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Lues Maligna in Immunocompetent Individuals: Two Case Reports

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Abstract

Lues maligna, also termed malignant syphilis or rupioid syphilis, is a rare and severe form of secondary syphilis. Clinically, the condition is characterized by unusual nodules and necrotic and ulcerated skin lesions covered by thick, lamellated crusts associated with severe constitutional symptoms. Most of the lues maligna cases have been observed in immunocompromised individuals, including Human Immunodeficiency Virus (HIV) co-infected patients, alcoholics, malnourished individuals, and patients with debilitating illnesses. However, immunocompetent individuals can also develop this form of illness. Herein, we present 2 cases of lues maligna in immunocompetent patients. The first case is a 38-year-old immunocompetent married female, while the second case is a 34-old married male, both presenting with multiple diffuse noduloulcerative lesions with rupioid crusts. Serological tests for syphilis were positive in both patients and a biopsy of both patients showed forms consistent with secondary syphilis.

Keywords: Fisher's criteria; Human immunodeficiency virus; Malignant syphilis; Rupioid syphilis; Ulceronodular-rupioid syphilis.

Introduction

Lues maligna, an uncommon form of secondary syphilis, is characterized by pleomorphic lesions, mostly nodular, ulcerative, and necrotic lesions, which are covered with thick, dark, lamellated rupioid crust resembling an oyster shell.[1] These nodulo-ulcerative lesions are followed by systemic manifestations like fever, malaise, or arthralgia.

It is still unclear why only a few Treponema pallidum-infected patients develop lues maligna. Studies have shown HIV co-infection as the most common association. However, malnourished individuals, alcoholics, patients with uncontrolled diabetes mellitus, and intravenous drug users (IVDUs) are also at higher risk of developing this form of illness.[2] The progressive and destructive course of this type of syphilis might be due to an immunocompromised status of the host or sometimes even due to a more virulent strain of T. pallidum. Though uncommon, immunocompetent individuals can also develop lues maligna.

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Fisher proposed criteria for lues maligna diagnosis, including the following features: 1) Compatible gross and microscopic morphology. 2) High-titer serologic test for syphilis. 3) Jarisch-Herxheimer (JH) reaction following treatment. 4) Dramatic response to antibiotic therapy.[3] Though rapidly progressive, lues maligna, if treated promptly, fortunately, has a good prognosis and responds well to multiple penicillin regimens, resulting in the complete resolution of lesions.

Case report

Case 1

A 38-year-old female, working as a laborer in Pokhara, married for the second time and currently living

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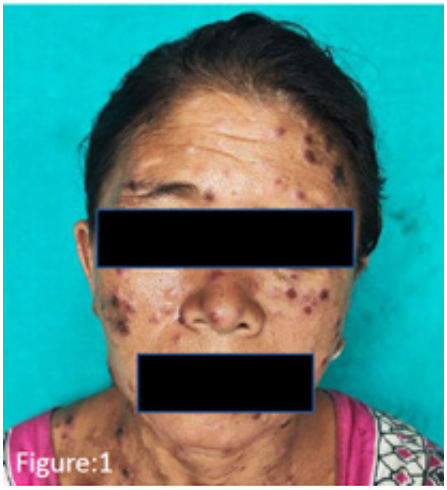

Figure 1: Multiple erythematous nodules over face

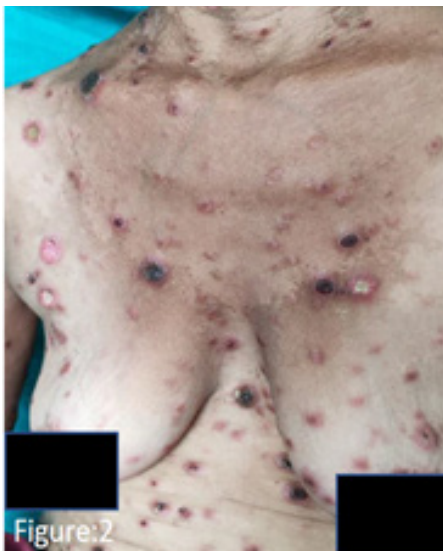

Figure 2: Extensive nodulo-ulcerative lesions with central necrosis over chest

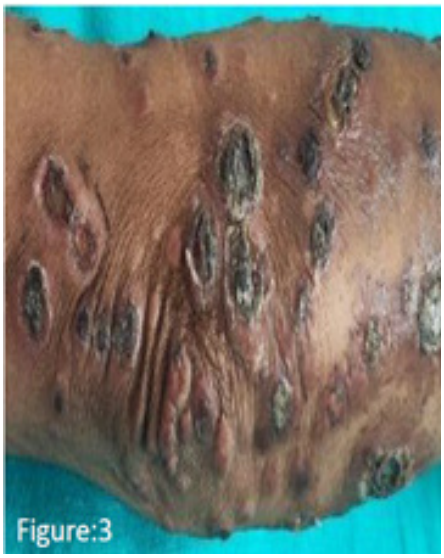

Figure 3: Thick, lamellated, rupioid crusts covering lesions of elbow extensor of right forearm

