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Neonatal Behçet's syndrome: a case report and literature review

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Abstract

Behçet's syndrome is a rare, chronic inflammatory disorder characterized by recurrent oral and genital ulcers, skin lesions, and eye inflammation. While most children born to mothers with Behçet's syndrome remain asymptomatic, some newborns may develop symptoms due to unclear pathological mechanisms. A male newborn, born at 39 weeks to a mother with a 14-year history of Behçet's syndrome, developed oral lesions on the 10th day of life. The lesions progressed, becoming ulcerated and causing painful feeding. Additional findings included a few facial pustules, pathergy, leukocytosis, and elevated inflammatory markers. Despite multiple therapies, the condition persisted. A biopsy of the tongue lesion was performed, and a diagnosis of neonatal Behçet's syndrome was made based on the clinical course, negative microbiological studies, and maternal history. The patient was treated with intravenous methylprednisolone, followed by oral steroids, with resolution within 3 months. Neonatal Behçet's syndrome is a very rare condition, with only a few cases reported in the literature. Most cases have mild clinical presentations, resolving spontaneously or with corticosteroids. However, severe cases with airway obstruction or neurological complications have been reported. This case demonstrates a favorable and self-limiting course. The underlying mechanisms causing symptoms in newborns of mothers with Behçet's syndrome remain unclear. Reporting these rare cases can help identify risk factors and improve early diagnosis.

Key words: neonatal Behçet syndrome, pediatric Behçet, oral ulcers, pathergy.

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Introduction

The diagnosis of Behcet's syndrome is based on a constellation of clinical features, as there are no pathognomonic laboratory findings. The most frequent symptoms are oral and genital ulcers, skin and eye lesions, and hyper-reactivity of the skin in response to minimal trauma (pathergy) (1). Vascular, neurological, and gastrointestinal symptoms may also be associated. Most children born to mothers with Behçet's syndrome during pregnancy remain asymptomatic. However, some newborns develop symptoms due to unclear pathological mechanisms.

Case Report

A male newborn was born at 39 weeks following a monitored and uneventful pregnancy. The mother had been diagnosed with Behcet's syndrome 14 years earlier due to severe oral and genital ulcers and dermatological symptoms. Maternal serological and genetic screening was negative for antinuclear antibody (ANA), anti-extractable nuclear antigen, and anti-double-stranded DNA antibodies, and HLA B51. During pregnancy, the disease was in remission under treatment with azathioprine (50 mg/day) and low-dose prednisolone. Previously, she was successfully treated with infliximab due to a severe disease course, with refractory necrotizing oral ulcers. Colchicine was discontinued before conception due to gastrointestinal intolerance.

The newborn developed a large ulcer on the dorsal aspect of the tongue on the 10th day of life, initially treated with topical antifungals (nystatin), which caused painful feeding. He also had rare facial pustules (Figure 1), with no other skin lesions, particularly in the genital area. He did not show fever, weight loss, or gastrointestinal symptoms. Due to the severity of the condition, he was admitted to his local hospital at 16 days old and received empirical treatment with ampicillin, cefotaxime, fluconazole, and acyclovir.

Laboratory investigations showed leukocytosis (maximum value of 21.8×10^9/L) with neutrophilia (maximum value 13.76×10^9/L), and elevated inflammatory markers [C-reactive protein (CRP) 95.6 mg/L, erythrocyte sedimentation rate (ESR) 15 mm/1st hour]. There were no alterations in renal or hepatic function, and blood, urine, and cerebrospinal fluid cultures were negative. Tongue ulcer swabs tested negative for fungi and herpes simplex virus 1 and 2.

Due to the lack of improvement, he was transferred to a tertiary hospital for further investigations. Upon surgical observation, there was a large ulcerated lesion located on the dorsal tongue, with loss of substance, 2-3 cm in diameter, a 1 cm lesion on the hard palate, and an infracentimetric lesion on the tonsillar pillar. Biopsy of the largest tongue ulcer yielded negative results for bac-

terial, mycobacterial, and fungal cultures, as well as negative polymerase chain reaction testing for Parvovirus B19, Varicella Zoster Virus, Herpes Simplex Virus 1, 2, and 8, Epstein-Barr Virus, Cytomegalovirus, *Treponema pallidum*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Candida albicans*. Histopathology revealed ulcerated borders with inflammatory infiltrates, with no malignancy.

The immunological study was unremarkable: immunoglobulin G 325 mg/dL, immunoglobulin A <6 mg/dL, immunoglobulin M 42 mg/dL, negative ANA and antineutrophil cytoplasmic antibodies. The HLA B51 was negative. During hospitalization, the development of pustules at puncture sites suggested pathergy (Figure 2).

