When ulcers do not heal: Recognising behçet's disease from recurrent oral ulcers in primary care

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SUMMARY

Oral ulcers are a common condition in primary care, usually benign and self-limiting. However, recurrent or persistent ulcers that do not respond to conventional symptomatic treatment should prompt a re-evaluation of the diagnosis and an investigation into underlying systemic disease. We present the case of a 35-year-old woman who repeatedly presented to primary care with painful, recurrent oral ulcers that substantially impaired her daily functioning. Initial investigations, including a biopsy, indicated a benign condition, so symptomatic management was pursued without achieving clinical resolution. Two years later, the development of genital ulcers prompted a diagnostic reassessment and the presence of cutaneous lesions resulting in a diagnosis of Behçet's disease. Although immunomodulatory treatment was initiated, symptom control was limited by suboptimal adherence. This case highlights the critical role of primary care in recognising mucocutaneous symptoms, maintaining diagnostic vigilance and ensuring longitudinal follow-up. Due to the multisystemic and clinically driven nature of Behçet's disease, it is essential to recognise it early and implement coordinated multidisciplinary management to reduce morbidity and optimise long-term outcomes.

INTRODUCTION

Individuals with oral ulcers often first seek care from a general practitioner or dental practitioner. While most ulcers are benign and self-limiting, a minority may represent malignant disease. It is estimated that aphthous ulcers occur in as many as 25% of individuals worldwide.[1]

Recurrent aphthous stomatitis (RAS), also known as canker sores, is a common but complex oral disorder characterised by recurrent painful ulcers on non-keratinized oral mucosa. Its exact aetiology remains uncertain, presenting challenges for both patients and clinicians. Several contributing factors have been implicated, including local trauma, psychological stress, smoking cessation, anaemia, and hematinic deficiencies. Gastrointestinal disorders such as Crohn's disease, ulcerative colitis, and malabsorption syndromes (e.g., coeliac disease) have also been associated with oral aphthous ulceration and other systemic conditions such as Behçet's disease or HIV infection.[2]

Recurrent oral ulcers constitute one of the diagnostic criteria for Behçet's disease, first identified by the famous Turkish dermatologist Hulusi Behçet. It is a chronic inflammatory disorder of uncertain aetiology that involves the oral mucosa, genitalia, eyes, skin, and joints. Mucocutaneous lesions are considered the hallmark feature and often represent the earliest manifestations. The occurrence of oral aphthous ulceration in conjunction with ulcerations at other anatomical sites should prompt consideration of Behçet's disease.[2] This case report discusses a patient with recurrent oral ulcers associated with Behçet's disease, highlighting the crucial role of multidisciplinary collaboration between primary and tertiary care in achieving optimal diagnosis and management.

CASE PRESENTATION

A 35-year-old Malay woman, Para 2 with a known thalassemia carrier status, presented to our primary care clinic in March 2023 with a one-week history of fever, sore throat, and painful oral ulcers unresponsive to over-the-counter topical treatment. The severity of the ulcers markedly limited her oral intake, resulting in a 4-kg weight loss over several weeks, as she could only tolerate fluids and soft foods. She reported similar episodes of painful oral ulcers during her adolescence, although these had previously resolved completely within a few days. Otherwise, she had no family history of oral malignancy or autoimmune disease.

On examination, she had injected pharynx, exudative tonsillitis, and multiple aphthous ulcers over the bilateral buccal mucosa, anterior tongue, and floor of mouth. She was treated as tonsillopharyngitis with oral amoxicillin–clavulanate 625 mg twice daily for 5 days, in addition to symptomatic medications. At follow-up a week later, the ulcers showed no improvement. Given the persistence of oral ulcers beyond two weeks, she was referred to the oral and maxillofacial surgery (OMFS) team to exclude oral malignancy.

Further history by the OMFS team revealed the onset of ulcers shortly after a dental filling procedure, raising suspicion of traumatic ulcer. However, as the ulcers persisted, an incisional biopsy was performed. Histopathology demonstrated benign ulcer margins. Due to the laboratory investigations also revealed microcytic hypochromic anaemia with underlying thalassemia carrier status (normal iron study findings), the impression was revised to recurrent aphthous ulcer secondary to anaemia, and she was discharged from the OMFS service in June 2023 and to continue follow up in primary care.

