COVID-19 *and* Behçet Disease

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Plan

COVID-19 and Behçet Disease:
Turkish Experience

Common pathogenic mechanisms ?

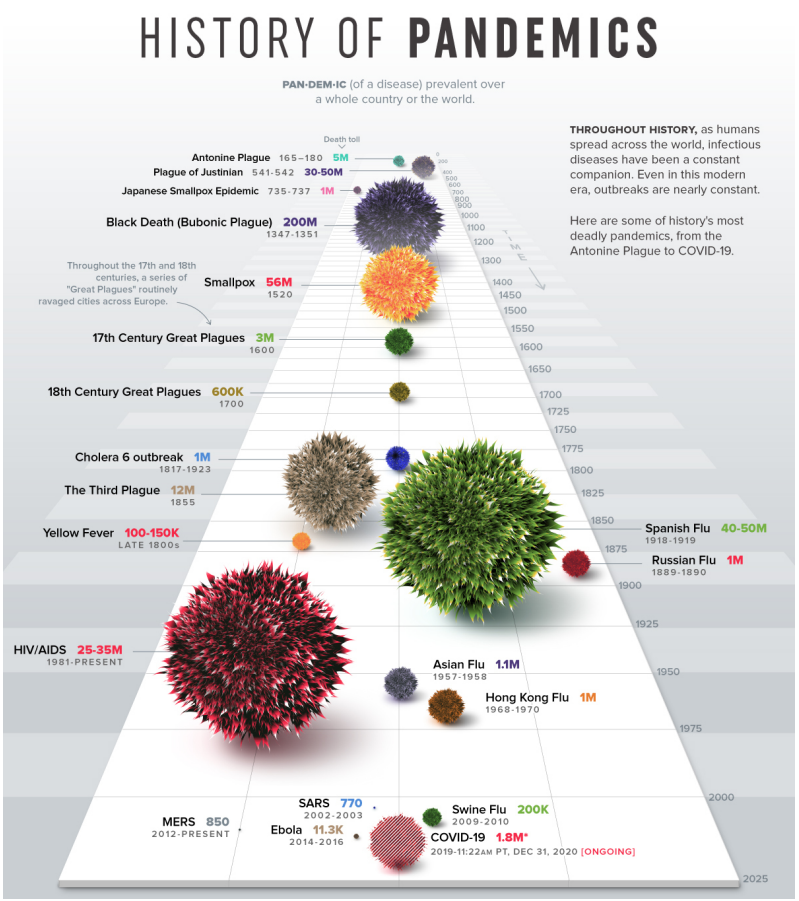
Follow-up and vaccination

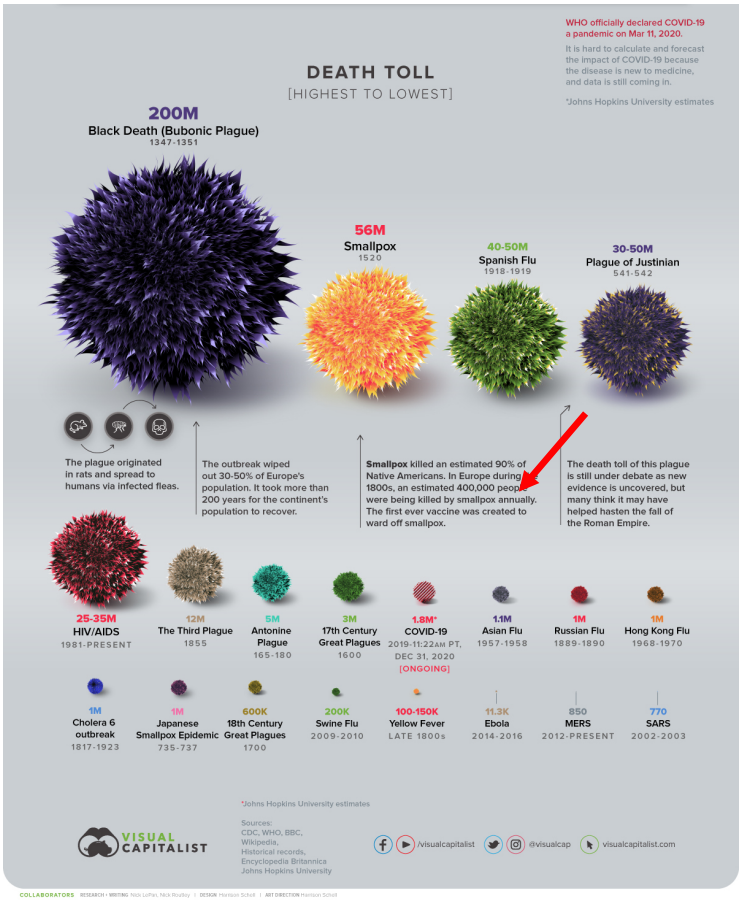
COVID-19 Pandemic

Vita brevis, ars longa, occasio praeceps, experimentum periculosum, iudicium difficile.

Life is short, the Art long, opportunity fleeting, experience perilous, and judgment difficult.

