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Multisystemic Manifestations of Behcet's Disease and Its Treatment Outcome: A Case Report and Review of the Literature

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ABSTRACT

Behcet's disease is a rare multisystem vasculitis that demands early diagnosis and prompt treatment. Clinicians must maintain a high index of suspicion, especially in patients presenting with recurrent oral and genital ulcers with systemic symptoms and adopt a multidisciplinary approach for the optimal management.

1 | Introduction

Behcet's disease (BD) is a multisystem inflammatory condition of unknown origin, categorized as both systemic vasculitis and neutrophilic dermatosis. Neutrophilic dermatoses refer to a group of skin disorders characterized by a dense inflammatory infiltrate predominantly made up of neutrophils [1]. This condition is characterized by recurrent oral aphthous ulcers, genital ulcers, and uveitis [2]. Because of its high prevalence in the Mediterranean and Middle East Asia, the condition is often referred to as the Silk route disease. It has the highest prevalence in Türkiye (14 to 20 cases per 100,000) [3], whereas prevalence estimates in the United States and Europe have varied from 0.12 to 7.5 per 100,000 [4].

Given the limited number of reported cases and only a single retrospective study published to date in Nepal, the prevalence of this condition in the country remains unknown [5]. Many clinicians, including dermatologists, general physicians, rheumatologists, neurologists, and ophthalmologists, remain unaware that BD is not uncommon in Nepali patients. They often seek medical attention too late due to the diagnostic dilemma, leading to significant local and systemic morbidity and mortality. This article aimed to raise awareness among healthcare professionals about BD and emphasizes the need for further research on this rare condition. Additionally, it highlights the effectiveness of colchicine and steroids in the treatment of BD.

2 | Case Presentation/Examination

A 21-year-old woman, referred case from another hospital with complaints of recurrent oral and genital ulcers for 5 years, presented to our dermatology out-patient department with oral and genital ulcers. She used to take vitamin B complex from the local health post in her village, and lesions used to relieve on their own and used to recur every 2 to 3 months. Three years back, she got pregnant. Her lesions began to increase in number and size in the gums, palate, and tongue. This caused her difficulty in swallowing, for which she was admitted in hospital for a few days. During her hospital stay, a biopsy done from her genital lesion revealed a granulomatous lesion. Unfortunately, she had a miscarriage during her 7 months of gestation. Since then, she has been having recurrent oral and genital ulcers almost every

month. The patient visited multiple clinics and hospitals for her lesions. She also noticed ulcers increasing during her menstrual period and acne-like lesions appearing on her face, neck, chest, buttocks, and back along with throat pain. There was a history of on and off low backache, abdominal distension, and difficulty in passing stool. On further inquiry, she reported symptoms of bilateral eye pain, blurring of vision, and itchiness for 1 month. She denies any history of fever, joint pain, neurological, cardiopulmonary, renal symptoms, or signs. There was no such history in the immediate family members.

On examination: There were few ulcers of size 0.5 × 0.5 cm with white in the middle and red in the periphery in the tongue, buccal mucosa (Figures 1 and 2), and multiple ulcers of size 1 × 1 cm to 2 × 2 cm in the labia majora and vagina with thick purulent discharge. The ulcers were tender on palpation (Figure 3). There were few erythematous papules and nodules on the temporal side of the face (Figure 4), acneiform-like eruptions over the forehead (Figure 5), papulopustular lesions on the chest (Figure 6), back, and axilla.

3 | Methods (Differential Diagnosis, Investigations, and Treatment)

On initial workup, blood investigations and serology tests were done. Complete blood count (CBC), renal function test (RFT), liver function test (LFT), and random blood sugar (RBS) were within normal limits. Hepatitis B surface antigen (HBs Ag), human immunodeficiency virus (HIV I and II), *Treponema Pallidum* hemagglutination (TPHA), and venereal disease research laboratory (VDRL) were negative, thus ruling out sexually transmitted diseases. Antinuclear antibody (ANA) test was also negative, which ruled out connective tissue diseases.