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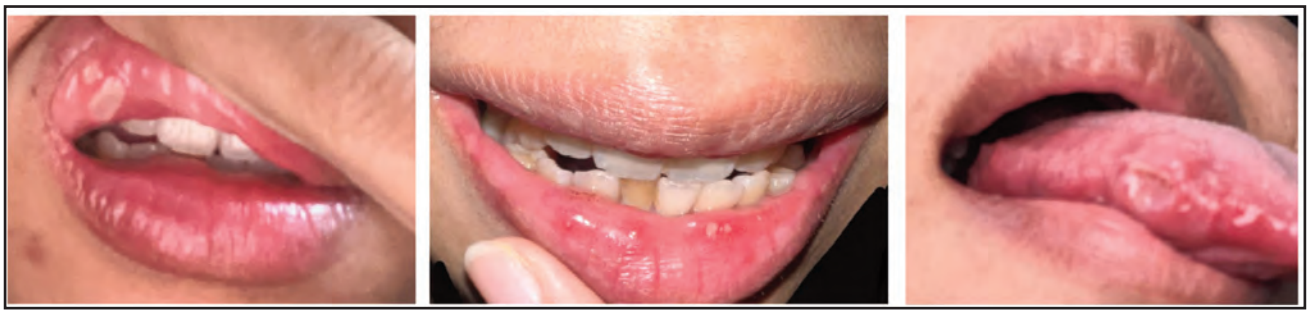

Fig. 1: Multiple aphthous ulcers over upper and lower lips and lateral tongue (Photo on 19.12.2024)

Manifestation	Definition
Recurrent oral ulceration	Observed by a physician or reported reliably by patient, recurring at least three times in one 12-month period
Plus any two of the following findings:	
Recurrent genital ulceration	Recurrent genital aphthous ulceration or scarring, observed by a physician or reported reliably by patient
Eye lesions	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; or retinal vasculitis observed by qualified physician (ophthalmologist)
Skin lesions	• Erythema nodosum-like lesions, observed by a physician or reported reliably by patient; • Pseudofolliculitis or papulopustular lesions; or acneiform nodules observed by a physician in post adolescent patients not receiving glucocorticoids
Positive pathergy test	Test interpreted as positive by a physician at 24–48 h, performed with oblique insertion of a 20-gauge needle or smaller under sterile conditions

Fig. 2: International Study Group criteria[10]

The patient re-presented in February 2024 with another episode of painful recurrent oral ulcers of two-week duration, again poorly responsive to topical treatment. She also reported fatigue, alopecia, and unquantified weight loss. Examination revealed multiple aphthous ulcers involving the lips, lateral tongue, and floor of mouth, ranging from 0.5 × 0.5 cm to 2 × 1 cm. Autoimmune screening was performed, showing ANA positivity (1:320) with elevated C3 and C4 (165 and 45.7mg/dL respectively). Anti-dsDNA, rheumatoid factor, and infectious disease screens were negative.

She was referred to rheumatology in March 2024, where detailed genital examination was also performed, revealing a solitary ulcer over the left labia majora (0.5 × 0.5 cm). A provisional diagnosis of Behçet's disease was made, and she was commenced on oral colchicine 0.6 mg daily. At subsequent primary care visits over the following months, she reported recurrent painful oral ulcers interfering with eating, speaking, and her job as a teacher. Symptomatic medications were provided while awaiting rheumatology follow-up.

By July 2024, review by the rheumatology team noted clinical improvement with colchicine, but worsening upon discontinuation. Colchicine, prednisolone, and hydroxychloroquine were initiated, and further blood investigations were performed, including anti-dsDNA, anti-ENA panel, complement (C3/C4), and HLA-B51/B52. The results were negative except for anti-SSA positivity, with normal complement levels and elevated ESR and CRP (65mm/hr and 2.69mg/dl respectively).

Despite receiving treatment, her medication adherence was inconsistent, largely due to work-related constraints and concerns about the long-term side effects of the newly prescribed oral therapies. Between July and December 2024, she presented to primary care four times with recurrent ulcers and reported that her symptoms worsened during the premenstrual period. At her rheumatology review in December 2024, her ulcers were noted to improve with good adherence but recur during periods of non-compliance. A clinical diagnosis of Behçet's disease was made with subsequent follow up also reveals presence of recurrent papulopustular lesions over left forehead, left axilla and recurrent erythema over lateral side of left ring finger nailbed.

In August 2025, at her consequent rheumatology follow-up, ongoing issues with non-adherence were noted. She had continued prednisolone but had not taken colchicine or hydroxychloroquine as prescribed. Azathioprine 50 mg daily was initiated, in addition to continuing hydroxychloroquine and prednisolone. She was referred for ophthalmology and gastroenterology assessments. Ophthalmological review, prompted by a past episode of right-eye redness (self-resolving within 4 days), showed no evidence of uveitis; meanwhile, her esophagogastroduodenoscopy and colonoscopy show no finding. At her latest rheumatology follow up in December 2025, patient has good compliance to the medication and this reflected on her marked reduction in both recurrence and the number of active oral lesions and skin lesions at any given time and better function in daily life

with marked reduction of CRP level more than 50% and normal ESR level.