Hippocrates (*Aphorisms)*





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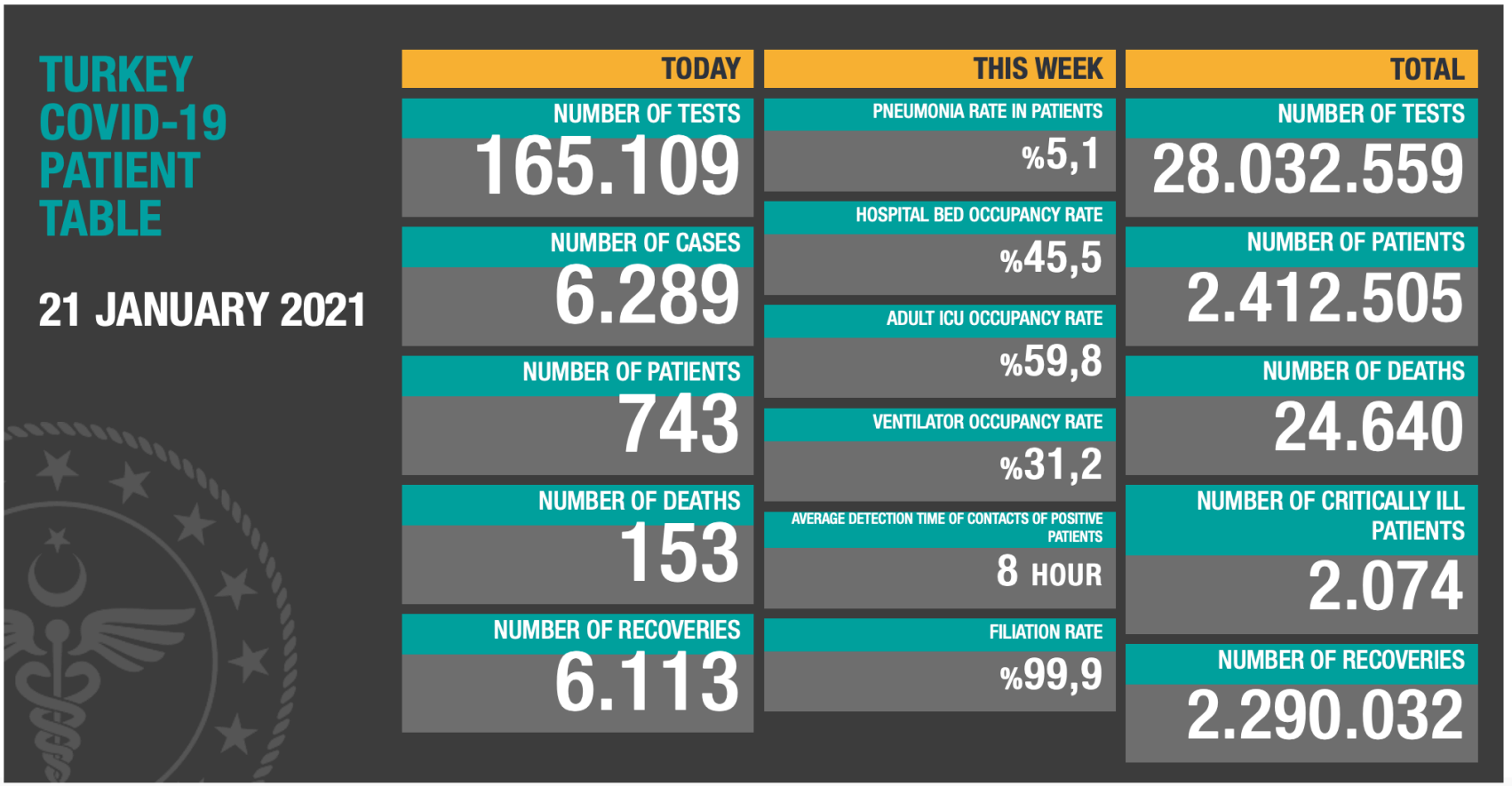
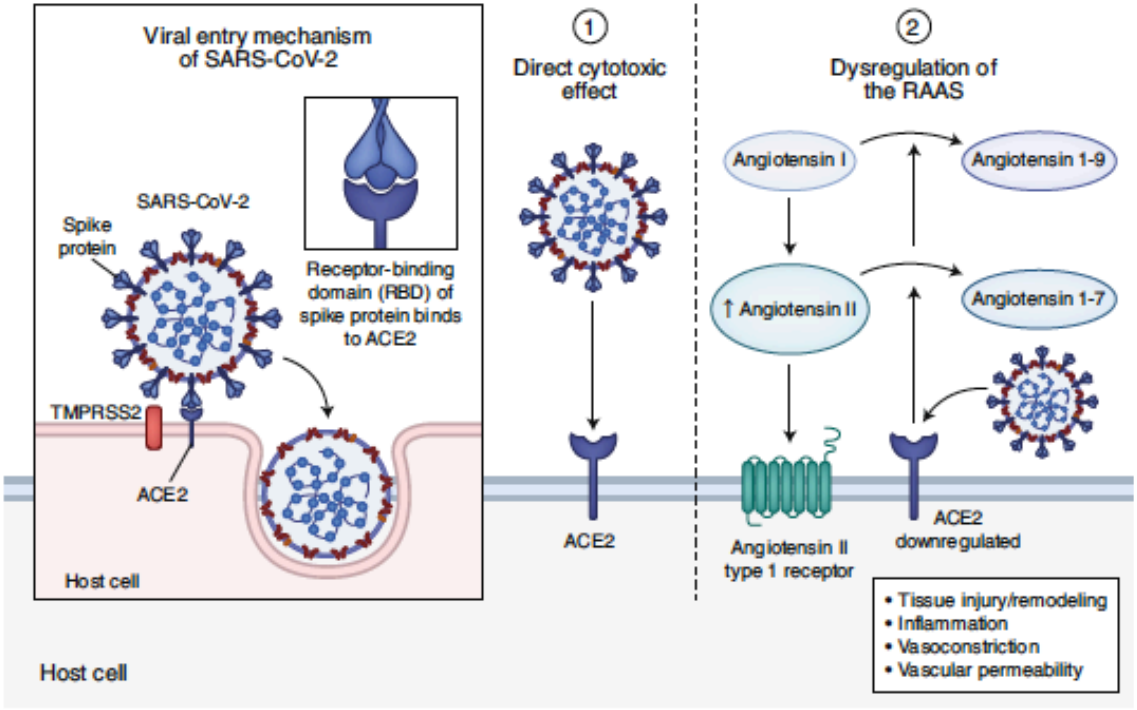
COVID-19 Pandemic



