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TEST YOUR KNOWLEDGE

Rash, red eyes, lip erosions and genital ulcer - What is the diagnosis?

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Abstract

Maculopapular eruptions are frequently described as large areas of rash characterised by red, small, confluent bumps. They are frequently puzzling for the attending clinician due to the multiple possible aetiologies. Accurate diagnosis is important because treatment varies depending on the aetiology, and some rashes can be life-threatening if not treated promptly. Common aetiologies implicated include drug allergies, infection-related (for example: viral exanthems, scarlet fever) and autoimmune conditions (for example: Still's disease). We report a case of maculopapular eruption associated with mucocutaneous involvement and systemic symptoms. The possible differential diagnoses and approach to the management of this patient are discussed.

Case Summary

A 26-year-old male presented with a 3-week history of rash involving the face, trunk, and limbs. There was associated fever, sore throat, red eyes, painless lip erosions, and left knee pain. He had no urethritis, but reported a painless, non-healing genital ulcer for 2 months. Examination revealed widespread erythematous maculopapular rash involving the face, chest, abdomen, bilateral arms, forearms, and thighs (Figure 1). The patient had bilateral conjunctivitis. The throat was injected without tonsillar enlargement. Superficial erosions were found on the lower lip (Figure 2). A clean-based ulcer with indurated border was seen on the penile shaft (Figure 3). He had tenosynovitis of the left knee and bilateral 'shotty' inguinal lymph nodes.

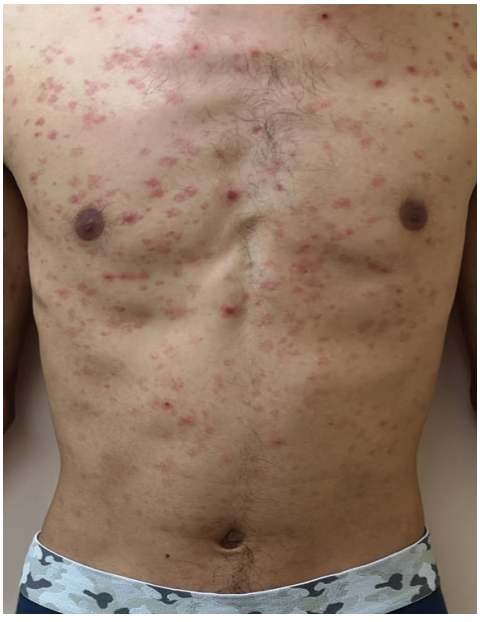

Figure 1. Widespread maculopapular rash on the trunk.

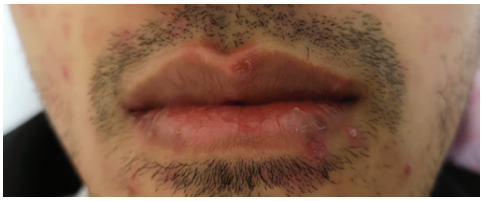

Figure 2. Well defined superficial erosions on the lower lip.

Figure 3. A clean-based ulcer with indurated border on the penile shaft.

Questions:

1. What further information would you like to elicit from history taking?
2. What differential diagnoses would you consider at this point?
3. What investigations would you like to perform?

Answers with discussion

1. What further information would you like to elicit from history taking?

    - History of recurrent oral, eye, or genital ulcers
    - History of recent initiation of drugs, traditional medications, or supplements
    - Sexual history
    - Other past medical history

The patient denied history of recurrent oral, eye, or genital ulcers. He also denied taking any medications or supplements. He admitted to being a male who had sex with males (MSM) and participated in unprotected anal and oral sex with multiple partners. His last sexual exposure was 3 months prior to presentation. He was positive for human immunodeficiency virus (HIV), which was detected 1 year prior.

2. What differential diagnoses would you consider at this point?

    - Stevens-Johnson syndrome
    - Disseminated gonococcal infection
    - Concurrent primary and secondary syphilis
    - Behcet's disease

Stevens-Johnson syndrome (SJS) is a life-threatening condition characterised by maculopapular eruption that spreads and forms blisters.[1] This condition is usually triggered by medications, such as antibiotics (penicillins and sulfonamides), anti-convulsants (phenytoin and carbamazepime), allopurinol, anti-retroviral therapy (nevirapine), and non-steroidal anti-inflammatory drugs (e.g., mefenamic acid, ibuprofen). typical exposure period is 4 days to 4 weeks. Treatment involves prompt withdrawal of the causative drug.[2] The rash of this patient was not characteristic of SJS. As the patient also denied recent drug initiation, SJS was an unlikely diagnosis.