Provisional diagnosis of BD was made. We scheduled a pathergy test and sent blood samples. Erythrocyte sedimentation rate

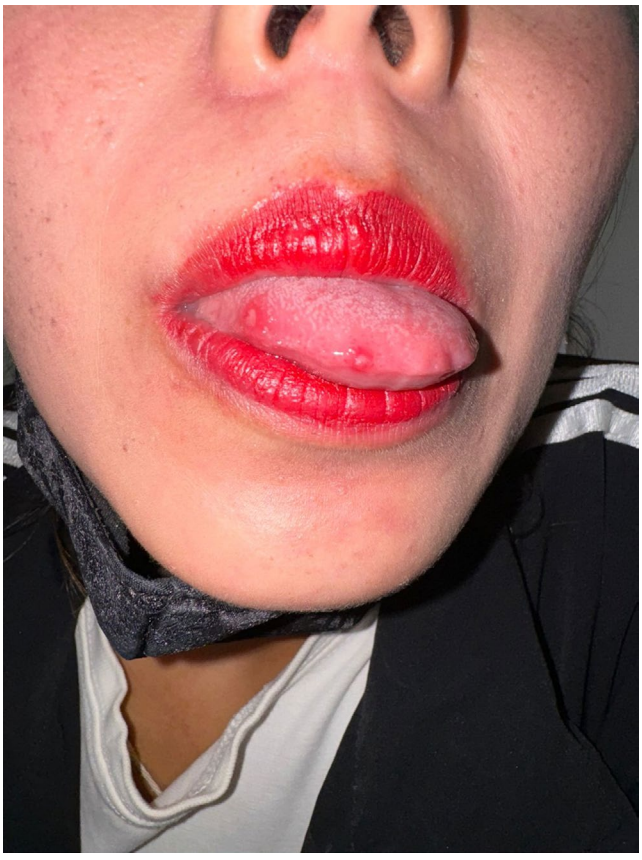

FIGURE 1 | Multiple aphthous ulcers on the tongue.

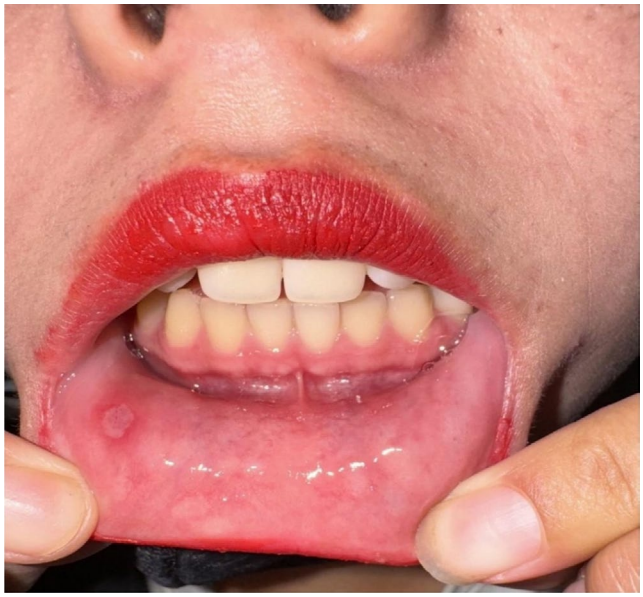

FIGURE 2 | Aphthous ulcer in buccal mucosa.