Given the clinical course (oral ulcers + facial pustules + pathergy), high inflammatory markers, negativity of multiple microbiological studies, and a maternal history of Behçet's syndrome, a diagnosis of neonatal Behçet's syndrome was made. Treatment was initiated with intravenous methylprednisolone at a dose of 1.5 mg/kg/day for 3 days, reduced to 0.75 mg/kg/day for 2 days, and changed to oral deflazacort at a starting dose of 2.5 mg/kg/day with a slow tapering regimen over 2 months.

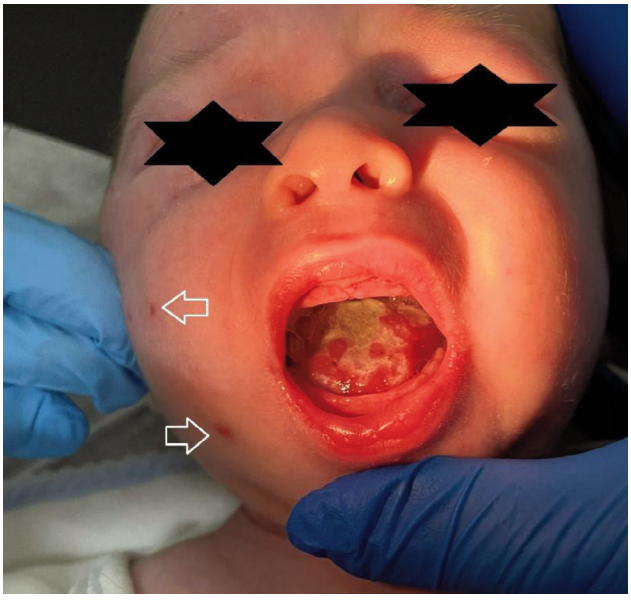

Figure 1. Large tongue ulcer with active borders and facial pustules (white arrows).

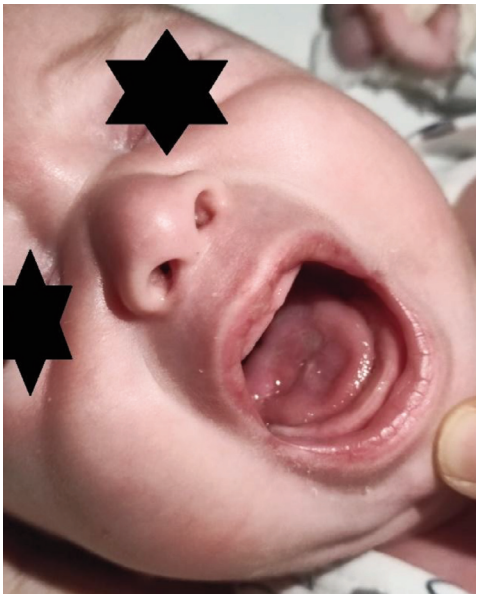

Figure 3. Tongue ulcer without active inflammation after a few days of steroids.

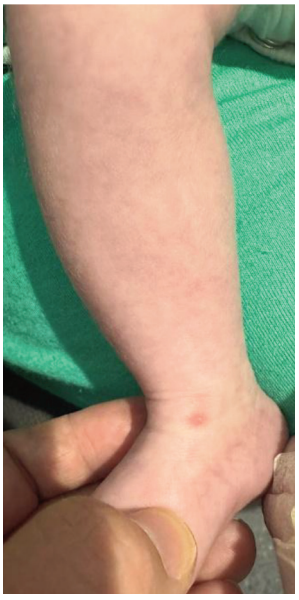

Figure 2. Pustule on the right leg on the day after venopucture (pathergy).

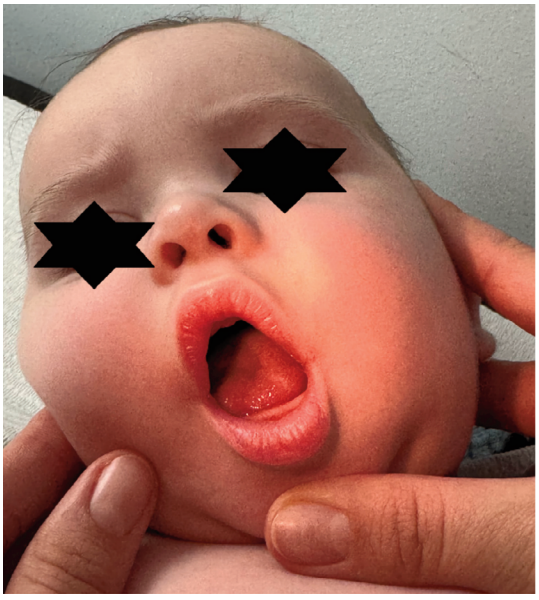

Figure 4. Tongue with minor scarring 3 months after treatment initiation.

