MS-like lesions in a patient after COVID-19

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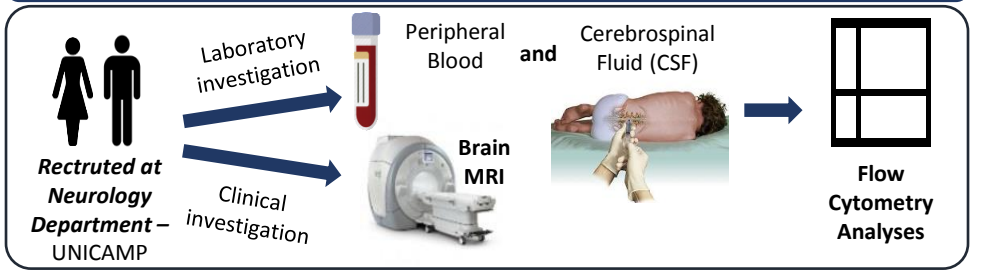
CASE PRESENTATION

Here we describe a patient who manifested CNS-demyelinating lesions resembling Multiple Sclerosis (MS) pattern after symptomatic infection due to coronavirus disease 2019 (COVID-19). Moreover, using high-dimensional flow cytometry analyses (umap), we identified strong cytotoxic signature (*CD27-, CD28-, CD195-, CD49d+, CD56+, CD57+, CD94+, CD215+*) from both CD8+ and CD4+ T cells, in the cerebrospinal fluid and peripheral blood, after patient's recovery for COVID-19.

MATERIAL AND METHODS



CLINICAL HISTORY AND EVOLUTION

A woman (36 years, right-handed, psychologist) presented COVID-19´s acute infection in November 2020, with fever, running nose, paresthesia in legs, dyspnea and fatigue. After 2 months, she persisted with "weakness and pain" in the legs (unable to walk since the infection). Physical examination exhibited a functional pattern, with normal neurological exam. Her sister has Multiple Sclerosis (MS). Although she had a normal MRI from 2019, the new 3T MRI revealed white matter lesions (some suggestive of microvascular lesions), and some ovoid lesions suggestive of demyelinating disease (**Figure 1A-D**). The neuropsychological evaluation revealed severe dysexecutive syndrome (motor and cognitive dysfunction) with anxiety and depressive symptoms. Blood tests showed low Vitamin-D (18 pg/mL) and high Erythrocyte Sedimentation Rate (51mm/h). ANA, complement, serologies and other exams were negative. Routine CSF was normal (with negative oligoclonal bands) glucose of 55mg/dL, protein of 23mg/dL, 1 leukocyte/mm³, 23 red cells/mm³, IgG of 1.76mg/dL. In the reevaluation (April 2021), she was walking and working (half-day), with mild dyspnea (under treatment). New MRI was identical, with normal brain FDG-PET and normal Electroneuromyography. She presented low levels of B12 (143pg/mL), spirometry with mild obstructive pattern (FEV1/FVC of 0.735 and FEV1 of 0.75). We prescribed vitamin B12 replacement.

