

A Clinical Odyssey: a case report on the diagnostic complexity and neurological management of Behçet's disease

Thaís Malta Romano ¹, Sandra Isamar da Silva Leandro ², Karoliny de Lima Nardin ³, Beatriz Mazzer Zamoner ⁴, Bruna Capello Gervásio ⁴, Fernanda Susy Bessa Menezes Cavalcante ⁵, Kelvin Corrêa Miranda Alves ⁶, Lavínnia Yáskara de Aquino Matoso ⁷, Francisco Ícaro Silvério de Oliveira ⁸, Paulo Guilherme Müller ⁹, Álvaro Moreira Rivelli ¹⁰, Marina Carvalho de Souza Lima ¹⁰, Roger Wilson Gonçalves de Oliveira ¹¹, Júlio César Claudino dos Santos ¹²

¹ Universidade Federal de São Paulo, São Paulo, SP, Brazil.

² Universidade Federal do Ceará, UFC, Fortaleza, Ceará, Brazil.

³ Centro Universitário Católico Salesiano Auxilium - UniSALESIANO, Araçatuba, SP, Brazil.

⁴ Centro Universitário Barão de Mauá - CBM, Ribeirão Preto, São Paulo, Brazil.

⁵ Universidade Federal do Ceará, UFC, Fortaleza, Ceará, Brazil; Centro Universitário INTA, UNINTA, Sobral, Ceará, Brazil.

⁶ Pontifícia Universidade Católica, PUCRS, Rio Grande do Sul, Brazil.

⁷ Universidade Potiguar, UNP, Mossoró, Rio Grande do Norte, Brasil.

⁸ Centro Universitário Leonardo Da Vinci - UNIASSELVI, Indaial, Santa Catarina, Brazil.

⁹ Universidade Federal de Pelotas - UFPel, Faculdade de Medicina, Pelotas, Rio Grande do Sul, Brazil..

¹⁰ Centro Universitário Governador Ozanam Coelho, Minas Gerais, MG, Brazil.

¹¹ Faculdade Metropolitana de Manaus - Fametro, Manaus, Amazonas, Brazil.

¹² Post-graduate Program in Morphofunctional Science. Federal University of Ceara, Ceará, Brazil.

* Correspondence: rafaromani@gmail.com.

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Abstract: Behçet's Syndrome (BS) is a pathological condition that encompasses a diverse spectrum of clinical manifestations of a polysystemic nature. It is a chronically progressive inflammatory vasculitis, characterized mainly by recurrent episodes of oral and genital aphthous ulcers, ocular involvement, and other clinical expressions, including skin lesions and gastrointestinal disorders. The aim of this study is to present an atypical case of BS, as well as its correlation with the medical literature, to elucidate particularities of relevant significance for medical practice.

Keywords: Behçet's syndrome; Behçet/optic neuritis, Behçet's syndrome/differential diagnosis, Behçet's syndrome/therapy.

1. Introduction

Behçet's disease (BD) is described as a multisystem vasculitis with heterogeneity that has a broad involvement in various body systems [1]. Its main characteristics are oral and genital ulceration, ocular inflammation, and skin lesions [2]. Neurological involvement (Neuro-Behçet's disease), which is rarer, is around 9%, ranging from 3% to 30% [3]. It generally affects more men and young adults [4] and may be the first manifestation or appear during the disease [5].

In this sense, ophthalmic involvement in BD is frequent and an important cause of morbidity. One of the most important ocular manifestations is uveitis, whose average age of onset is between 20 and 30 years in male patients and 30 years in female patients [6]. In addition, extraocular manifestations with visual repercussions are also characteristic, such as neuritis, a rare condition characterized by inflammation of the optic nerve, which can

lead to symptoms such as loss of vision, blurred vision, ocular pain and altered color perception, which can cause permanent damage [7]. With this information, the treatment of ophthalmic manifestations, such as biotechnological agents, is remarkably effective, improving intraocular inflammation, visual acuity and helping to reduce acute exacerbations. They also help to reduce the use of systemic immunosuppressants, including corticosteroids [8].