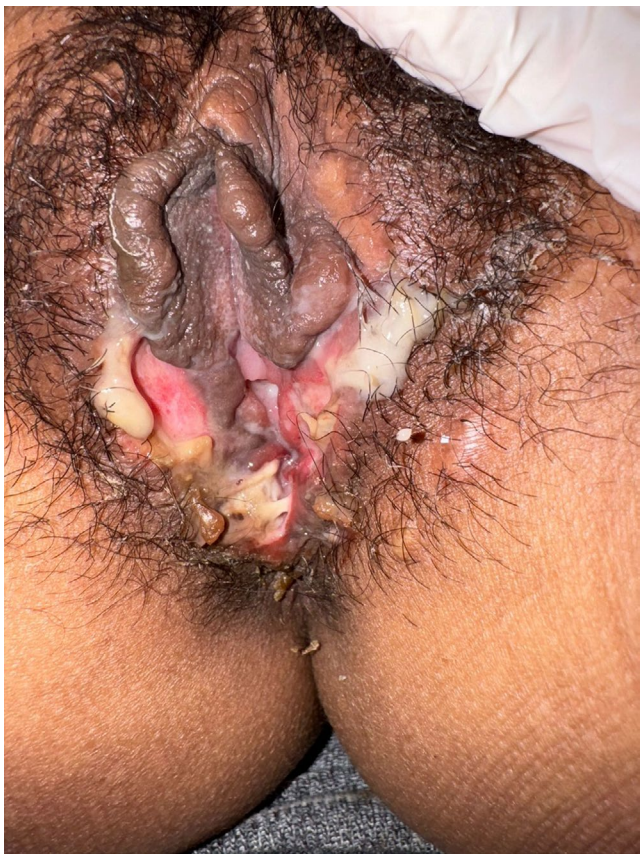

FIGURE 3 | Multiple ulcers on the vulva along the labia majora with thick purulent discharge.

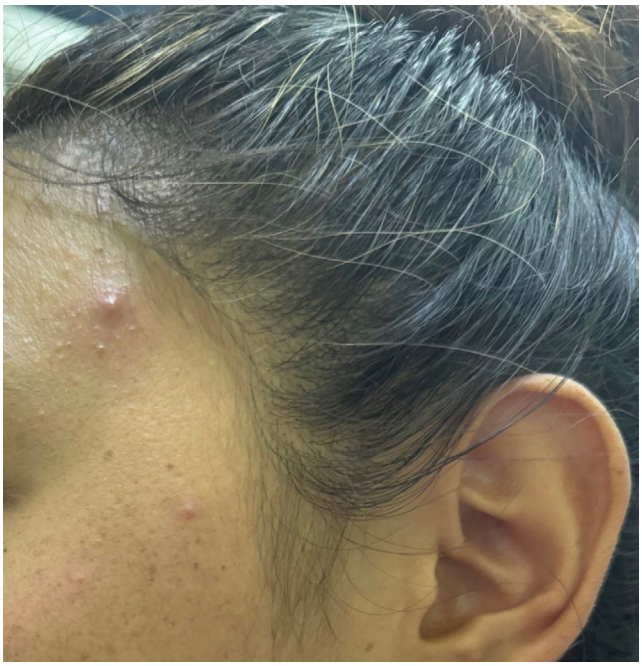

FIGURE 4 | Erythematous nodule on the temporal area.

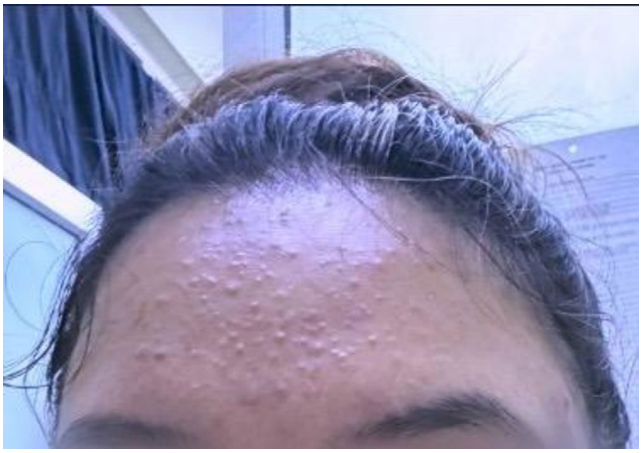

FIGURE 5 | Acneiform-like eruption on forehead.

(ESR) and C-reactive protein (CRP) turned out to be 37 mm/h (normal range: 0 to 10 mm/h) and 77 mg/L (normal range: 0.1 to 1 mg/L), respectively.

A pathergy test was done using a 20-gauge needle on both the right and left forearm, and the results, read after 48 h, yielded a positive result (Figure 7).

The patient was referred to ophthalmology and ENT for her ocular complaints and throat pain.

