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Case Report

A complex presentation of complicated secondary syphilis with ulcerated lesion progression

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Abstract

Secondary syphilis is commonly associated with well-known cutaneous and mucosal manifestations, including maculopapular rashes and condylomata lata. However, clinical presentation can vary significantly, often resembling other dermatological or infectious conditions, which can lead to diagnostic delays and challenges, particularly in immunocompetent individuals. We report the case of a 26-year-old heterosexual Asian man working as a baggage handler at a busy international airport, who presented with a rapidly progressive, painful rash. Initially treated with flucloxacillin, his condition worsened, spreading to his face, trunk, and mucous membranes, accompanied by fever, tachycardia, and difficulty swallowing. Physical examination revealed widespread umbilicated vesicles, haemorrhagic blisters on his right lower leg, and ulcers in the oral cavity. Despite negative results for common viral infections (HSV, VZV, HIV) and autoimmune disorders, serological testing for syphilis revealed a positive rapid plasma regain test, confirmed by a positive treponemal antibody EIA test and subsequent clinical improvement with appropriate antibiotic therapy. Following the diagnosis of secondary syphilis, the patient was treated with benzathine penicillin and supportive care. He experienced a mild Jarisch-Herxheimer reaction, which resolved with monitoring. A subsequent infection of a fungating lesion (bacteria superimposition) on the right shin was managed with amoxicillin/clavulanic acid. By the patient's follow-up visit, the skin lesions had markedly improved, and he was discharged with ongoing care and penicillin treatment. This case highlights the importance of considering syphilis in the differential diagnosis of atypical cutaneous and mucosal lesions, especially when presenting with systemic symptoms. The diagnosis of secondary syphilis can be challenging due to its diverse clinical manifestations, which may mimic other infectious or autoimmune conditions. A careful diagnostic approach, including serological and polymerase chain reaction testing, is essential for accurate diagnosis and effective treatment. This case also emphasizes the need for timely public health intervention and education in high-risk populations.

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Introduction

Syphilis, a sexually transmitted infection (STI) caused by the bacteria spirochete *Treponema Pallidum* exhibits four stages (primary, secondary, latent, and tertiary) of disease progression [1, 2]. Primary syphilis' typical presentation is a single painless sore called a chancre, which can be found anywhere with regional lymphadenopathy [2]. If not correctly treated, it can progress to secondary syphilis. Manifestation of secondary syphilis may include a diffuse mucocutaneous rash, headache, myalgia, generalised lymphadenopathy, and ulceration on the mucosa [2]. Patients with secondary syphilis recover after 3-6 weeks without treatment and enter the latent phase; however, around a quarter will relapse and have further episodes [3]. Approximately a third of patients in the latent phase will develop into late syphilis, formerly known as tertiary syphilis, with involvement of cardiac, neurological, and gummatous manifestations [2, 3]

Syphilis is most common among gay, bisexual, and other men who have sex with men (GBMSM) aged 25 to 34, with a significant proportion of them also living with HIV. In 2023, England reported a total of 12,588 new cases of syphilis, of which 76% (9,513) were infectious and 3,075 were acquired [4]. This resulted in an 11% jump in cases in 2023 compared to 2022. Furthermore, 76% of these occurred in GBMSM. Of these cases, 26% were among individuals living with HIV [4]. The incidence of infectious syphilis diagnoses in 2023 by ethnicity is white (61%), Asian (9%), Black African (6%), Black Caribbean (6%), Other Black (2%), Mixed (5%), Other (3%), and Unknown (8%). [4]

The main investigations for a presumed diagnosis of syphilis are two serological tests: a non-treponemal test, e.g., rapid plasma reagin (RPR) or Venereal Disease Research Laboratory (VDR), and a treponemal test, e.g., immunoblots, enzyme immunoassays (EIAs), Treponema Pallidum passive particle agglutination test (TP-PA), rapid treponemal assays, and chemiluminescence immunoassays (CLIAs). Both types of serological tests are needed to confirm the diagnosis [2, 5]. There are various management protocols for syphilis. The British Association for Sexual Health & HIV (BASHH) UK guidelines recommend for early syphilis (primary, secondary or early latent) a single dose of Benzathine Penicillin 2.4 MU IM. For late latent (neurological/cardiovascular and gummatous syphilis), a weekly dose of Benzathine Penicillin 2.4 MU IM for 3 weeks is recommended [6].

