



Editorial

Brain fog across the Mediterranean



When I sat down to write the first sentences of this document, everything was blurred, hazy, and shrouded, as though I were in a dense, cloudy fog that I could not quite describe. About 10 years ago, I was a young infectious disease (ID) physician working in a ward at the largest university hospital in Tunis, Tunisia, designed to accommodate about 60 patients. Despite working in a country where we sometimes lacked logistical resources and technical facilities and platforms, we never lacked willpower and thoroughness. We sometimes ran through the long corridors of the old buildings to perform exams and transfer patients, even using our own cars to travel from one department to another. Everything was justified by the goals of caring for our patients and saving lives.

During one night shift, I was called by my best friend, a neuroradiologist who worked in the same university hospital. He described a young female patient who presented to the emergency room with neurological disorders and fever. Multiple brain abscesses associated to the “concentric target sign” were confirmed on brain magnetic resonance imaging, and neurotoxoplasmosis with untreated human immunodeficiency virus was the diagnosis. This patient was homeless, with malnutrition, cachexia, and skin manifestations such as bedsores (pressure ulcers) likely caused by several days of immobility on the streets of Tunis. Beyond starting treatment for cerebral toxoplasmosis followed by highly active antiretroviral therapy, I (along with nurses) personally took charge of the care of the wound on the patient’s sacral region until complete healing was achieved. My co-interns and I brought her favorite dairy and cheese products every morning to promote weight gain and better nutrition. We decided to keep her hospitalized; our ID ward became her home, yet her future was ultimately as uncertain as mine. Together with my superiors, I called social services and the

authorities to establish her identity, but no one could help with this. The patient could not help either; she was simply “lost,” and her brain condition made things more complicated.

Fate led me to pursue my professional career elsewhere. I decided to settle in Franche-Comté, France, in 2017, and I lost track of the patient’s outcome.

During the first wave of coronavirus disease 2019 (COVID-19) in France, the prevalence rate of patients with SARS-CoV-2 infection in the Franche-Comté region was one of the highest among French metropolitan regions; my colleagues and I took this very seriously and assumed a leadership role in our hospital. We were among the first ID teams to describe the clinical features of our initial COVID-19 patients, especially the olfactory disorders seen at a time when no-one else was talking about them; our report [1] made a track record of hundreds of citations. Subsequently, together with the Nord Franche-Comté Hospital multidisciplinary team, we highlighted that the anti-interleukin-6 receptor monoclonal antibody tocilizumab reduced intensive care unit admissions and/or mortality in COVID-19 patients [2]. We even managed to publish our initial papers in Infectious Diseases Society of America journals [3,4]. What a triumph!

Later, along with Dr. Timothée Klopfenstein, who is both my colleague and pair mentor, we quickly decided to investigate whether COVID-19 patients presented with residual symptoms, with the purpose of characterizing a syndrome that was little known at that time (i.e., in 2021) and initially referred to as “post-COVID-syndrome” [5]. This concept is likely analogous to what we observed in our patients with neuroborreliosis in the Franche-Comté region—or maybe not; I do not know in retrospect... please excuse me, I have just had a major episode of brain fog...

Abbreviations: ID, infectious disease; COVID-19, coronavirus disease 2019; LC, long COVID; PASC, post-acute sequelae of severe acute respiratory syndrome coronavirus 2 infection.

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On the evening of December 15, 2021, my phone rang. It was my best friend, “the neuroradiologist,” with whom I had grown up and studied medicine in Tunis before we eventually both became doctors. We had worked very hard together for years, constantly exchanging ideas regarding our life plans, ambitions, and childhood dreams. Life determined that we had to part ways and forge our own paths and futures, as dictated by professional and family requirements.

He told me he had received his fourth dose of the COVID-19 vaccine and subsequently sought care for symptoms including palpitations, chest tightness and pain, shortness of breath, and fatigue. Pericarditis was quickly diagnosed and treated. Unfortunately, he was infected again with severe acute respiratory syndrome coronavirus 2 in July 2022; and that is when it all began.

He reported little-known symptoms that no-one took seriously: a heart rate that would suddenly jump from 60 to 120 bpm, dizziness, post-effort malaise with muscle pain and weakness, headache, and concentration and memory disorders with a brain fog that only he could describe. This fog could arrive without warning, persist for days, and cause sleep disturbance. People around him thought that he was suffering from migraines, whereas others—even people in the medical field—suspected anxiety or depression. During this period, my friend lost his autonomy and could no longer fly to see me. We were both sad about this, but at least I could visit him, and his condition became our daily life battle.

He said the following to me: “It feels like you don’t have the same brain as before. Sometimes, it’s hard to think clearly, and the worst part is that you’re compelled to stop working while interpreting patients’ exams and brain magnetic resonance imaging, and concluding regarding the imaging findings. The anxiety and fear stem from the impression that it’s irreversible for long periods, like a plane flight with constant turbulence—you panic, but there’s no choice, you have to wait for it to end.” He then added the following: “Every day, I checked to be sure if people’s brains were suffering or not; today, mine is suffering so much but nobody has checked it, except maybe you.” The third “pillar” of our family tree was a friend and Professor of neurosurgery. Everything in our history relates to the brain; he was there the whole time, but we did not ask him anything regarding his skills, and so much the better!

All laboratory and imaging exams were normal, and the initial empirical treatments did not improve the symptoms. We finally understood that it was postural orthostatic tachycardia syndrome, the symptoms of which are highly correlated with those of long COVID (LC) or the post-acute sequelae of severe acute respiratory syndrome coronavirus 2 infection (PASC).

There might also be an opportunity to raise the alarm about this condition in countries where resources can sometimes be lacking, and where there is a lack of understanding and will in terms of medical policy. Patients with LC or PASC are currently underdiagnosed and improperly managed, with inevitable medical and social repercussions.

I quickly started reading, thanks to my friend. We reviewed the latest medical literature daily, again thanks to him. We had to find solutions even though we were both truly in a fog, though his was surely much more extensive. We wrote emails to experts in France and other countries, and we thought about treatments we could start while awaiting clinical trial results. I decided to fly to Madrid, Spain to attend the first “Demystifying Long COVID International Conference.” It was important to hear from experts such as Professor Monica Gandhi and Daniel Kuritzkes, and to learn from their experiences. I also met other specialists and acquired new competencies that would be useful for my own care and that of my friend.

I later decided to influence my small circle to improve and optimize care in our hospital, and within our team, training other healthcare professionals like general practitioners and physiotherapists. Patients are now better managed thanks to diagnostic scores and imaging modalities such as brain positron emission tomography/computed tomography. In collaboration with experts from other specialties, a project to implement vagus nerve stimulation treatment is underway. As for my friend, treatments are changing his life for the better, with rehabilitation and pacing also helping despite “mild” relapses. The overall outlook is certainly positive after more than 2 years of fighting.

I learned some time ago that my patient with toxoplasmosis was well; she found her family and had almost no neurological sequelae. It is probably thanks to my friend and I that this patient was treated quickly and able to recover. This is our reason for practicing and waking up to fight every day. When your best friend is the focus, it becomes your life battle as an ID specialist.

Today, my friend is finally able to fly. The thick cloud of fog between two continents has been cleared; his brain fog has been overcome such that we can share time together, although I still feel like I am swimming in a large sea of fog together with several patients suffering from LC/PASC who I am currently following.

Soon, the fog will disappear forever, permanently clearing a path across the Mediterranean.

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CRedit authorship contribution statement

Souheil Zayet: Conceptualization, Methodology, Project administration, Resources, Validation, Writing – original draft.

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Not applicable.

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