Based on the established diagnostic criteria of BD by the international study group [6], our patient fulfilled several key features, including recurrent oral ulcers, recurrent genital ulcers, skin lesions, and a positive pathergy test. To manage her condition, she began a treatment plan including oral colchicine (0.5 mg twice-daily), triamcinolone gel 0.1%, and analgesic/healing gel containing choline salicylate, benzalkonium chloride, and

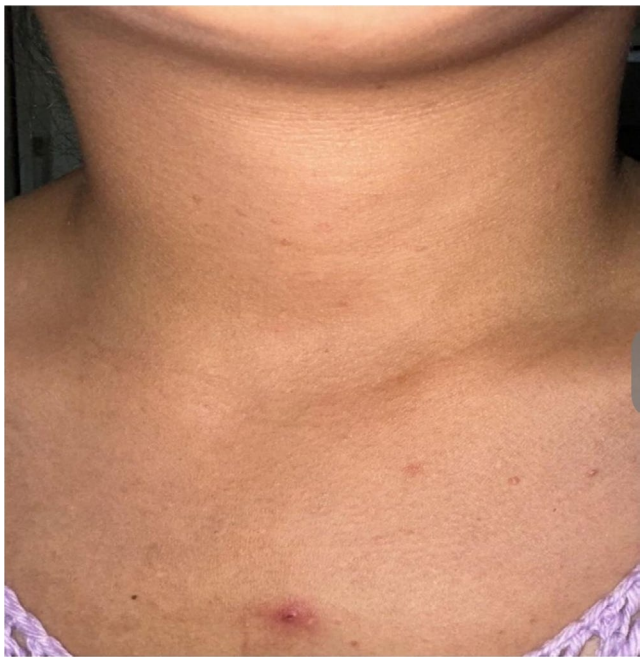

FIGURE 6 | Papulopustular lesion in anterior chest.

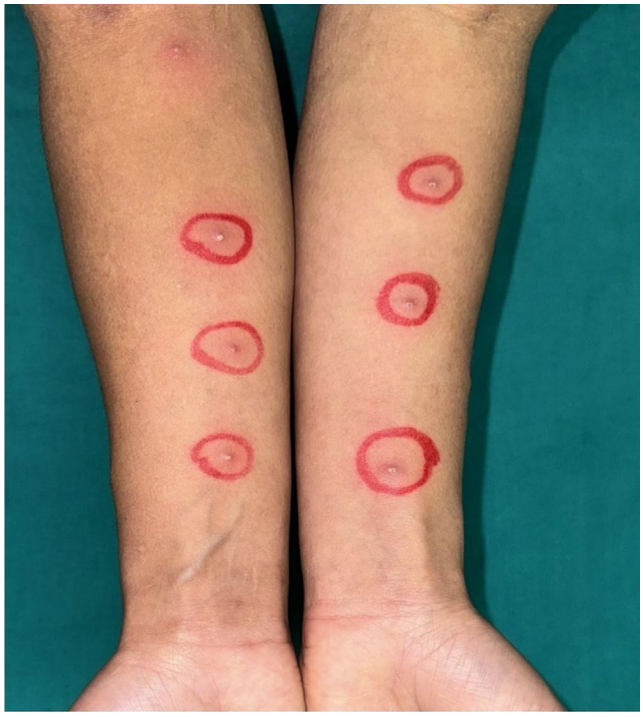

FIGURE 7 | Positive pathergy test in bilateral forearm.

lignocaine hydrochloride for oral ulcers, as well as topical betamethasone and fusidic acid cream for genital lesions.

4 | Outcome and Follow-Up

After 2 weeks, her lesions improved but remained persistent, prompting the addition of oral prednisolone for 2 weeks alongside colchicine. After one and a half months of treatment, her

lesions healed (Figure 8), and she continued with colchicine for the next month. After two and a half months following treatment, she briefly discontinued colchicine on her own. While previous lesions had healed, two to three new oral lesions appeared but none in the genital area. She was re-prescribed colchicine for the next 1 month and oral prednisolone 20 mg for 2 weeks. Oral prednisolone was tapered slowly over the next 2 months. Monthly CBC and RFT tests remained normal throughout her treatment. After 4 months of treatment with colchicine and intermittent oral prednisolone, her oral ulcers ceased (Figures 9 and 10). She is currently being maintained with oral colchicine 0.5 mg twice-daily with proper monitoring. The patient is satisfied with her treatment after previously having visited multiple hospitals. She is also advised on potential eye manifestations of the disease and recommended to have regular eye checkups.