DISCUSSION

The assessment of chronic oral ulcers in primary care must begin with careful exclusion of malignancy. According to Paleri V et al. (2010), malignant oral ulcers are typically non-healing and painless, persisting for more than three weeks. They often exhibit induration with minimal surrounding inflammation and may have a rolled, thickened edge. Risk factors such as male, smoking, alcohol consumption, and older age further increase clinical suspicion. Additional red flags include a previous history of a premalignant lesion or oral squamous cell carcinoma, as well as the absence of local or systemic factors that could otherwise explain the ulceration.[1]

Conversely, features that reduce suspicion of malignancy include recurrent ulcers that heal between episodes, multiple or clustered ulcers, or lesions associated with systemic or autoimmune diseases. Following this, other benign or systemic conditions should be considered.[1]

For primary care physicians (PCPs), the decision to refer a patient with a chronic oral ulcer of more than 3 weeks of duration is guided by the lesion's clinical characteristics and the clinician's diagnostic certainty. Ulcers exhibiting features suspicious for malignancy should be referred urgently within two weeks. Whereas, cases involving isolated traumatic ulcers or recurrent aphthous ulceration can be managed within primary care, provided the diagnosis is secure. This stratified approach supports timely identification of potentially malignant disease while ensuring efficient use of specialist services.[1]

Behçet's disease remains a primarily clinical diagnosis as no specific laboratory test exists to confirm it. The diagnosis of Bechet's disease for this patient satisfies the International Study Group criteria (ISG) as shown in the figure below.[10] Investigations such as brain MRI or blood tests may aid in assessing systemic involvement or ruling out alternative diagnoses, but they are not diagnostic. While HLA-B51 positivity is linked to increased disease risk, it is not a prerequisite for diagnosis.[3]

The identification of genital ulcers on detailed examination during rheumatology follow-up, together with the history of ocular involvement and other skin lesions underscores the importance of thorough history taking and physical examination during earlier primary care visits. The hallmark manifestation of Behçet's disease is recurrent, painful oral ulceration, which occurs in more than 95% of patients. These ulcers are thought to arise from dysregulation of the immune system, leading to overproduction of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). The resulting mucosal inflammation contributes to ulcer formation and persistence.[3]

Genital ulcers, though less common, are another characteristic feature. Their immunopathogenesis parallel that of oral ulcers, driven largely by T-cell–mediated immune responses and cytokine-driven mucosal injury. Unlike oral ulcers, genital ulcers often heal with scarring, which can aid in clinical differentiation.[3] Skin lesions such as erythema nodosum–like lesions, acneiform nodules, and pseudofolliculitis may occur, driven by vasculitis and neutrophil-mediated inflammation.[3]

Although Behçet's disease is a chronic condition characterised by alternating periods of remission and flare, many patients can maintain a good quality of life with appropriate treatment and monitoring.[7] Symptomatic relief of pain and inflammation in Behçet's disease may be achieved with nonsteroidal anti-inflammatory drugs (NSAIDs).[4] Corticosteroids are frequently employed for their potent anti-inflammatory effects and can be administered topically, orally, or intravenously depending on the severity and site of involvement.[5] In more severe or treatment-resistant cases, immunosuppressive agents are indicated to control disease activity, reduce the frequency of flares, and prevent long-term complications.[6]

Disease activity is often pronounced in the early years following diagnosis, with a tendency to decrease in severity over time.[3] Adherence to therapy is crucial for disease control and quality of life in patients with Behçet's disease. Patient's role as a mother and teacher highlights the impact of recurrent flares on daily functioning and underscores the importance of consistent treatment compliance. The unpredictable nature of disease flares can contribute significantly to psychological distress, as patients often experience anxiety and uncertainty regarding the timing and severity of future exacerbations. This emotional burden may impact adherence to treatment and overall quality of life, highlighting the need for holistic management that addresses both physical and psychological aspects of care.[8] In addition, the chronic pain associated with Behçet's disease has been linked to an increased risk of depression.[9]

PCPs plays this pivotal role as the first point of contact during disease exacerbations, allowing timely symptom management, reinforcement of treatment adherence, providing psychosocial support and coordination with the rheumatology team. In this case, the patient's early non-adherence was partly due to fear of medication side effects. This emphasizes the need for clear counselling to address patient concerns and support treatment compliance; PCPs are well-positioned to provide patient education, address misconceptions about medications, and empower patients to take an active role in their long-term management. Regular follow-up and multidisciplinary care are essential to optimise symptom control and to monitor for systemic involvement and complications.[3]

CONCLUSION

This case highlights the importance of maintaining a broad differential diagnosis when evaluating patients with persistent or recurrent oral ulcers in primary care. Early recognition of Behçet's disease requires detailed history taking and comprehensive examination. Long-term outcomes are influenced by treatment adherence, patient education, and effective communication to dispel

misconceptions about therapy. Ultimately, coordinated multidisciplinary care between primary care providers and specialists is essential to ensure optimal disease control and preserve the patient's quality of life.

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DECLARATIONS

No conflicts of interest declared.

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