Diagnosis is essentially clinical, and inflammatory diseases are characterized by multifaceted episodes of idiopathic origin, without the identification of a specific antigen or antibody that defines the immune response [9]. Complementary tests help in the differential diagnosis and exclusion of potential complications, such as cerebrospinal fluid analysis, magnetic resonance imaging and computerized tomography [10, 11]. However, it is understood that BD is potentially serious, especially when the uvea, central nervous system and great vessels are affected. It is therefore necessary for doctors to be familiar with the forms of BD, its natural evolution, as well as its diagnosis and treatment, to improve the patient's prognosis. This case report emphasizes the importance of recognizing optic neuritis as a possible presenting symptom of BD, which is a rare clinical feature.

2. Case Report

This clinical case discusses a 24-year-old male patient from Belo Horizonte, Brazil, seen at the Internal Medicine and Rheumatology center, who presented in 2022 with an episode of optic neuritis in the left eye > right eye responsive to corticosteroids. Despite the fact that, at the time, there was no etiology in the clinical and propaedeutic evaluation, but there was a good progression and, therefore, recovery of visual acuity, the patient did not follow the treatment until, in the same year, he manifested a headache, a sensation of paresthesia in his lower limbs and an ulcer on his genitals (Figure 1).



Figure 1: Genital ulcer in a patient with Behcet syndrome.

With this condition, clinical and laboratory tests tested negative for Sexually Transmitted Diseases (STDs). The headache and complaints of paresthesia ceased with the use of corticosteroids and, although he still had an ulcer on his glans, the patient had no systemic symptoms. The pathogen test was negative, and magnetic resonance imaging (MRI) and magnetic angiography (MRA) (including the venous phase) showed no axial or extra-

axial involvement. Biochemical tests within reference: Creatine 1.1 mg/dL, CRP 0.3 mg/l, TGP 18 U/l, Anti HCV and HBC IgG not reactive, red series and white series within reference standards. Given this information, the patient continues to be monitored on an outpatient basis using Azathioprine 50mg and Colchicine 0.5mg, with the aim of reducing the inflammation of the mucosa and preventing new neurological manifestations.

3. Discussion and conclusion

Behcet's Syndrome is a pathological condition that encompasses a diverse spectrum of clinical manifestations of a polysystemic nature. The disease usually manifests itself in the 30s and 40s, with a predominance of males [12, 13]. However, the above-mentioned patient is in his second decade of life and has no positive laboratory or imaging results for BD but has ocular symptoms such as neuritis and genital ulcers. It should be noted that ocular involvement is a manifestation present in approximately half of all cases of BD, with the possibility of amaurosis occurring in up to 20% of affected patients. The ocular lesions observed in the patient are characterized by being bilateral, non-granulomatous, recurrent and inflammatory in nature.

The prognosis becomes unfavorable when the posterior segment of the eye is involved, and can manifest itself in conditions such as periphlebitis, diffuse vascular process, retinitis and vitritis [14, 15]. Therefore, the diagnosis of Behcet's Disease is essentially clinical due to the heterogeneity of its presentation. In 1990, the International Study Group for Behcet's Disease (ISGBD) introduced additional diagnostic criteria. However, it is essential to emphasize that these criteria should not be used in isolation to diagnose individual cases.

The disease is usually treated with immunosuppressive drugs and corticosteroids, such as Azathioprine and Cyclosporine A [16], with good results with alpha-interferon [17]. In this case, the treatment prescribed was Azathioprine 50mg, which has the characteristic of controlling inflammation and the symptoms of the disease, such as oral ulcers, specific lesions, and ocular inflammation. However, Azathioprine can promote the generation of reactive oxygen species with mutagenic potential, making it a possible carcinogenic agent [18]. This risk becomes more significant after a period of continuous treatment of approximately 10 years or when the accumulated dose reaches 600 grams or more [18].

Furthermore, the medication Colchicine, with an initial prescription of 0.5mg, has been widely used as a fundamental approach to treating the disease, due to its ability to exert beneficial effects in inhibiting the functions of neutrophils, due to their hyperactivation in BD [19]. Despite showing limitations in cases of more severe manifestations, treatment with colchicine results in a reduction in the incidence of oral and genital ulcers and erythematous lesions, as well as providing relief from the symptoms of arthritis [20, 21].