5 | Discussion

BD is a rare systemic vasculitis characterized by relapsing and remitting episodes of acute inflammation affecting vessels of all sizes [7]. The peak incidence of BD is seen in the age group between 20 and 40 years, but juvenile onset has also been reported [8, 9] as was our reported case of a 21-year-old woman. The exact cause of BD is unknown, but it is thought to involve aberrant immune responses triggered by an external factor, such as an infection, in genetically predisposed individuals. The disease features both autoimmune and autoinflammatory elements, with key mechanisms including genetic influences linked to specific HLA and non-HLA genes, altered host bacterial responses, changes in innate immune function, disrupted hematopoietic cell populations and cytokines, immune complexes and autoantibodies, vascular endothelial activation, hypercoagulability, and neutrophil activation, as well as epigenetic modifications [10]. The most common clinical feature of BD is the occurrence of recurrent and generally painful mucocutaneous ulcers. Other manifestations of the disorder can vary widely between different patients and populations, which includes oral, ocular, urogenital, neurologic, vascular, renal, gastrointestinal, and joint involvement [11, 12].

Most patients with BD initially have recurrent oral aphthous ulcers that are more extensive and painful than common ulcers, often affecting eating. Our patient was also unable to swallow food due to oral cavity ulcers needing admission. BD ulcers range from a few millimeters to two centimeters (cm),

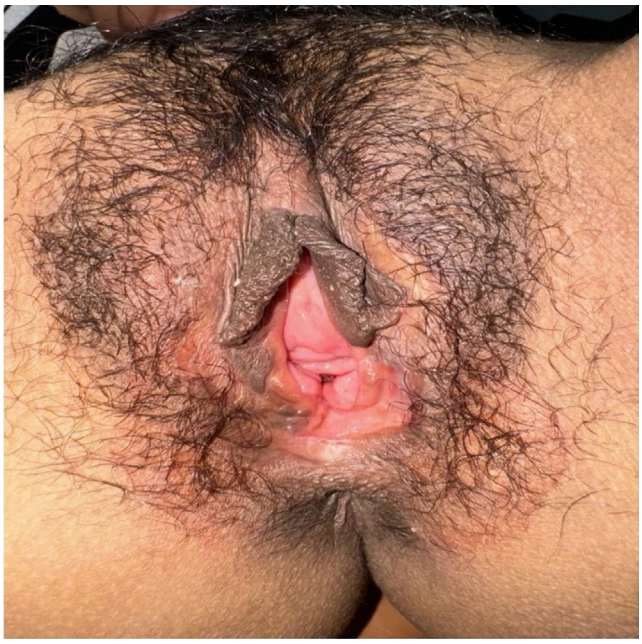

FIGURE 8 | Healing of genital lesions after one and a half months of treatment.

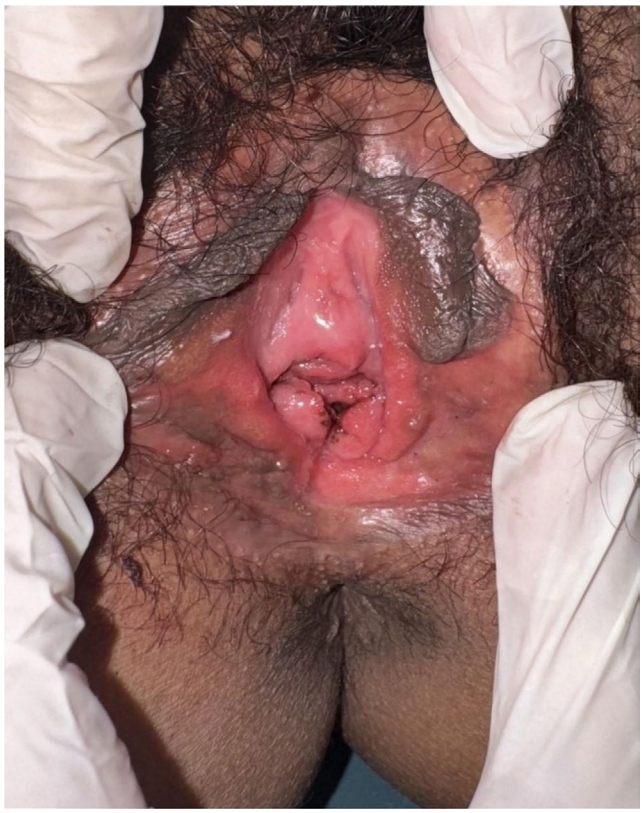

FIGURE 9 | Healed scar in genital area after 4 months of treatment.