COVID-19

- Symptomatic cases
  - Pulmonary and other clinical findings
  - Systemic inflammatory findings and cytokine storm
  - Vascular findings



Gupta et al. Nat Med 2020; 26: 1017-32

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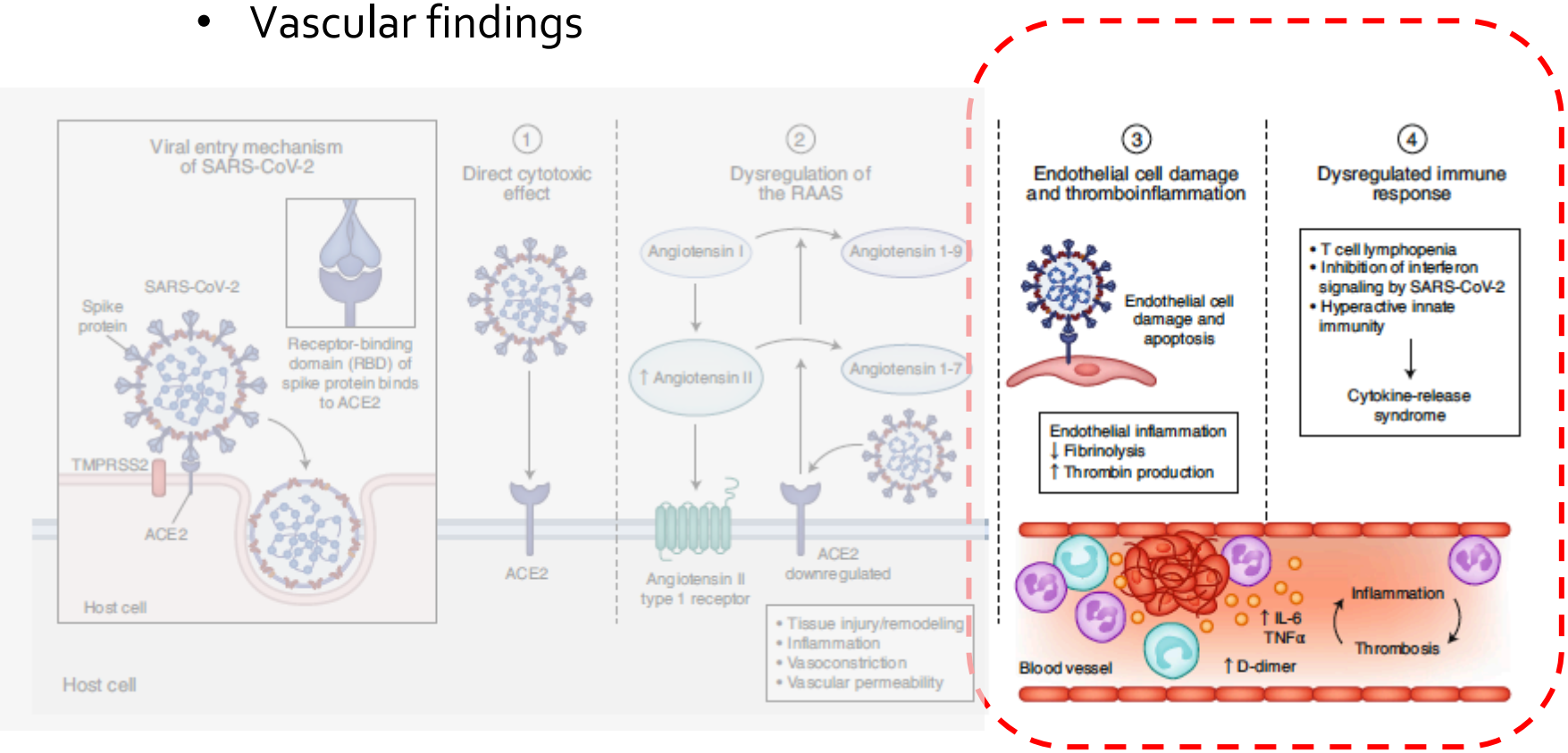