There is a recognised underrepresentation of darker skin in medical education. This can affect the ability of clinicians to diagnose skin rashes and lesions in people of colour. A dermatological study assessed 424 images with identifiable skin types. Skin lesions in light skin were portrayed in 47.6% of all images compared to 41.7% of intermediate skin and 10.7% of dark skin. Responses to the challenge correctly diagnosed pathology in 50.4% of light skin, compared to 50.5% of intermediate skin and 44.3% of dark skin [7]. Our case study highlights a case of secondary syphilis in a person of colour with an initial diagnostic dilemma, while treated as cellulitis twice before a re-presentation with more severe symptoms.

Case Presentation

We present the case of a 26-year-old Asian heterosexual man with a single female partner. The patient initially presented with painful blisters, erythematous vesicular rash with central crusting on some lesions, and swelling on both lower legs, progressing over several days. Following initial treatment with flucloxacillin, his rash spread to the face, trunk, arms, and mouth, with painful mucosal lesions. The patient also had difficulty swallowing and systemic symptoms, including fever and perception of fast heart beat. Physical examination revealed widespread umbilicated vesicles, haemorrhagic blisters on the right lower leg, and ulcers in the oral cavity with tender cervical lymphadenopathy (see figures 1 A and B). No prior dermatological disorders were reported. He is unclear about his childhood vaccination status.

Figure 1A:

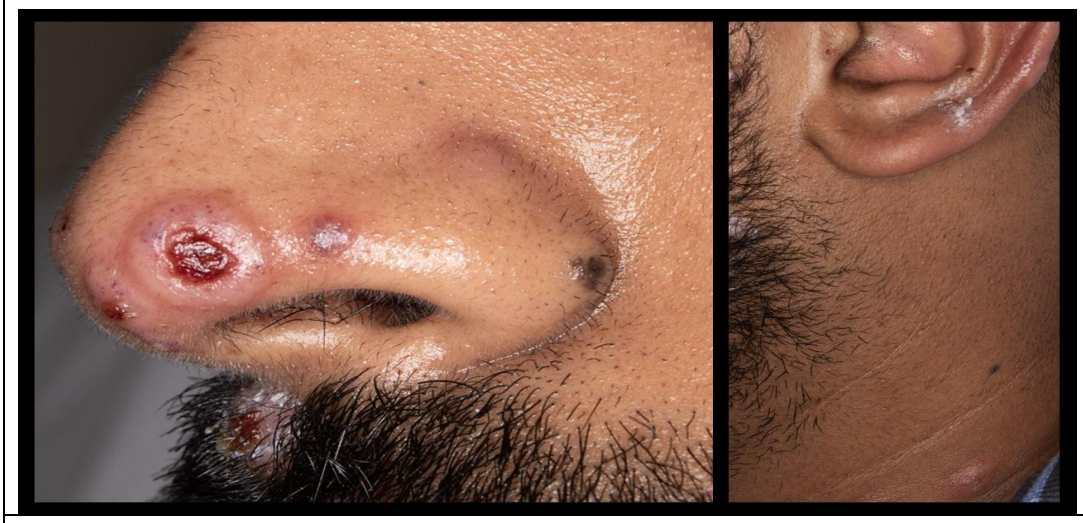

Figure 1B:

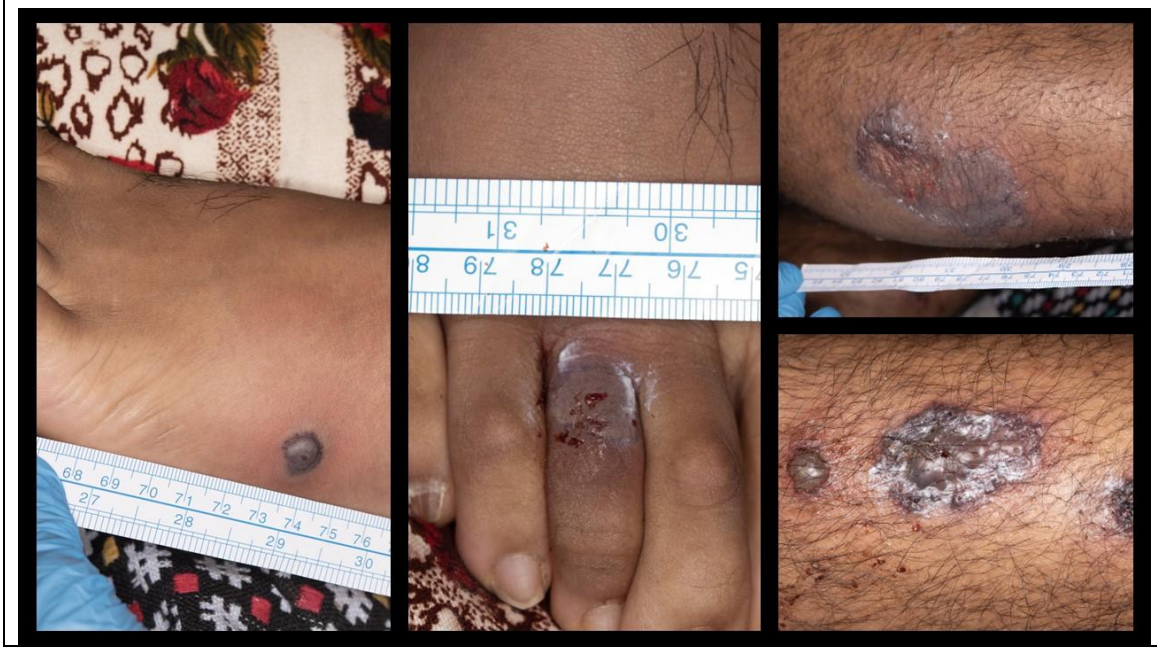

Figure 1A: showing multiple blistering lesions with central crusting and Figure 1B: showing hyperpigmented multiple blistering lesions of different sizes present in different parts of the body.

Investigations and Diagnosis

Initial microbiology investigations, including syphilis serology (RPR 1:16), were suggestive of secondary syphilis. Swabs for orthopox virus were initially reactive. Further testing, including Polymerase chain reaction (PCR) for Herpes Simplex Virus (HSV), varicella zoster virus (VZV), and mpox, were negative. HIV and other viruses, such as rubella and hepatitis viruses, were all negative. A confirmatory syphilis diagnosis was made after a positive treponemal antibody EIA test. Dermatological consultation initially raised suspicion for autoimmune skin conditions like pemphigus vulgaris, but the conclusion was to treat for syphilis, and if there was no response, request for a biopsy.

Management

The patient was initially treated with broad-spectrum antibiotics (meropenem, clindamycin, Doxycycline) and antivirals (acyclovir). This was necessary to cover for secondary bacterial infection. He developed Jarisch-Herxheimer reactions, evidenced by new fever and transaminitis within 24 hours of antibiotics. Fever settled within 24 hours, but transaminitis took a week to completely resolve. Following confirmation of secondary syphilis, treatment was switched to benzathine penicillin with supportive care. The patient responded well to treatment, with significant improvement in his rash and systemic symptoms.

Outcome and Follow-up

By the end of the second week, the patient's lesions were improving, and he was discharged with a follow-up plan for continued penicillin treatment. At his follow-up visit, a month later, although he felt generally well, a fungating (ulcerated) lesion on his right shin was noted, likely related to secondary syphilis (see figure 2). A wound swab was obtained, and he commenced amoxicillin/clavulanic acid for secondary bacterial infection on an outpatient basis. The wound swab grew *Staphylococcus aureus* with sensitivity to amoxicillin/clavulanic acid. At telephone follow-up about 2 weeks later, the patient reported healed ulcers with no complications. This case highlights the complex presentation of secondary syphilis and the diagnostic challenges associated with skin lesions in an immunocompetent individual. A thorough differential diagnosis, including viral, bacterial, and autoimmune aetiologies, is crucial for proper management.

Figure 2:

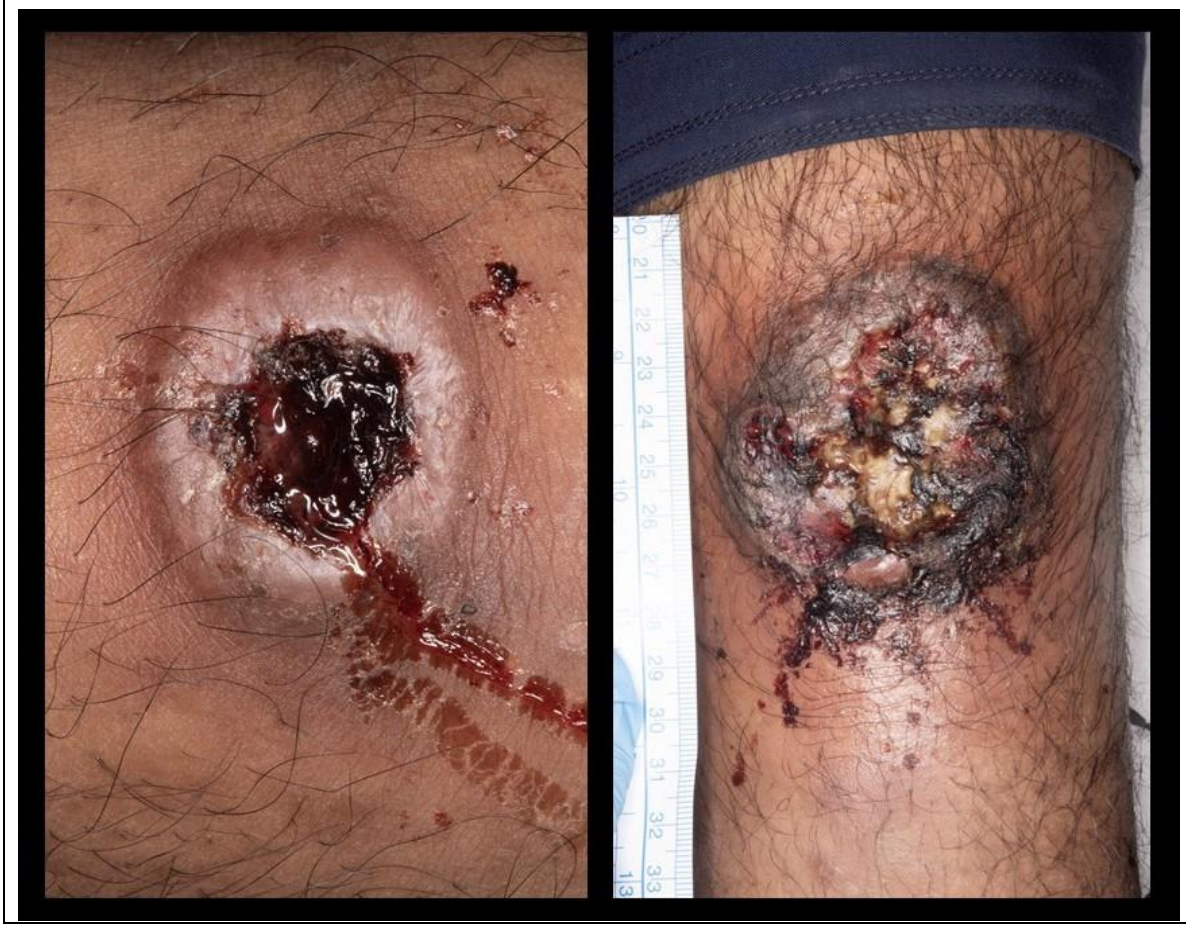

Figure 2: showing a fungating (ulcerated) lesion on his right shin.

Discussion

This case underscores the diagnostic challenges associated with complex presentations of secondary syphilis, particularly in immunocompetent individuals. While syphilis typically manifests well-characterized stages, the variable and often nonspecific presentation of secondary syphilis can complicate diagnosis, especially when skin lesions and systemic symptoms diverge from classical features. This patient's progression from localized blisters to systemic involvement, including fever, tachycardia, mucosal ulcers, and a generalized rash with subsequent fungating ulcer, exemplifies such complexity. On top of this, there is no multiple sexual contact, and the patient is a baggage handler in a busy international airport, which makes him a high risk for imported high-consequence infectious disease such as the mpox virus. The difficulty in identifying the condition highlights the importance of a comprehensive diagnostic approach, integrating clinical findings with microbiological and histopathological investigations.

Secondary syphilis is generally recognized by its characteristic cutaneous manifestations, including maculopapular rashes, condylomata lata, and mucosal lesions [8]. However, a complex presentation, such as the one observed in this case, is not uncommon, particularly when lesions resemble other dermatological or infectious conditions, such as pemphigus vulgaris, herpes simplex virus (HSV), varicella-zoster virus (VZV) infections, or mpox. The patient's rash, consisting of painful vesicles, haemorrhagic blisters, and mucosal ulcers, could easily be mistaken for viral exanthems or even autoimmune blistering diseases like pemphigus vulgaris [9]. Furthermore, the spread of lesions to the face, trunk, and extremities, combined with systemic symptoms like fever, suggested a more severe or disseminated infectious process [10], which initially led to the consideration of other diagnoses such as HSV, varicella, or even rubella, all of which were eventually ruled out. Furthermore, the patient's occupation in an international airport, which may expose him to contact with imported high-consequence infectious diseases such as the mpox virus, underscores the necessity of further screening for orthopox virus.