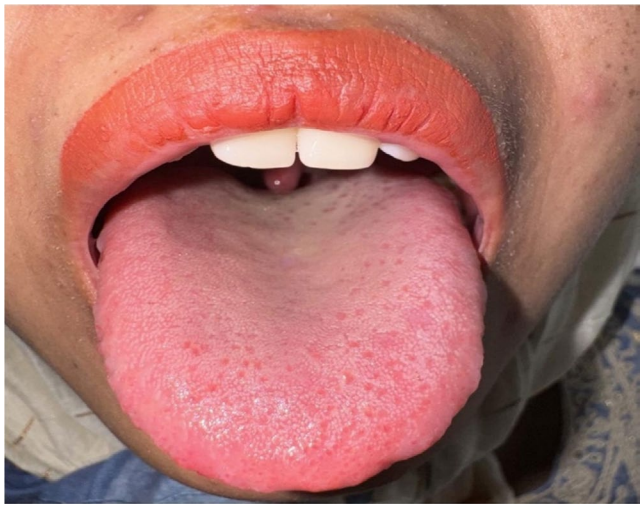

FIGURE 10 | No new lesion in the oral cavity after 4 months of treatment.

TABLE 1 | International Study Group for Behcet's disease (ISG) diagnostic criteria.

Required clinical features	Description
Recurrent oral ulceration	Aphthous (idiopathic) ulceration, as noted by either the clinician or patient, occurring at least three times within a 12-month period
Plus, any 2 of the following	
Recurrent genital ulceration	Aphthous ulceration or scarring, noted by either the clinician or the patient
Eye lesions	Anterior or posterior uveitis with cells in the vitreous observed during a slit-lamp examination, or retinal vasculitis documented by an ophthalmologist
Skin lesions	Erythema nodosum-like lesions observed by either the clinician or patient, along with papulopustular skin lesions or pseudo folliculitis with distinctive acneiform nodules noted by the clinician
Positive pathergy test	Interpreted by the clinician within 24 h to 48 h

TABLE 2 | International Criteria for Behcet's disease (ICBD) for diagnosis of BD.

Required clinical features	Points
Ocular lesions	2
Genital aphthosis	2
Oral aphthosis	2
Skin lesions	1
Neurological manifestations	1
Vascular manifestations	1
Positive pathergy test[a]	1

[a]The pathergy test is optional and not included in the primary scoring system. However, if the pathergy test is performed and results are positive, an additional point may be awarded.

with well-defined borders, a white-yellow necrotic base, and surrounding erythema, comparable to our case findings. Minor ulcers are under 1 cm, while major ones are at least 1 cm and may scar. Healing typically occurs spontaneously within 1 to 3 weeks, though some patients experience continuous lesions due to frequent recurrences [13]. Our patient also reported minor, non-scarring oral ulcers, and they used to recur every 2 to 3 months for 5 years (Figures 1, 2, and 10).

Genital ulceration, the most specific finding of BD, occurs in over 75% of patients. These ulcers resemble oral aphthae and are usually painful [6]. They commonly appear on the scrotum in men and the vulva in women. Recurrence is less frequent than with oral ulcers, but scar formation is common with genital lesions [14]. Our patient too displayed the presence of recurrent genital ulcer at the vulva along the labia majora with scarring after the healing of ulcers (Figures 3, 8, and 9).

In BD, cutaneous lesions are observed in 41 to 97% of patients. These skin manifestations can vary widely and may include erythema nodosum, pyoderma gangrenosum-type lesions, acneiform lesions, erythema multiforme-like lesions, nodules, papulopustular eruptions, skin ulcers, superficial thrombophlebitis, pseudofolliculitis, and Sweet's syndrome-like lesions [15]. Our reported case has concurrent findings such as erythematous nodules on the face (Figure 4), acneiform eruptions on the forehead (Figure 5), a papulopustular lesion over the chest (Figure 6), back, and axilla. Acneiform lesions might be more prevalent in individuals with accompanying arthritis [16]. It can be correlated with the history of lower back pain in our patient.

Pathergy test is a specific test for BD, and it refers to an erythematous papule or pustule that appears within 48 h after a skin prick with a 20-gauge needle, reflecting a hyper-reactive response to local trauma [17]. We also reported a positive pathergy test in our patient.