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The patient's clinical condition improved significantly following the initiation of corticosteroids, with normalization of inflammatory markers and immediate improvement of mucocutaneous symptoms (Figure 3). At 3 months of age, the largest tongue lesion now shows some scarring changes (Figure 4); the remaining findings have regressed. Blood tests reveal negative blood counts and negative CRP and ESR.

Discussion and Conclusions

Autoimmune diseases are rare in fetuses and neonates due to their immature immune systems, with relative immunodeficiency and inability to overreact to self. Most neonatal autoimmune conditions arise from maternal antibodies crossing the placenta and targeting fetal or neonatal antigens (2). This is further illustrated by the self-limited nature of these conditions, as washout of the antibodies occurs during the first year of life.

The exceptions are some rare genetic autoinflammatory syndromes (SAI), like cryopyrin-associated periodic syndromes and deficiency in interleukin-1 receptor antagonist, that can present very early in life. Some interferonopathies, such as stimulator of interferon genes-associated vasculopathy of infancy and chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature, and nuclear factor-kB-related disorders, such as otulipenia, have also been described in the first month of life. Autoinflammatory disorders should be considered in an infant with unexplained fevers, rash, and evidence of systemic inflammation with a negative infectious workup (3).

Some manifestations can be common to secondary neonatal autoimmune diseases, but SAI are not self-limited and require lifelong treatment. Whenever neonatal presentations are organ and/or life-threatening, if the mother is asymptomatic or does not carry pathogenic antibodies, or if manifestations are not self-limited, primary SAI should always be excluded.

The better-known neonatal secondary autoimmune diseases are neonatal lupus and antiphospholipid syndrome. Others include neonatal Behçet's syndrome, Graves' disease, and, more rarely, myasthenia gravis. In some, including Behçet's syndrome, the specific target antigen remains unidentified (2).

Even in the most common prototypic neonatal lupus, the mechanisms driving secondary autoimmune diseases in newborns remain unclear, though they are often linked to antibodies against Ro and La. Since many mothers with these antibodies have unaffected infants, additional factors beyond the direct effect of transplacental antibodies should be at work. Key theories include cardiac cell apoptosis, maternal microchimerism, autoantibody cross-reactivity with heart tissue, T cell dysregulation, inhibitory receptors, and genetic predisposition (2).

The pathogenesis of Behçet's syndrome is complex, and both autoimmune and autoinflammatory features seem to be involved. Autoantibodies have been described against several targets, including oral mucosal antigens, endothelial cells, killer immunoglobulin-like receptors, T cell costimulatory molecule CTLA-4, kinectin, and oxidized low-density lipoprotein (4-9). Anti-saccharomyces cerevisiae antibodies have been observed in patients with Behçet's syndrome (10, 11).

Behçet's syndrome with a neonatal presentation is a very rare clinical entity, with only 15 cases described in the literature (12-26). The majority of them presented mild clinical features, typically involving oral and/or genital ulcers with associated skin lesions that resolved spontaneously or with corticosteroids.

Only two severe cases have been reported, one with airway obstruction and the other with neurological complications (17, 26). Three additional cases showed intestinal involvement, characterized by diarrhea, poor feeding, and delayed weight gain (14, 24). In only a few cases with non-affected mothers, the neonates' clinical presentations were consistent with Behçet's syndrome (14, 21, 24). Interestingly, all reported cases with intestinal involvement exhibited this discrepancy. Despite a benign course, some cases exhibited scarring from mutilating lesions in the oral mucosa (15, 16, 20). The most frequently described laboratory abnormalities were elevated inflammatory markers and leukocytosis with neutrophilic predominance. Our patient exhibited these same alterations. In nearly all cases, a differential diagnosis of herpesvirus infection was excluded, as in our patient.

This case had a favorable and self-limiting course. The underlying mechanisms causing symptoms in newborns of mothers with Behçet's syndrome remain unclear. Interestingly, this newborn presented with the same most severe and refractory manifestation as the mother, severe oral ulcers resulting in scarring. This is possibly due to an unidentified antibody against oral mucosal antigens.

Reporting these rare cases can help identify risk factors and improve early diagnosis, potentially avoiding unnecessary hospital stays, tests, and treatment. The baby exhibits normal growth and development so far, with no other health issues.

