Adamantiades-Behçet's disease and COVID-19

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Introduction

COVID-19 results in a multi-faceted inflammatory disease and immune-mediated organ damage. There is a reasonable cause for concern that it may occur in patients with autoimmune/autoinflammatory diseases.

Adamantiates-Behçet's disease (ABD) is a rare, multisystemic, hyper-ergic, inflammatory disease characterized by variable vasculitis/ perivasculitis and relapsing–remitting course. Only rudimentary data on COVID-19 in ABD patients exist, and there is no information about the optimal management of ABD patients during the pandemic period.

Aim, patients and methods

Patients registered in the German Registry of Adamantiades-Behçet's disease (GeR-ABD), who were reported infected with SARS-CoV-2 during the period of 1 March 2020 to 31 October 2022, were prospectively evaluated with the aim to describe the main characteristics of the disease coincidence and to highlight possible management implications. All patients fulfilled the International Diagnostic Criteria of ABD[1]. Demographic and clinical data were collected.

Results

During the study period, 14/900 (1.6%) registered patients, who have been infected with SARS-CoV-2 were identified. The patients were middle-aged (median 45-year-old, IQR 42–56) without sex prevalence (6 female, 8 male) and of different nationalities (9 of German, 2 of Iranian, 2 of Turkish, 1 of Syrian origin). The duration since ABD diagnosis ranged from 1 to 22 years (Table 1) with 9 patients (64.3%) having systemic involvement. Thirteen patients received systemic treatment (4 immuno-suppressive, 9 immunomodulatory) at the time of COVID-19. Twelve patients had undergone investigation for HLA-B51, with 7 being positive, including five German, one Turkish and one Iranian patient. All nine patients who had undergone vitamin D level investigation had hypovitaminosis D (5.41–59.9 nmoL/L; reference range>75), which continued beyond starting supplementation. Patients were infected with SARS-CoV-2 between March 2020 and September 2022, a time period with marked differences in the prevalence of SARS-CoV-2 variants. In 13 patients (92.9%), symptoms ranged from asymptomatic status to moderate fatigue and transient myalgia. Loss of taste was reported in the two patients (14.3%) infected in 2021. No hospitalization and no changes in ABD medication was required in 13 patients (92.9%), and no COVID-19-specific treatment has been introduced in 10 patients (71.4%). All patients recovered completely, although two patients (14.3%) had long-term sequelae.

Discussion

The prevalence of COVID-19 in patients of the GeR-ABD ςαs with 1.6% substantially lower than the median seroprevalence in Germany (2.93%)[2]. Our observations are compatible with the report of the International Society for ABD in January 2021, showing lower COVID-19 prevalence in ABD patients compared with the general population[2]. This might be due to extra precautions advised in risk groups. Indeed, ABD patients, especially those being immunosuppressed/ immune regulated, were commonly apprehensive during the pandemic. However, underreporting of COVID-19 in ABD patients is possible, especially in asymptomatic cases3. In addition, in case series from Spain, Italy, the Netherlands, Turkey and Iran1 lower hospitalization, intensive care and death rates of COVID-19-infected ABD patients were observed in 2021/2022, when compared to those in 2020 (Table 2)[2,4]. Our only hospitalized patient has also been infected in 2020. ABD is an exception among autoimmune/autoinflammatory diseases regarding, probably due to the young age of ABD patients[5] Our data suggest that systemic ABD involvement is not necessarily associated with a severe COVID-19 course and that the medication-induced immunosuppressed/ immunomodulated ABD state does not predispose to SARS-CoV-2 infection. Therefore, ABD therapy should be personalized by balancing the risks of severe COVID-19 with that of ABD relapse.

Table 1. Patients of the German Registry of Adamantiades-Behçet's disease reported to be infected with SARS-CoV-2