BD may negatively impact pregnancy; although rare, it can cause an increased rate of miscarriage [18]. The likely cause of third trimester abortion in our case could be due to BD. Disease activity in BD is influenced by the menstrual cycle, with female sex hormones playing a role. The sudden drop in progesterone at the onset of menstruation is associated with disease flare-ups in BD, as shown in one of the studies where disease worsened in 18 (66.7%) patients, but only 11 (40.7%) of them exhibited exacerbation of BD during menstruation [19]. This similar but rare pattern of disease activity is reported in our case with a history of exacerbation of symptoms during menses.

Gastrointestinal tract involvement in BD occurs in 4 to 38% of patients and can present with a variety of symptoms, including abdominal pain, abdominal distension, diarrhea, dysphagia, vomiting, abdominal mass, constipation, and bloody stools [20]. Our patient also reported abdominal distension and constipation warranting a thorough gastrointestinal evaluation.

Diagnosis of BD is based on clinical findings as there is no pathognomonic laboratory test till date. At present, two widely used criteria for diagnosis of BD are International Study Group (ISG) published in 1990 (Table 1) [6] and International Criteria for BD (ICBD) developed in 2013 (Table 2) [21]. In ISG criteria, the presence of recurrent oral ulceration plus any two of the following among recurrent genital ulceration, eye lesions, skin lesions, and positive pathergy test yields a diagnosis of BD, whereas in ICBD criteria among various features, a score > 4 indicates a diagnosis of BD (Table 2).

Our patient presented with recurrent oral ulcers, recurrent genital ulcers, typical skin lesions, and a positive pathergy

test, fulfilling the diagnostic criteria for BD according to the ISG criteria and with a total scoring of 6 (2 points for each of genital and oral ulcers, 1 for each of skin lesion and positive pathergy test), hence meeting the diagnosis of BD as per ICBD guidelines.

The goals of treatment for BD are to quickly suppress inflammatory flare-ups and recurrences to prevent irreversible organ damage. A multidisciplinary approach is essential for optimal care, with treatment individualized based on age, gender, type and severity of organ involvement, and patient preferences. Ocular, vascular, neurological, and gastrointestinal involvement can be linked to a poorer prognosis. However, many patients may experience improvement in disease manifestations over time. For mucocutaneous involvement, topical steroids should be used to treat oral and genital ulcers. Colchicine is recommended as the initial treatment to prevent recurrent mucocutaneous lesions, particularly if erythema nodosum or genital ulcers are predominant. Papulopustular or acne-like lesions can be managed with topical or systemic treatments similar to those for acne vulgaris. In selected cases, medications such as azathioprine, interferon-alpha, TNF-alpha inhibitors, or apremilast may be considered [22]. Similarly, we initiated treatment with topical corticosteroid to address inflammation. Also, we prescribed oral colchicine, given that the dominant lesion was vulval ulceration and to prevent recurrence of mucocutaneous lesions. Additionally, we recommended local anesthetics to alleviate pain and discomfort from both oral and genital lesions, as well as an antibacterial and steroid cream for the genital ulcers.

With each follow-up every week to four weeks, the condition of the patient improved significantly.

6 | Conclusion

BD should be considered as one of the differentials in a patient presenting with recurrent oral and genital ulcers, skin lesions, gastrointestinal, obstetric, and gynecological symptoms. Due to its multisystem and vital organ involvement, this condition should be taken cautiously, especially by dermatologists, and should be investigated further with a multidisciplinary approach consulting different specialties for early diagnosis to reduce morbidity and mortality associated with this disease.

Additionally, this case report warrants comprehensive research studies to know the exact prevalence of BD in a developing country such as Nepal and to further explore its pathogenesis, multisystem involvement, diagnosis, and treatment outcome with colchicine, steroids, and other newer drugs.

Author Contributions

Mohan Bhusal: conceptualization, project administration, resources, writing – original draft, writing – review and editing. **Chanda Shrestha:** resources, writing – original draft, writing – review and editing. **Sanjay Dhungana:** writing – original draft, writing – review and editing. **Smriti Piya:** resources, writing – review and editing. **Binita Thapa:** resources, writing – original draft.

Consent

Written informed consent was obtained from the patient to publish this report and any accompanying images in accordance with the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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