with her second husband, presented with multiple painful, non-itchy, diffuse erythematous papules, and nodules over her face, chest, and trunk for 4 weeks. The lesions started as circular macules which became nodular, ulcerated, and oozed foul-smelling yellowish pus discharge predominantly over the upper and lower extremities and later developed thick black crusts with the largest lesion measuring 2cm x 1cm (Figure 1,2). The relatively older papules and nodules of the face, trunk, and extremities had heaped up crusts giving rise to "limpet-like" crusts resembling an "oyster shell, i.e., typical dirty looking, adherent, rupioid lesions (Figure 3). There was no involvement of palms, soles, oral, and genital mucosa. The patient also complained of fever, which was recorded as 101.40 F, headache, and fatigue after a few days of the appearance of skin lesions. Few, non-tender, fluctuant inguinal and axillary lymph nodes were palpable, with the largest measuring about 2cm x 1cm, were palpable. Other systemic examinations including neurological examination were unremarkable.

Past medical history and drug history were non-significant. However, she has a history of multiple unprotected sexual exposure with multiple partners in the past. Her last sexual exposure with her second husband was 2 months back. She and her husband deny having any form of genital lesions in the past.

Hematological parameters were found to be within normal limit. Serological tests showed Treponema Pallidum Hemagglutination Assay (TPHA) to be positive, and Reagin plasma reagin (RPR) titre to be 1:128. However, the HIV test was negative, and the serological markers for hepatitis B and C infection were also negative. Patient's cerebrospinal fluid (CSF) analysis showed CSF-VDRL titre at 1:4, cell count as 3 lymphocytes/mm3 (reference range (RR):0-4 lymphocytes/mm3), and total protein as 50 mg/dl (RR:15-45 mg/dl). Magnetic Resonance Imaging (MRI) of the brain and spine showed no significant findings. Echocardiogram (ECHO) findings were also normal. Histopathological examination revealed dense subepithelial and periadnexal lymphoplasmacytic infiltrate admixed with few histiocytes and scattered epithelioid cells (Figure 4). Periodic Acid Schiff (PAS) stain and Fite stain were negative for the given specimen. The patient's husband's serological test showed positive TPHA with RPR titre 1:16 with no HIV, hepatitis B and C infection.

The patient was admitted to the hospital, and after an antibiotic sensitivity test, the patient received 2.4 million units of intramuscular (IM) benzathine penicillin and 1.2 million units in each buttock. Within 72 hours, the lesions stopped draining. Patient received two additional weekly doses of benzathine penicillin. During the treatment course, the patient was admitted to the hospital. The lesions of the patient had completely resolved in three weeks. Based on clinical, histopathological, and serological findings along with a rapid response to treatment, the patient had three

out of four positive Fisher's criteria i.e presence of characteristic nodulo-ulcerative lesions with rupioid crusts; a strong RPR titre 1:128; patient's dramatic response to therapy. However, JH reaction was not experienced by this patient.

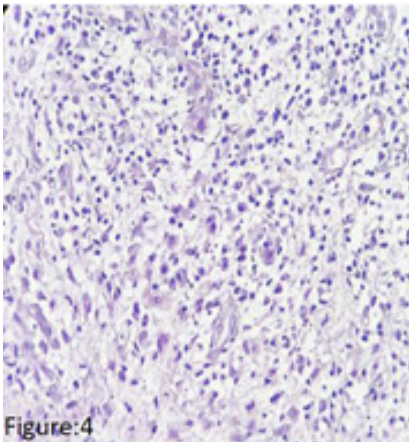

Figure 4: Histopathology of skin lesions showing dense infiltrate of lymphocytes and plasma cells with few histiocytes in dermis (Hematoxylin and eosin stain; x40)

Figure 5: Multiple erosions and ulcers over prepuce and scrotum with serosanguinous discharge

Figure 6: Diffuse nodules covered with rupioid crusts over trunk and extremities

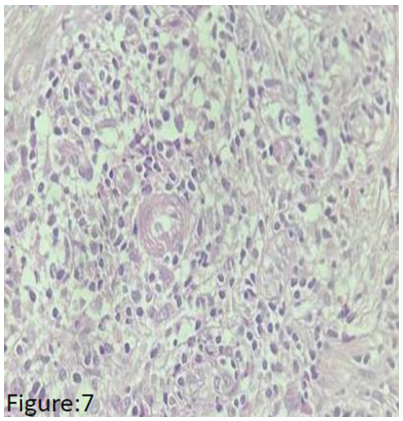

Figure 7: Histopathology of skin lesions showing ill-defined granuloma and dense inflammatory cell infiltrates comprising lymphocytes, plasma cells, and histiocytes (Hematoxylin and eosin stain; x40)