Colchicine is commonly employed in the treatment of Behçet's disease due to its anti-inflammatory and immunomodulatory properties. This autoimmune disease is characterized by chronic inflammation of small and medium-sized blood vessels, affecting various parts of the body. Colchicine acts by inhibiting microtubule formation, interfering with the processes of chemotaxis and phagocytosis, resulting in reduced leukocyte migration and, consequently, decreased inflammation. Additionally, colchicine demonstrates efficacy in controlling specific symptoms associated with Behçet's disease, such as recurrent oral aphthae, through the suppression of the inflammatory response, which may contribute to improving the quality of life for patients [10, 12, 21, 22]. It is worth noting that BD is one of the main causes of long-term morbidity and mortality in its sufferers, making its recognition and treatment essential for a better outcome [22]. For this reason, it is important to carry out differential diagnosis and scientific disclosure of less frequently reported diseases.

4. Conclusion

Research focused on Behçet's cases in young individuals is of paramount importance to the scientific community, encompassing various perspectives. Firstly, the epidemiological approach is crucial for understanding the prevalence of the disease. Colchicine is commonly employed in treating Behçet's disease due to its anti-inflammatory and immunomodulatory properties. This autoimmune disease is characterized by chronic inflammation of small and medium-sized blood vessels, affecting various parts of the body. Colchicine acts by inhibiting microtubule formation, interfering with the process of chemotaxis and phagocytosis, resulting in reduced leukocyte migration and, consequently, decreased inflammation. Additionally, colchicine demonstrates efficacy in controlling specific symptoms associated with Behçet's disease, such as recurrent oral aphthae, through the suppression of the inflammatory response, potentially contributing to improving patients' quality of life.

In this specific age group, identifying incidence patterns and specific risk factors is essential. Furthermore, analyzing diagnostic and therapeutic challenges in young individuals highlights specific issues related to early diagnosis and condition management, providing essential insights to tailor therapeutic strategies to the peculiarities of this population. Evaluating the impact on the quality of life and psychosocial development of affected young individuals is fundamental for formulating appropriate interventions and support. Moreover, investigating these cases substantially contributes to the global knowledge of Behçet's disease, potentially leading to discoveries benefiting both young individuals and the general population by providing valuable information on underlying mechanisms, disease progression, and possible therapeutic approaches. The identification of specific risk factors is crucial for developing preventive strategies and targeted screening protocols, aiming to reduce the incidence or achieve early detection of the disease in this specific population.

In summary, researching Behçet's disease in young individuals represents a significant contribution to scientific advancement, enriching the understanding of this complex condition and providing valuable insights to improve clinical practice and public health. As this is a clinical case with many non-specific manifestations, some patients tend to mischaracterize the classic symptoms of the disease. Therefore, a differential analysis is extremely important, considering new diagnostic options and understanding different levels of functioning to contribute to a more effective approach to the available therapeutic options. A multidisciplinary approach is necessary for better outcomes. Larger cohort studies and unpublished reports are needed to enhance the literature on Behçet's disease.

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References

1. Hatemi G, Seyahi E, Fresko I, Talarico R, Hamuryudan V. One year in review 2020: Behçet's syndrome. *Clin Exp Rheumatol.* 2020;38 Suppl 127(5):3–10.
2. Yurdakul S. Epidemiology of Behçet Syndrome and Regional Differences in Disease Expression. In: Yazici Y, Hatemi G, Seyahi E, Yazici H, editors. *Behçet Syndrome*. Springer, Cham; 2020. <https://doi.org/10.1007/978-3-030-24131-5>.
3. Kidd DP. Neurological complications of Behçet's syndrome. *J Neurol.* 2017;264(10):2178–2183.
4. Noel N, Bernard R, Wechsler B, Resche-Rigon M, Depaz R, Le Thi Huong Boutin D, et al. Long-term outcome of neuro-Behçet's disease. *Arthritis Rheumatol.* 2014;66(5):1306–1314.