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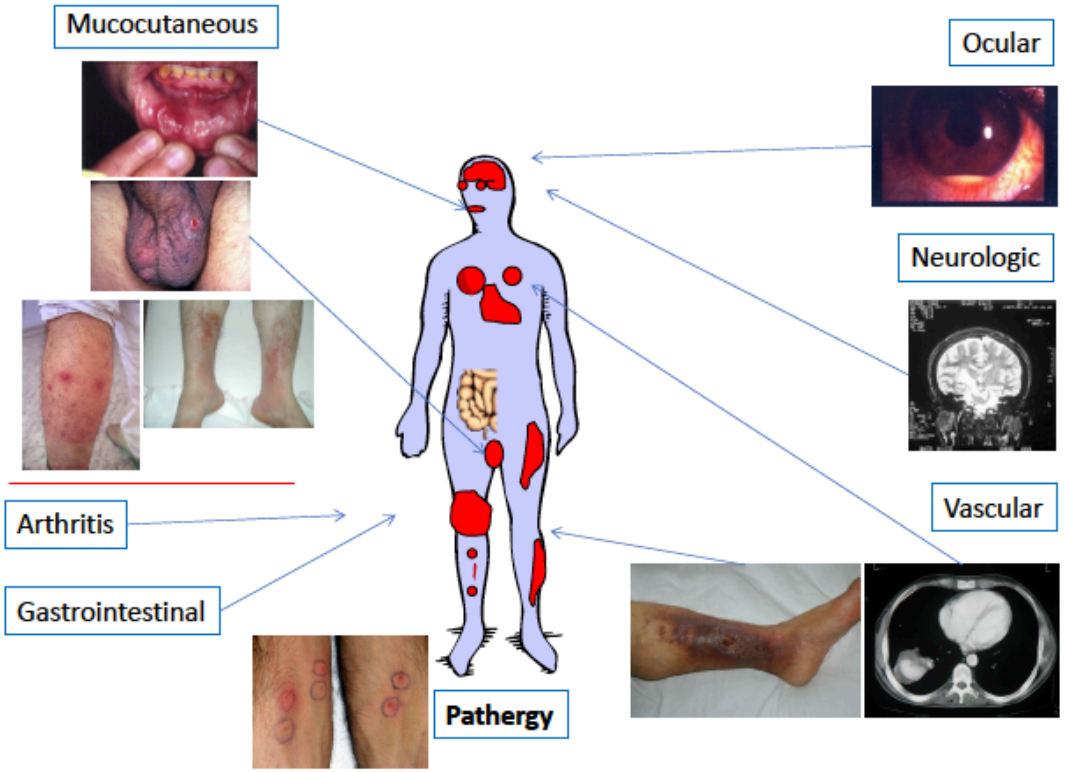
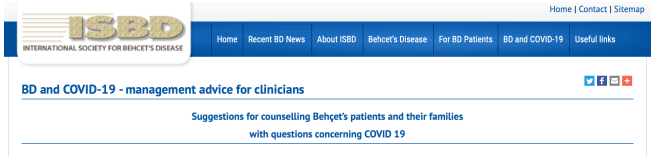
COVID-19 and Behçet Disease

- No data about the course of CVID-19 in patients with systemic inflammatory diseases or vasculitidis; and no data about the effects of anti-inflammatory/biologic agents on the disease