In this case, despite a serological indication of syphilis through positive RPR and confirmatory treponemal antibody test, the unusual presentation of blisters and ulcers raised initial confusion, particularly given the patient's unclear vaccination history, lack of prior dermatological disorders, no multiple sexual contacts, and occupation as a baggage handler in an international airport. The initial reactive results for the orthopox virus, which led to a PCR test, further complicated the diagnostic landscape. This could be explained as a false positive result due to cross-reactivity. This case emphasizes that while serological testing remains pivotal in the diagnosis of syphilis, clinicians must remain vigilant for potential cross-reactivity in initial screenings and consider the full spectrum of differential diagnoses before finalizing treatment plans [11].

The patient's development of a Jarisch-Herxheimer reaction (JHR) following the initiation of antibiotic treatment is a well-documented phenomenon in syphilis, typically presenting with fever, chills, and worsening of the rash [12]. JHR occurs because of the release of endotoxins from the dying spirochetes, and whilst it can be distressing, it is generally self-limiting [12]. In this patient, the JHR was marked by fever and transaminitis, both of which resolved following supportive care. It is critical to differentiate JHR from disease progression or secondary infections, particularly in cases where patients present with complex or escalating symptoms [13]. Prompt recognition and management of JHR can prevent unnecessary modifications to treatment protocols, ensuring the continuation of the effective regimen.

The management of secondary syphilis primarily involves the use of penicillin, typically in the form of benzathine penicillin G [6], as was administered to this patient once the diagnosis was confirmed. Despite the challenging presentation, the patient responded well to treatment, with significant improvement in

both cutaneous and systemic symptoms. However, the development of a fungating lesion on the right shin during follow-up suggests the possibility of secondary bacterial infection or complications associated with syphilitic ulcerations. This necessitated the addition of amoxicillin/clavulanic acid to address potential secondary bacterial pathogens. The patient's ongoing dermatological follow-up is essential to monitor for any further complications or relapse of symptoms. It is important to note that while penicillin remains the gold standard for treating syphilis, there are concerns about the increasing incidence of syphilis-related complications, including treatment failures and the potential for coinfections, particularly in high-risk populations [14, 15, 16].

Limitations:

This case report describes a single patient, which inherently limits the generalizability of its findings. While the presentation was unusual and instructive, conclusions drawn from a single clinical encounter may not apply to broader populations. Individual factors such as the patient's age, ethnicity, occupational exposure, and sexual history may have influenced both presentation and diagnostic challenges in ways that are not representative of other cases of secondary syphilis.

Another limitation is the incomplete exclusion of all possible coexisting conditions that could have contributed to the patient's presentation. Although a broad range of infectious and autoimmune differentials were investigated, including mpox, HSV, VZV, rubella, and pemphigus vulgaris, no skin biopsy was ultimately performed due to the patient's clinical improvement. This means that certain dermatological conditions, which can mimic or coexist with syphilis, could not be definitively ruled out. Lastly, diagnostic interpretation in this case was further complicated by the initial reactive orthopox virus result, which was later deemed a false positive. While follow-up PCR testing was negative, this raises the possibility of cross-reactivity or laboratory error, neither of which was fully investigated. Such uncertainties highlight the challenges of interpreting serological results in complex cases and underscore the potential for diagnostic delay or misdirection in similar clinical settings.

Key lessons

This case illustrates several key lessons in the diagnostic and management approach to secondary syphilis. Firstly, a thorough differential diagnosis is essential, particularly in the context of complex presentations, occupation of the patient, vaccination, and sexual history. Given the overlap in clinical manifestations between syphilis and other viral or autoimmune blistering diseases, a combination of clinical suspicion, serological testing, PCR, and decision for further histopathological examination is crucial to establish a definitive diagnosis. Furthermore, the management of secondary syphilis requires not only the correct use of antibiotics but also vigilant monitoring for treatment-related reactions and potential complications, including JHR and secondary infections.

Conclusion

Secondary syphilis can present with a wide range of clinical manifestations, some of which may be complex and difficult to distinguish from other infectious or autoimmune conditions. This case emphasizes the importance of a comprehensive diagnostic approach, careful consideration of differential diagnoses, and close follow-up to manage potential complications effectively. Early recognition and appropriate treatment of syphilis not only prevent further disease progression but also reduces transmission risks, underscoring the critical role of timely diagnosis and intervention.

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