolved | Lesions resolved | Lost follow up | Lost follow up | Lost follow up | Patient lost to follow up |
| Remarks | - | Partner VDRL 1:32, TPHA (1:64) - Reactive, same treatment given | - | - | - | - |

In the absence of primary genital lesions, the clinician's index of suspicion regarding syphilis is tested even more. None of the subjects in our case series had a history of primary syphilitic chancre, and five out of six (83%) subjects denied a history of any form of sexual contact. The denial of risky sexual exposure, drug abuse, and blood transfusion further escalates the diagnostic challenge.

Four of the six (66%) patients had enlarged, rubbery, discrete, and non-tender lymph nodes. Lymphadenopathy involving two or more groups is seen in 60%–100% of patients with secondary syphilis.[3] The severity of the presenting illness is unrelated to the degree of lymphadenopathy, and glands seldom expand to the proportions associated with malignancies, including lymphomas.[6] The existence of lymphadenopathy along with asymptomatic scaly palmoplantar lesions goes more in favor of secondary syphilis as the underlying diagnosis as concomitant lymphadenopathy is uncommon with the other common dermatoses with scaly palmoplantar lesions.

One of the patients (16%) had palpitations and was diagnosed with supraventricular tachycardia. Cardiovascular complications in secondary syphilis are rare but myocarditis and ventricular arrhythmias in secondary syphilis are well-documented.[7,8]

JHR was noted in one patient 4 hours after treatment with Benzathine penicillin. JHR occurs due to the spontaneous release of lipopolysaccharides on bacterial cell membranes upon exposure to antibiotics and can be accompanied by an inflammatory response manifesting with fever, arthralgia, myalgia, nausea, and headache.[9] Its occurrence should be anticipated in all patients receiving antibiotic treatment for syphilis (especially secondary syphilis) and should not be mistaken for a drug reaction to penicillin.

Non-sexual treponemal transmission in early acquired or congenital forms through direct contact with exposed lesions is unlikely. Other rare modes of transmission include direct transfusion of contaminated blood and exposure to infected fomites.[10,11] Clinical scenarios wherein there is no history suggestive of the possibility of usual modes of transmission emphasize the need for further research into lesser-known modes, such as through fomites.

Earlier studies have shown that aberrant morphologies can be found in up to 29.6% of secondary syphilis cutaneous lesions.[12] Patients can be undiagnosed or misdiagnosed as an allergic response for long periods of time before being finally identified as secondary syphilis based on newly discovered sexual history or serological and pathological investigations.[13]

The major strategy for successful management of patients with sexually transmitted infections (STIs) has been to incorporate STI services into the current healthcare system and to follow the syndromic management recommendations. Primary care physicians need to be familiar with such cutaneous manifestations of such an atypical yet common multisystem disease. Early diagnosis and counseling of index patients should be routinely incorporated into the practice of primary care physicians with an aim to increase partner notification and minimize fear and stigma associated with STIs. For patients presenting at the primary care level with non-specific bilateral, asymptomatic palmoplantar lesions, we suggest a routine VDRL/RPR screening. If found to be reactive (VDRL/RPR), they may be referred to a specialist (dermatovenereologist) for further appropriate management. Such an intervention at the primary care level could go a long way towards reducing the transmission of syphilis.

Doxycycline post-exposure prophylaxis (PEP) has the potential to reduce syphilis incidence but has received limited attention. A study evaluated the long-term population impact of prophylactic doxycycline and indicated that doxycycline PEP may be most suited as a secondary infection prevention strategy, following condoms and improved screening.[14] Another study revealed that individuals who received PEP with a single 200 mg doxycycline treated within 72 hours following a high-risk sexual contact had a 73% lower risk of developing syphilis.[15]

This case series portrays the heterogeneous and subtle presentations of this "great imitator" and further highlights the significance of including syphilis as a differential diagnosis for maculopapular eruptions of palms and soles. Routine syphilis serological screening is advised in such patients to facilitate early detection and treatment of syphilis, curbing further progression of the disease and remaining prudent of the deceitful treponeme.

**Note**: check ethical and institutional permission taken and duly mentioned in the manuscript.

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## Conflicts of interest

There are no conflicts of interest.

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