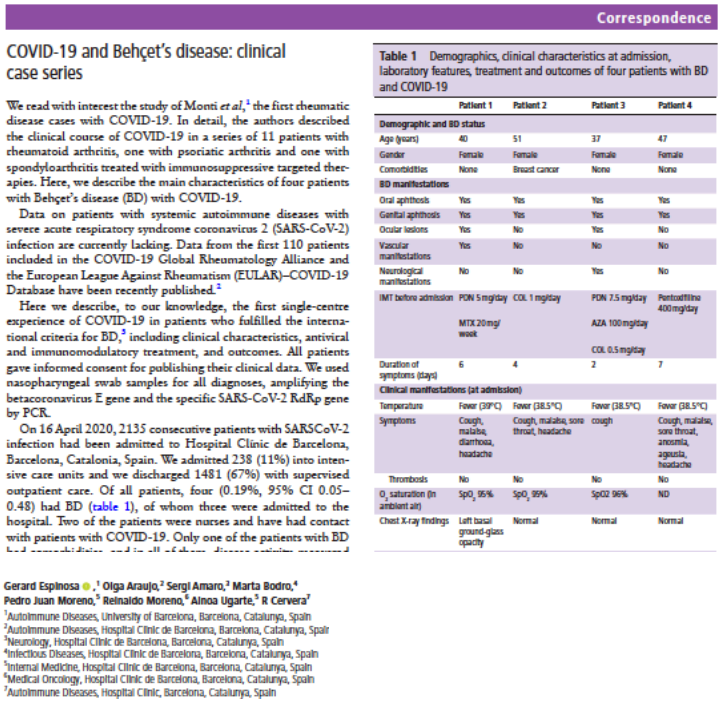




- There is no evidence that BD *per se* increases the susceptibility to viral diseases in general.
- Viral disease may lead to an exacerbation of BD.
- Some or all immunosuppressive drugs may increase the risk of acquisition COVID-19.
- There are ongoing discussions about immunosuppressive drugs, including biologics, potentially being beneficial for late complications by preventing the cytokine storm responsible for development of complications such as ARDS.

COVID-19 and Behçet Disease

- Limited number of publications



Correspondence

COVID-19 and Behçet's disease: clinical case series

We read with interest the study of Monti *et al*,[1] the first rheumatic disease cases with COVID-19. In detail, the authors described the clinical course of COVID-19 in a series of 11 patients with rheumatoid arthritis, one with psoriatic arthritis and one with spondyloarthritis treated with immunosuppressive targeted therapies. Here, we describe the main characteristics of four patients with Behçet's disease (BD) with COVID-19.

Data on patients with systemic autoimmune diseases with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are currently lacking. Data from the first 110 patients included in the COVID-19 Global Rheumatology Alliance and the European League Against Rheumatism (EULAR)–COVID-19 Database have been recently published.[2]

Here we describe, to our knowledge, the first single-centre experience of COVID-19 in patients who fulfilled the international criteria for BD,[3] including clinical characteristics, antiviral and immunomodulatory treatment, and outcomes. All patients gave informed consent for publishing their clinical data. We used nasopharyngeal swab samples for all diagnoses, amplifying the betacoronavirus E gene and the specific SARS-CoV-2 RdRp gene by PCR.

On 16 April 2020, 2135 consecutive patients with SARSCoV-2 infection had been admitted to Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain. We admitted 238 (11%) into intensive care units and we discharged 1481 (67%) with supervised outpatient care. Of all patients, four (0.19%, 95% CI 0.05–0.48) had BD (table 1), of whom three were admitted to the hospital. Two of the patients were nurses and have had contact with patients with COVID-19. Only one of the patients with BD

Table 1 Demographics, clinical characteristics at admission, laboratory features, treatment and outcomes of four patients with BD and COVID-19

