

Erythema nodosum in Behçet's disease in remission: Think COVID-19?

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Abstract

The coronavirus disease has several manifestations related to the activation of the immune system. Because of such activation, autoimmune diseases, including vasculitis, have been reported to occur. Behçet's disease, a variable vessel vasculitis, has been discussed in the context of coronavirus disease. Rarely, the induction of Behçet's disease flare or exacerbation has been reported necessitating aggressive treatment. The presentation of Behçet's disease flares secondary to coronavirus disease is variable, including mucocutaneous lesions and eye or joint involvement. We highlight the case of a 35-year-old woman with pre-existing Behçet's disease in remission on colchicine presenting with new onset erythema nodosum-like lesions on her right shin being diagnosed with coronavirus disease infection a few days after. Despite treatment with systemic corticosteroid, the lesions did not resolve, necessitating the initiation of anti-interleukin-6 therapy.

Keywords

Coronavirus disease, Behçet's disease, erythema nodosum, positron-emission tomography imaging

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Introduction

By dysregulating the immune system, infection with SARS-CoV-2 can trigger the onset or exacerbate specific immune-mediated diseases.¹ As a result of such immune dysregulation, coronavirus disease (COVID-19) can have different presentations. For example, unusual dermatological manifestations—such as livedo reticularis, pityriasis rosea, or erythema multiforme—have been linked to COVID-19.^{2,3} Various types of vasculitides—including cutaneous vasculitis, immunoglobulin A (IgA)-associated vasculitis, or antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis—have been reported in the context of COVID-19.⁴

Behçet's disease (BD) is a variable vessel vasculitis that has been rarely studied in the setting of COVID-19 infection. Limited data suggest a similar clinical course in COVID-19 patients with BD and COVID-19 patients with no BD.⁵ Interestingly, BD flares with multisystem involvement following COVID-19 have been described.⁵

We present the case of a 35-year-old woman with BD who was in remission while on colchicine for 2 years, until erythema nodosum (EN) lesions appeared on her right shin, testing positive for SARS-CoV-2 a few days later.

Case report

A 35-year-old woman with past history of BD in remission presented with a 4-day history of painful, tender, erythematous lesions anteriorly over the right shin affecting ambulation.

A few years prior to the current presentation, she presented with recurrent orogenital ulcerations, arthralgia, and bilateral anterior uveitis and was found to be HLA-B51 positive. There were no EN lesions. She was diagnosed with BD. She has been in remission for 2 years while on colchicine until the appearance of the painful lesions over the right shin. The pain was worse in the morning. She started coughing and complained of severe pain anterior to the left tragus

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radiating to the back of the head. She tested positive for SARS-CoV-2. Both eyes became erythematous with no discharge or blurry vision. The lesions became larger and spread to behind the medial malleolus with similar but milder lesions over the left leg. Despite complaints of arthralgias, she denied recurrence of orogenital ulcers.

Physical examination revealed EN-like lesions over the right shin and to a lesser extent over the left shin. Bilateral erythema of the eyes with a small hypopyon was evident. No detailed examination by a specialist was done. The right temporomandibular joint was tender. Temporal, carotid, and peripheral pulses were present.

A computed tomography (CT) of the neck demonstrated a diffuse intimal thickening of the aortic arch as well as the carotid arteries. Subsequent carotid Doppler ultrasonography revealed a diffusely thickened intima-media complex of extracranial carotid system on both sides.

The findings of the intimal thickening prompted an F-18 fluorodeoxyglucose (FDG) positron-emission tomography (PET)/CT of the body to assess an active BD flare. Multifocal mild FDG uptake was noted along the upper third of the right superficial femoral artery and the lower two-thirds of the right posterior tibial artery as well as around the medial aspect of the right ankle and the muscular branches of the left anterior tibial artery representing active vasculitis (Figure 1).

For the uveitis, topical corticosteroids resolved the symptoms. Clopidogrel was started because of the carotid intimal thickening and prednisolone 40 mg a day.

One month later, the left mandibular pain and the uveitis resolved. However, EN persisted prompting the initiation of anti-interleukin (IL)-6 therapy with tocilizumab (TCZ). A follow-up 2 months after initiation of TCZ demonstrated resolving EN lesions and decreased pain sensation.

Discussion

Within a few weeks following the emergence of the COVID-19 pandemic, a state of multisystem inflammation resembling shock, similar to Kawasaki disease, was described.⁶ With that, the possible association between COVID-19 and vasculitis was extensively discussed in the literature.