Disseminated gonococcal infection (DGI) occurs 2–3 weeks after primary gonococcal infection.[3] DGI is characterised by a triad of tenosynovitis, dermatitis, and polyarthralgia. Cutaneous lesions usually involve the extremities and are described as tender and sparse papulo-pustules on a haemorrhagic base.[4] Treatment is intravenous or intramuscular ceftriaxone 1 g daily, continued for 24–48 hours after improvement of symptoms, before switching to an oral agent for a total treatment course of at least 7 days.[5]

Concurrent primary and secondary syphilis is an uncommon presentation of syphilis. It is seen more often in HIV-infected patients due to the rapid progression of the disease from primary to secondary stage, and the delayed healing of the genital ulcer.[6-8]

Behçet's disease (BD) is a rare and severely debilitating vasculitis that manifests as recurring orogenital ulcers and skin lesions. Diagnosis is made after excluding all other causes of orogenital ulcerations. Based on the International Study Group Criteria for BD, recurrent oral ulcerations at least 3 times in a 12-month period, plus any two of genital ulceration, eye lesions (anterior uveitis, posterior uveitis, cells in vitreous on slit lamp examination, or retinal vasculitis), skin lesions (erythema nodosum or papulopustular lesions), or a positive pathergy test supports the diagnosis of BD.[9] As this patient denies history of recurrent oral ulcers, BD is a less likely diagnosis.

3. What investigations would you like to perform?

    - Venereal Disease Research Laboratory (VDRL test) or *Treponema pallidum haemagglutination* (TPHA) test, blood culture and sensitivity
    - Swab for Gram stain and culture and sensitivity from the urethral, anal, pharyngeal, and scrotal ulcers
    - Urine/urethral swab for nucleic acid amplification test (NAAT)

The blood, urethral, anal, pharyngeal ulcer, and scrotal swab cultures were negative. NAAT of the urine specimen was negative for *Neisseria gonorrhoea*. These negative results ruled out disseminated gonococcal infection. VDRL was positive with a titre of 1:32, and they patient's TPHA was positive, confirming the diagnosis of syphilis. The genital ulcer represented a chancre, which is a feature of primary syphilis, whereas conjunctivitis, tenosynovitis, and maculopapular eruptions supported secondary syphilis. These findings indicated that the patient had concomitant primary and secondary syphilis. He was given a 2.4 MU stat dose of IM benzathine penicillin, which resulted in complete symptom resolution within 1 week.

Discussion

Syphilis is a common sexually transmitted disease caused by *Treponema pallidum*.[10] In Malaysia, it is found mainly in HIV-positive patients and men who have sex with men (MSM).[11]

Syphilis occurs in three phases: primary, secondary, and tertiary. Primary syphilis occurs after an incubation period of 21 days and is characterised by chancre, a painless ulcer at the inoculation site. Untreated, the chancre resolves, and the infection progresses into secondary syphilis 6 weeks later, signifying the haematogenous spread of *T. pallidum*. This secondary phase is characterised by a widespread macular rash with palmoplantar involvement and systemic symptoms.[12] *T. pallidum* may also inoculate other organs, such as the eye and musculoskeletal system. Ocular manifestations in secondary syphilis include conjunctivitis, episcleritis, scleritis, keratitis, iridocyclitis, anterior uveitis, posterior segment involvement, and acute posterior placoid chorioretinopathy (APPC).[13] In the musculoskeletal system, periostitis, osteochondritis, osteitis, and less commonly, tenosynovitis and syphilitic arthritis, may occur.[14] Latent syphilis follows secondary syphilis. If untreated, up to 25% of cases will progress to tertiary syphilis, characterised by cardiovascular and neurologic features and gummatous lesions.[9]

In HIV-positive patients, clinical presentation of syphilis is often atypical due to compromised humoral and cell-mediated immunity. Chancres can be numerous, large, and deep, with delayed healing, leading to persistence into secondary syphilis. Cutaneous manifestations in HIV-positive patients are also highly variable, with papulosquamous, lenticular, annular, and pustular lesions being described[12]

Conflict of interest

The authors declare no conflicts of interest.

How does this paper make a difference to general practice?

- Syphilis in HIV-positive patients can be atypical, and it is important to have a high index of suspicion when encountering a HIV-positive patient with a skin rash.

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