	Patient 1	Patient 2	Patient 3	Patient 4
Demographic and BD status				
Age (years)	40	51	37	47
Gender	Female	Female	Female	Female
Comorbidities	None	Breast cancer	None	None
BD manifestations				
Oral aphthosis	Yes	Yes	Yes	Yes
Genital aphthosis	Yes	Yes	Yes	Yes
Ocular lesions	Yes	No	Yes	No
Vascular manifestations	Yes	No	No	No
Neurological manifestations	No	No	Yes	No
IMT before admission	PDN 5 mg/day MTX 20 mg/week	COL 1 mg/day	PDN 7.5 mg/day AZA 100 mg/day COL 0.5 mg/day	Pentoxifilina 400 mg/day
Duration of symptoms (days)	6	4	2	7
Clinical manifestations (at admission)				
Temperature	Fever (39°C)	Fever (38.5°C)	Fever (38.5°C)	Fever (38.5°C)
Symptoms	Cough, malaise, diarrhoea, headache	Cough, malaise, sore throat, headache	cough	Cough, malaise, sore throat, anosmia, ageusia, headache
Thrombosis	No	No	No	No
O_2 saturation (in ambient air)	SpO_2 95%	SpO_2 95%	SpO2 96%	ND
Chest X-ray findings	Left basal ground-glass opacity	Normal	Normal	Normal

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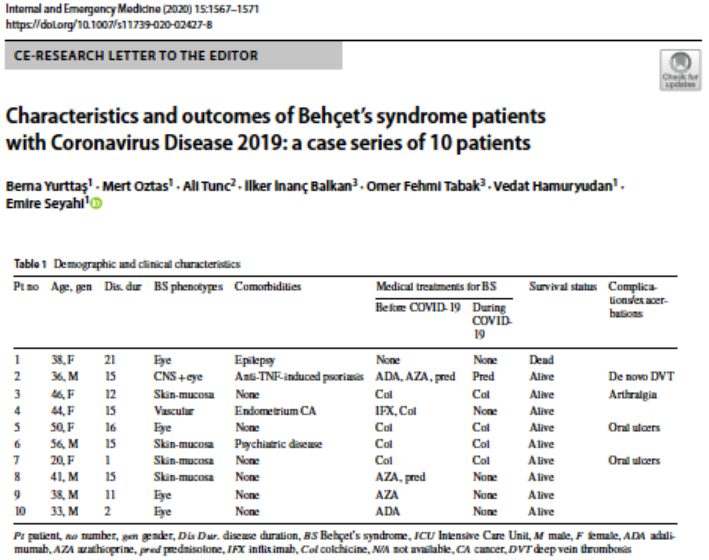

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CE-RESEARCH LETTER TO THE EDITOR

Characteristics and outcomes of Behçet's syndrome patients with Coronavirus Disease 2019: a case series of 10 patients

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Table 1 Demographic and clinical characteristics

Pt no	Age, gen	Dis. dur	BS phenotypes	Comorbidities	Medical treatments for BS		Survival status	Complications/exacerbations
					Before COVID-19	During COVID-19		
1	38, F	21	Eye	Epilepsy	None	None	Dead	
2	36, M	15	CNS + eye	Anti-TNF-induced psoriasis	ADA, AZA, pred	Pred	Alive	De novo DVT
3	46, F	12	Skin-mucosa	None	Col	Col	Alive	Arthralgia
4	44, F	15	Vascular	Endometrium CA	IFX, Col	None	Alive	
5	50, F	16	Eye	None	Col	Col	Alive	Oral ulcers
6	56, M	15	Skin-mucosa	Psychiatric disease	Col	Col	Alive	
7	20, F	1	Skin-mucosa	None	Col	Col	Alive	Oral ulcers
8	41, M	15	Skin-mucosa	None	AZA, pred	None	Alive	
9	38, M	11	Eye	None	AZA	None	Alive	
10	33, M	2	Eye	None	ADA	None	Alive	

Pt patient, *no* number, *gen* gender, *Dis Dur.* disease duration, *BS* Behçet's syndrome, *ICU* Intensive Care Unit, *M* male, *F* female, *ADA* adalimumab, *AZA* azathioprine, *pred* prednisolone, *IFX* infliximab, *Col* colchicine, *N/A* not available, *CA* cancer, *DVT* deep vein thrombosis