As a type of vasculitis, BD has been studied in the setting of COVID-19. The prevalence of COVID-19 among BD patients was found nearly similar to the general population.⁷ BD patients have the same risk of acquiring COVID-19 as the general population, suggesting that BD treatment does not predispose to COVID-19.^{6,8}

Several reports highlighted the occurrence of BD flares in the setting of COVID-19 (Table 1). The manifestations of the BD flare are variable including oral ulcers, genital ulcers, or uveitis. Patients who discontinue or decrease the dose of the immunosuppressives are more likely to have BD flares.⁹ Notably, BD flares are also reported post COVID-19.⁹

EN is a delayed hypersensitivity reaction to multiple antigenic stimuli.¹⁵ Examples include infections such as

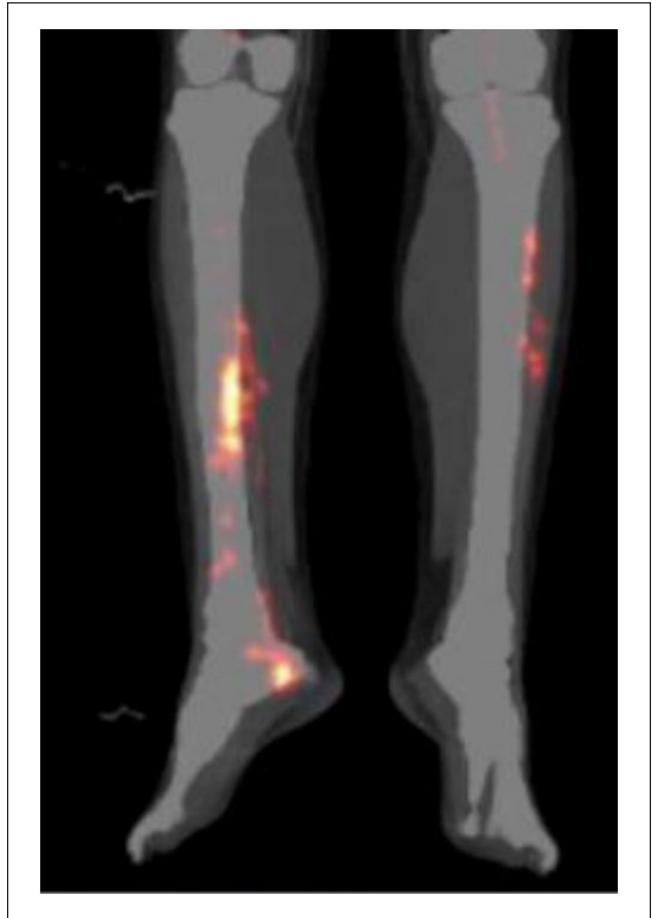


Figure 1. Multifocal segmental activity related to the lower limb arteries representing active vasculitis on F-18 FDG PET/CT of the body.

tuberculosis and streptococcal infection, drugs, neoplasia, and inflammatory diseases, such as Behçet's and inflammatory bowel disease. EN lesions have been reported in 44% of patients with BD.¹⁶ They were described in 4.4% of patients with BD as the initial manifestation of the disease.¹⁶ Interestingly, EN is considered as a disease criterion in the International Study Group International Criteria for BD.¹⁷ Importantly, no other case in the literature, as far as we know, reported EN as an initial manifestation of BD flare secondary to COVID-19.

Conclusion

In conclusion, despite being a rare entity, BD flare can occur secondary to COVID-19. While most flare signs resolve with the continuation of the remission treatments, some flares need aggressive treatment such as systemic corticosteroids. In most cases, the presentation of the flare can involve the eyes or the orogenital mucosa. However, atypical presentation, such as EN, can sometimes be an initial presentation of a BD flare in the setting of a SARS-CoV-2 infection.

Table 1. Literature data on the characteristics of BD flares induced by COVID-19.

| Study | Number of patients with flare | Presenting symptom | Management |
|--------------------------------|-------------------------------|---|---|
| Yurttaş et al. ¹⁰ | 3 | Oral ulcers or arthralgias | Colchicine |
| Espinosa et al. ¹¹ | 2 | Oral and genital aphthosis 1 with EN | Colchicine |
| AlBloushi et al. ¹² | 2 | Uveitis | Adalimumab |
| Ozcifci et al. ⁹ | 36 | 22 with oral ulcers 7 with genital ulcers 10 with uveitis 14 with various skin lesions | NA |
| Shahram et al. ⁵ | 16 | NA | NA |
| Polat et al. ¹³ | 19 | 12 with oral ulcers 10 with arthralgias 1 with DVT | NA |
| Trevisini et al. ¹⁴ | 3 | Mucocutaneous, ocular, neurological, joint, and vascular involvement | Systemic corticosteroids or azathioprine |
| Current report | 1 | EN lesion | Systemic corticosteroids and tocilizumab |

BD: Behçet's disease; DVT: deep vein thrombosis; NA: not applicable; EN: erythema nodosum.

Therefore, more literature description is crucially needed to elaborate on the presentation of COVID-19 in patients with BD and the outcomes of possible BD flares.

Author contributions

G.E.H. reviewed the literature and drafted the manuscript. A.S.M.J. critically revised the manuscript. I.U. provided data and critically revised the manuscript.

Declaration of conflicting interests

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