Case 2

A 34-year-old married male laborer from Baglung presented with a 3-week history of erythematous oozing, non-painful erosions on the genitalia, starting as papules on the prepuce and progressing to more extensive erosions and ulcers extending to the scrotum (Figure 5). The erosions oozed non-foul-smelling serosanguinous fluid and were associated with mild dysuria but no urethral discharge. Additionally, within 8 days, he developed painful nodulo-ulcerative and necrotic lesions on the face, ears, neck, chest, and extremities. These began as erythematous macules, evolving into papules, nodules, and ulcerated lesions with thick black crusts and oozing foul-smelling yellow pus (Figure 6). The largest lesion measured 2 × 1cm. Palms, soles, and oral mucosa were spared. Unilateral, non-tender inguinal lymphadenopathy (2 × 1cm) was noted on the left side. The patient had no episodes of fever. Past medical history and drug history were non-significant. The patient reported unprotected sexual contact with a sex worker 8 months prior. Hematological parameters were normal, but serological tests revealed positive TPHA and RPR titre of 1:8, with negative HIV status. There was no evidence of hepatitis B and C infection. Histopathology showed ill-defined granuloma comprising lymphoplasmacytic infiltrates admixed with histiocytes (Figure 7). Both PAS stain and Fite stain were negative for the given specimen.

After admission to the hospital, followed by an antibiotic sensitivity test, the patient was treated with 2.4 million units of deep intramuscular benzathine penicillin, 1.2 million units in each buttock. The patient received two more weekly doses of IM benzathine penicillin. The lesions ceased oozing within days, and complete healing occurred within 4 weeks, leaving hyperpigmentation and scarring. The compatible nodulo-ulcerative lesion with rupioid crust, high RPR titre, and rapid response to penicillin fulfilled three out of four Fisher's criteria with no Jarisch-Herxheimer reaction during therapy.

Discussion

In 1859, Bazin coined the term "malignant" for this severe form of syphilis. However, Dubuc later defined the condition as malignant syphilis. Since then, different terms like lues maligna, ulceronodular syphilis, rupioid syphilis, ulceronodular-rupioid syphilis (UNRS) have been used.[4] Lues maligna is characterized by rapidly progressing nodulo-ulcerative lesions covered with typical thick, lamellated, cone-shaped, rupioid crusts.[1] Between 2014 and 2018, about 45 overall cases of lues maligna have been published, of which 73% of the cases were associated with HIV-infected patients.[2] To our knowledge, no case of lues maligna has been published in Nepal. The pathogenesis and course of lues maligna depend upon the host's immune status. A strong delayed-type hypersensitivity (DTH) response, mediated by CD4 cells, is crucial to the control of syphilis.[5] In HIV-infected individuals, defective CD4 cell function in the setting of uncontrolled viremia leads to rapid development of lesions in lues maligna.[4] People living with HIV/AIDS are 60 times more likely to present with this form of syphilis.[6] Only few cases of immunocompetent, healthy individuals have been reported to develop lues maligna.[7,8] Though hypervirulent strain of Treponema pallidum could be a potential cause of lues maligna in immunocompetent patients, there is no sufficient evidence to substantiate this hypothesis.[7] As in our case, both patients had no comorbidities yet developed this form of rapidly progressive syphilis. Fisher established criteria for diagnosing lues maligna, which include gross and microscopic features of lesions, elevated rapid plasma reagin (RPR) test levels, a rapid response to treatment, and the presence of the Jarisch–Herxheimer (JH) reaction.[3] Both our patients met only three out of four Fisher's criteria, i.e., nodulo-ulcerative lesions covered with rupioid crust, high RPR titre, and rapid response to penicillin with no JH reaction in both cases. These findings were similar to those of other studies in which patients did not fulfill all of Fisher's criteria.[1,6] Lues maligna should be differentiated from other conditions like cutaneous lymphoma, bacillary angiomatosis, mycobacterial, and fungal infections. Compared to the tertiary syphilis, lesions in lues maligna are rather multiple, round or oval with lamellar crusting.[4] Though the lesions are widely disseminated, patients with lues maligna show rapid improvement with intramuscular injection of benzathine penicillin. For patients allergic to penicillin, other available alternative treatments like ceftriaxone, doxycycline, and minocycline can be used.[4,9] However, if left untreated, patients may develop complications in the form of uveitis, osteitis, and neurosyphilis.[4,8,10]

The limitations of this case report arise from the inability to perform CSF analysis in the second patient, and hence, complications like neurosyphilis could not be ruled out. The other limitation was tracking the serological status of the wife of the same patient due to the patient's fear of stigma in family and society.

Conclusion

Lues maligna is a rare complication of a common disease. Though it is most commonly associated with HIV infection and other immunocompromised conditions, the sudden and diffuse appearance of nodulo-ulcerative lesions in immunocompetent individuals should arouse the suspicion of lues maligna. So, appropriate serological tests should be carried out in such cases. Early diagnosis and treatment of lues maligna not only alleviates morbidity but also arrests the disease progression and prevents further systemic complications of the infection.

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