5. Domingos J, Ferrão C, Ramalho J, Rodrigues T, Moreira B, Santos E, et al. Characteristics of neuro-Behçet's disease in a case-series from a single centre in Northern Portugal. *Eur Neurol.* 2015;73(5-6):321-328.
6. Saadoun D, Cassoux N, Wechsler B, Boutin D, Terrada C, Lehoang P, Bodaghi B, Cacoub P. Ocular manifestations of Behçet's disease. *Rev Med Interne.* 2010;31(8):545-550. doi: 10.1016/j.revmed.2009.04.014.
7. Saadoun D, Wechsler B. Behçet's disease. *Orphanet J Rare Dis.* 2012 Apr 12;7:20. doi: 10.1186/1750-1172-7-20.
8. Martín-Varillas JL, Calvo-Río V, Beltrán E, Sánchez-Bursón J, Mesquida M, Adán A, et al. Successful Optimization of Adalimumab Therapy in Refractory Uveitis Due to Behçet's Disease. *Ophthalmology.* 2018;125(9):1444-51.
9. Owlia MB, Mehrpoor G. Behçet's Disease: New Concepts in Cardiovascular Involvements and Future Direction for Treatment. *ISRN Pharmacol.* 2012;2012:760484. doi: 10.5402/2012/760484.
10. Silva L, Correia J, Santos E. Diagnóstico e Tratamento de Neuro-Behçet: Uma Atualização Clínica. *Porto Acta Med [Internet].* 2023, 21 de junho [citado em 26 de agosto de 2023]. Disponível em: <https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/19734>.
11. Borhani-Haghighi A, Kardeh B, Banerjee S, Yadollahikhales G, Safari A, Sahraian MA, Shapiro L. Neuro-Behçet's disease: An update on diagnosis, differential diagnoses, and treatment. *Mult Scler Relat Disord.* 2020 Apr;39:101906. doi: 10.1016/j.msard.2019.101906. Epub 2019 Dec 23. PMID: 31887565.
12. Yazici H, Fresko I, Yurdakul S. Behçet: manifestações da doença, manejo e avanços no tratamento. *Nat Clin Pract Rheumatol.* 2007;3(3):148-155.
13. Sachdev N, Kapali N, Singh R, Gupta V, Gupta A. Espectro da doença de Behçet na população indiana. *Int Ophthalmol.* 2009;29(6):495-501.
14. Kidd D, Steuer A, Denman AM, Rudge P. Neurological complications in Behçet's syndrome. *Brain.* 1999;122(Pt 11):2183-94.
15. Kanski JJ. *Clinical ophthalmology. Uveitis* (6): 3rd ed.
16. Yazici H, Pazarli H, Barnes CG, Tuzun Y, Ozyazgan Y, Silman A, Serdaroglu S, Oguz V, Yurdakul S, Lovatt GE et al. A controlled trial of azathioprine in Behçet's syndrome. *N Engl J Med.* 1990;322:281-5.
17. Yazici H, Yurdakul S, Hamuryudan V. Behçet's syndrome. *Curr Opin Rheumatol.* 1999;11:53-7.
18. Borhani-Haghighi A, Kardeh B, Banerjee S, Yadollahikhales G, Safari A, Sahraian MA, Shapiro L. Neuro-Behçet's disease: an update on diagnosis, differential diagnoses, and treatment. *Multiple sclerosis and related disorders.* 2020;39:101906.
19. Confavreux C, Saddier P, Grimaud J, Moreau T, Adeleine P, Aimard G. Risk of cancer from azathioprine therapy in multiple sclerosis: a case-control study. *Neurology.* 1996;46(6):1607-1612.
20. Hirohata S, Kikuchi H. Behçet's disease. *Arthritis Res Ther.* 2003;5(3):139-46.
21. Yurdakul S, Mat C, Tüzün Y, Ozyazgan Y, Hamuryudan V, Uysal O, et al. A double-blind trial of colchicine in Behçet's syndrome. *Arthritis Rheum.* 2001;44(11):2686-92.
22. Davatchi F, Sadeghi Abdollahi B, Tehrani Banihashemi A, Shahram F, Nadji A, Shams H, et al. Colchicine versus placebo in Behçet's disease: randomized, double-blind, controlled crossover trial. *Mod Rheumatol.* 2009;19(5):542-9.
23. Caruso P, Moretti R. Focus on neuro-Behçet's disease: A review. *Neurol India.* 2018 Nov-Dec;66(6):1619-1628. doi: 10.4103/0028-3886.246252.