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14
Age at COVID-19 diagnosis (years)	50	43	55	65	45	45	56	32	44	42	40	60	59	37
Gender	Male	Male	Male	Female	Female	Female	Male	Male	Female	Female	Female	Male	Male	Male
Origin	Germany	Turkey	Iran	Germany	Syria	Turkey	Germany	Germany	Germany	Iran	Germany	Germany	Germany	Germany
Clinical signs (ABD phenotype)	Recurrent oral and genital aphthae Vascular manifestations (systemic)	Recurrent oral and genital aphthae Recurrent pustular folliculitis Arthralgia (mucocutaneous)	Recurrent oral aphthae Recurrent pustular folliculitis Recurrent scleritis, hypopyon Severe arthralgia (systemic)	Recurrent oral and genital aphthae Deep vein thrombosis Arthritis (systemic)	Recurrent oral and genital aphthae Recurrent pustular folliculitis Arthralgia (mucocutaneous)	Occasional oral aphthae Sporadic arthralgia (mucocutaneous)	Recurrent oral and genital aphthae, Recurrent pustular folliculitis, Thrombophlebitis, skin ulcers, Recurrent retinal vasculitis and bilateral uveitis, Spondylitis. Neuropathy, Peripheralm Pyelonephritis (systemic)	Recurrent oral aphthae Recurrent pustular folliculitis, erythema nodosum Bilateral panuveitis (systemic)	Recurrent oral and genital aphthae Recrrent pustular folliculitis, erythema nodosum Chronic seronegative polyarthritis (mucocutaneous)	Recurrent oral aphthae Severe unilateral panuveitis Neurological manifestations (systemic)	Recurrent oral and genital aphthae (mucocutaneous)	Recurrent oral and genital aphthae Multiple erythema nodosum Recurrent bilateral uveitis Unilateral deep vein thrombosis (systemic)	Recurrent oral aphthae Recurrent pustular folliculitis Erythema nodosum Chronic bilateral iridocyclitis (systemic)	Recurrent oral and genital aphthae Recurrent pustular folliculitis Central oculomotor disorder Cephalgia Lung artery aneurysm (systemic)
Year of ABD diagnosis	2016	2017	2019	2013	2011	2009	2004	2011	2007	2000	2005	2007	2002	2021
ABD medication at presentation	Azathioprine Colchicine	Apremilast	Apremilast	Methotrexate	Azathioprine Colchicine	Triamcinolone oral paste	Infliximab Colchicine	Pegylated Interferon-α 2a	Adalimumab	Azathioprine	Pegylated Interferon-α 2a	Pegylated Interferon-α 2a Colchicine	Apremilast Methylprednisolone Etoricoxib	Colchicine
Date of COVID-19 infection	03/2020	05/2020	11/2020	04/2021	09/2021	02/2022	02/2022	03/2022	03/2022	04/2022	04/2022	04/2022	0720/22	09/2022
COVID-19 symptoms	Moderate cough, Severe sore throat, Fever, Severe fatigue Severe myalgia Severe diarrhoea Severe dyspnoea Respiratory distress	Mild fatigue Mild myalgia	Moderate cough	Mild flu symptoms (cough, rhinitis, fever) Aching limbs Loss of appetite Loss of taste	Fever Headache Moderate myalgia Loss of taste and smell	Moderate fatigue Moderate myalgia Moderate dyspnoea Arthralgia	Severe headache	Moderate fever Moderate sore throat Moderate arthralgia	Mild headache Mild nausea Moderate myalgia	Mild rhitinis	No reported symptoms	Mild fatigue	Mild cough Mild rhinitis	Fever Fatigue Moderate myalgia Arthralgia
Change to ABD symptoms	Intensification of oral aphthae, Athralgia	No change	No change	No change	No change	No change	No change	No change	No change	No change	No change	No change	No change	No change
COVID-19 medication	Multiple, including: Lopinavir/Ritanovir Ribavirin Hydroxychloroquine Respiratory ventilatory support	None	None	None	None	Doxycycline	Ribavirin	None	None	None	None	None	None	Paracetamol
Changes to ABD medication	Stop azathioprine and colchicine Commence apremilast after COVID-19 recovery	No change	No change	No change	No change	No change	No change	No change	No change	No change	No change	No chenge	No change	No change
Outcome	Hospitalised 3 weeks, 1 week in intensive care Recovery with sequlae (exhaustion, acitivity limitation, lack of concentration)	No medical intervention Recovery without sequelae	No medical intervention Recovery with sequelae (exertional dyspnoea)	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae	No medical intervention Recovery without sequelae

Table 2. Studies on COVID-19 amongst patients with Adamantiades-Behçet's disease in Europe and Asia [4]

	Number of patients	Date of publication	Country of publication	Age, years, median (IQR)	Duration of disease, years, median (IQR)	Hospitalisation, n (%)	Intensive care, n (%)	Death, n (%)
Europe								
Correa-Rodriguez et al.	36	12/21	Spain	43 (13)	8.5 (14)	1 (2.9)	N/A	N/A
Accorinti et al.	8	01/22	Italy	47 (18.5)	N/A	1 (12.5)	N/A	0 (0)
den Otter et al.	30	02/22	Netherlands	42.5 (17.5)	N/A	4 (13)	1 (3)	1 (3)
This study	14	12/22	Germany	45 (18)	12 (10)	1 (7.1)	1 (7.1)	0 (0)
Asia								
Yurttaş et al.	10	06/20	Turkey	39.5 (11.75)	14(7)	8 (80)	2 (20)	1 (10)
Polat et al.	59	05/21	Turkey	40 (23.5)	N/A	3 (5)	0 (0)	0 (0)
Shahram et al.	59	11/21	Iran	45 (20)	13.5 (16.25)	15 (25.4)	N/A	1 (1.7)
Enginar et al.	18	12/21	Turkey	39 (17)	N/A	2 (11.1)	1 (5.6)	1 (5.6)

References

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The Departments of Dermatology, Venereology, Allergology and Immunology, Staedtisches Klinikum Dessau, Dessau, Germany are health care providers of the European Reference Network for Rare and Complex Skin Diseases (ERN Skin).

Deutsches Register Morbus Adamantiades-Behçet e.V.