References

1. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. Lancet 1990; 335: 1078-80.
2. Chang C. Neonatal autoimmune diseases: a critical review. J Autoimmun 2012; 38: J223-38.
3. Stolberg NG, Verbsky JW. Autoinflammatory disorders with perinatal onset. Clin Perinatol 2020; 47: 41-52.
4. Aydìntug AO, Tokgöz G, D'cruz DP, Gürler A, Cervera R, Düzgün N, et al. Antibodies to Endothelial Cells in Patients with Behçet's Disease. Clin Immunol Immunopathol 1993; 67: 157-62.
5. Direskeneli H, Keser G, D'Cruz D, Khamashta MA, Akoğlu T, Yazici H, et al. Anti-endothelial cell antibodies, endothelial proliferation and von Willebrand factor antigen in Behçet's disease. Clin Rheumatol 1995; 14: 55-61.
6. Matsui T, Kurokawa M, Kobata T, Oki S, Azuma M, Tohma S, et al. Autoantibodies to T cell costimulatory molecules in systemic autoimmune diseases. J Immunol 1999; 162: 4328-35.
7. Matsui T, Otsuka M, Maenaka K, Furukawa H, Yabe T, Yamamoto K, et al. Detection of autoantibodies to killer immunoglobulin-like receptors using recombinant fusion proteins for two killer immunoglobulin-like receptors in patients with systemic autoimmune diseases. Arthritis Rheum 2001; 44: 384-8.
8. Örem A, Çimşit G, Değer O, Vanizor B, Karahan SC. Autoantibodies against oxidatively modified low-density lipoprotein in patients with Behçet's disease. Dermatology 1999; 198: 243-6.
9. Feng XGG, Ye S, Lu Y, Xu XJ, Gu YY, Shen N, et al. Antikinectin autoantibody in Behçet's disease and several other autoimmune connective tissue diseases. Clin Exp Rheumatol 2007; 25: s80-5.
10. Choi CH, Kim T Il, Kim BC, Shin SJ, Lee SK, Kim WH, et al. Anti-saccharomyces cerevisiae antibody in intestinal Behçet's disease patients: relation to clinical course. Dis Colon Rectum

2006; 49: 1849-59.
11. Cheng L, Li L, Liu C, Yan S, Li Y. Meta-analysis of anti-saccharomyces cerevisiae antibodies as diagnostic markers of Behçet's disease with gastrointestinal involvement. BMJ Open 2020; 10: e033880.
12. Patel D, Cook N, Newell B, Becker M. Fever, irritability, and ulcerations in an infant. Pediatr Dermatol 2013; 30: e287-8.
13. Johnson EF, Hawkins DM, Gifford LK, Smidt AC. Recurrent oral and genital ulcers in an infant: neonatal presentation of pediatric Behçet disease. Pediatr Dermatol 2015; 32: 714-7.
14. Wu PS, Chen HL, Yang YH, Jeng YM, Lee PI, Chang MH. Intestinal Behçet disease presenting as neonatal onset chronic diarrhoea in an 11-month-old male baby. Eur J Pediatr 2005; 164: 523-5.
15. Fam AG, Siminovitch KA, Carette S, From L. Neonatal Behcet's syndrome in an infant of a mother with the disease. Ann Rheum Dis 1981; 40: 509-12.
16. Fain O, Mathieu E, Lachassinne E, Buisson P, Bodemer C, Gaudelus J, et al. Neonatal behçet's disease. Am J Med 1995; 98: 310-1.
17. Stark AC, Bhakta B, Chamberlain MA, Dear P, Taylor P V. Life-threatening transient neonatal Behcet's disease. Br J Rheumatol 1997; 36: 700-2.
18. Thivolet J, Cambazard F, Genvo MF. Maternally-transmitted severe neonatal aphthosis. Ann Dermatol Venereol 1982; 109: 815-6. [Article in French].
19. Schuberth K, Kniess N, Johann Müller M, Seeliger S. Neonatal Behçet Disease. Klin Padiatr 2018; 230: 270-4. [Article in German].
20. Lewis MA, Priestley BL. Transient neonatal Behçet's disease. Arch Dis Child 1986; 61: 805-6.
21. Chang Y Sen, Yang YH, Chiang BL. Neonatal Behçet's disease without maternal history. Clin Rheumatol 2011;1641-5.
22. Antonelou M, Braha N. Transient neonatal Behçet's disease. BMJ Case Rep 2013; 2013; bcr2012007589.
23. Clarke K, Shastry D, Chetcuti P, Wood M, Morgan A. Neonatal Behçet's disease. Arch Dis Child 2017; 102: 1062.
24. Chong SK, Wright VM, Nishigame T, Raafat F, Isaacs D, Morson BC, et al. Infantile colitis: a manifestation of intestinal Behçet's syndrome. J Pediatr Gastroenterol Nutr 1988; 7: 622-7.
25. Fernández-Fructuoso JR, Gil-Sánchez S, Gómez-Santos E, Lloreda-García JM, Sevilla-Denia S, Leante-Castellanos JL. Neonatal Behçet's disease with Raynaud phenomenon. J Neonatal Perinatal Med 2016; 9: 423-5.
26. Jog S, Patole S, Koh G, Whitehall J. Unusual presentation of neonatal Behcets disease. Am J Perinatol 2001; 18: 287-92.

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