- No specific signal indicating increased susceptibility of patients with Behçet disease for COVID-19
- No specific signal for patients on biologic agents (anti-TNF) and immunosuppressive drugs

COVID-19 and Behçet Disease

- 4 out of 928 hospitalized patients at Istanbul Faculty of Medicine had Behçet disease
  - None required mechanical ventilation
  - None required anti-cytokine treatment
  - One of them was on adalimumab and had a mild course

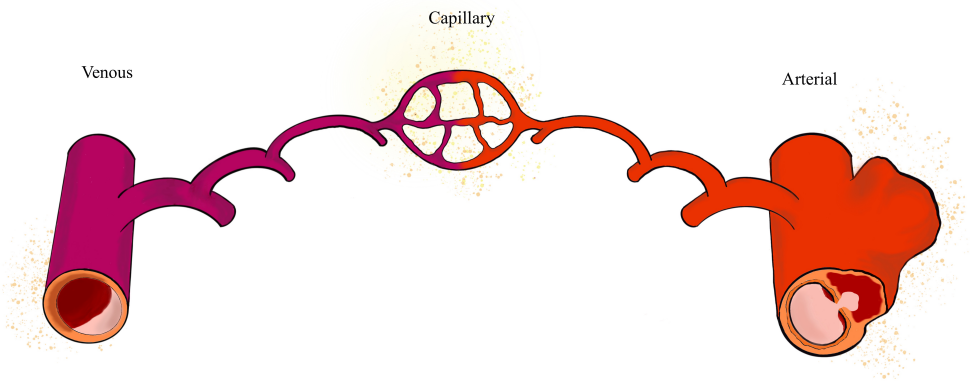
  - Another patient with juvenile onset Behçet disease from our cohort, with severe ocular involvement, vascular involvement and stroke, had COVID-19. He was on 10 mg/kg infliximab every 4w, and he did very well without hospitalization

COVID-19 and Behçet Disease

- Ministry of Health Database
  - Searching for patients with inflammatory rheumatic disorders (March-July 2020)
  - 313/7190 (4.3%) patients with Behçet disease
  - Better disease course in patients with SpA, FMF and BD compared to the patients with systemic vasculitis (AAV and others), myositis, gout
  - Data clearing regarding specific treatments is ongoing, and this analysis will be compared with the new dataset of September-December period

Common pathogenic mechanisms ?

- Behçet disease
  - Inflammatory disorder with strong innate immune activation
  - Vascular endothelial activation with a tendency for thrombosis
  - A tendency for the venous side of the vasculature



- COVID-19
  - Viral disease
  - Worse disease course in a subset with hyperinflammatory response (pulmonary macrophage activation syndrome)
  - Endothelial activation and a tendency for thrombosis
    - More capillaries compared to the medium-large vessels
  - A second wave of endothelial activation after developing antibody response to SARS-CoV-2
    - MIS-C/A
      - Kawasaki like manifestations
      - Systemic inflammatory response and other manifestations

Common pathogenic mechanisms ?

- Favorable response of moderate-severe COVID-19 patients to glucocorticoids
  - Recovery trial for dexamethasone
  - Other trials with glucocorticoids
    - Better survival in patients requiring oxygen support

- Role of anti-aggregants and anti-coagulants on the course of severe COVID-19 patients
  - Isolated favorable effects ?
  - Combination of anti-inflammatory treatments (glucocorticoids, anti-TNF, anti-IL-1, …)

Follow-up and vaccination

- Continuing to recruite patients for long-term follow-up
  - Different clinical subsets
  - Different treatment responses

- For those who had COVID-19
  - Findings of long COVID-19 ?
  - Vascular complications

- Vaccination responses
  - Re-activation of Behçet manifestations
  - Vascular complications
  - Antibody response to vaccinations