RESULTS

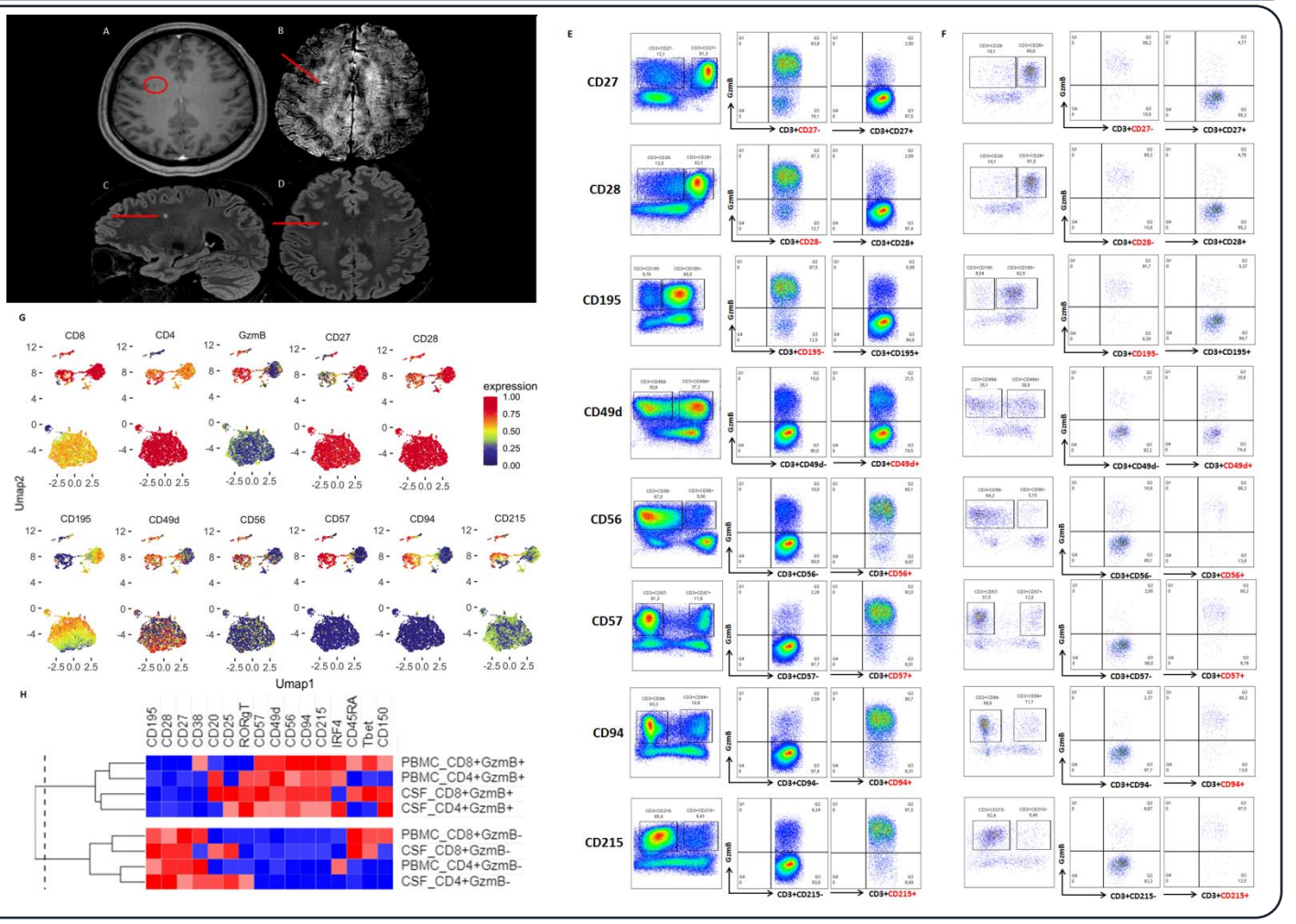


Figure 1: **Brain MRI and Flow Cytometry Analyses of T cell markers from PBMC and CSF after COVID-19.** (**A**) Gd+ T1 without lesion enhancement. (**B**) SWI showing perivenular lesion. (**C**) Sagittal FLAIR. (**D**) Axial FLAIR. (**E**) Representative gate strategy for assessment of serine-protease granzyme-B (GzmB) expression according to distinct immune-associated markers in CD3+ T cells from the peripheral blood (PBMCs) and (**F**) cerebrospinal fluid (CSF). (**G**) Uniform Manifold Approximation and Projection (Umap) for CD3+ T cells derived from PBMCs and CSF. (**H**) Heatmap of median fluorescence intensity (MFI) from immune-associated markers in subsets of cytotoxic (CD8+GzmB+ and CD4+GzmB+) and non-cytotoxic (CD8+GzmB- and CD4+GzmB-) T cells from PBMCs and CSF.

DISCUSSION AND FINAL COMMENTS

Despite their positive role during antiviral and antitumor immune responses, persistent cytotoxic T cells are known to cause tissue damage in diverse conditions. Particularly, in MS patients, these subsets can be found in the CNS-parenchyma during severe relapses, as well as in inflamed meninges during progressive disease. Recently, *Palao* and coworkers (2020) reported the first case of CNS-demyelinating and non-enhancing perivascular lesions in a patient who met the diagnosis criteria for MS shortly after COVID-19. They speculate that the demyelination may not be driven by SARS-CoV-2 virus itself, but that the infection triggered immune-associated mechanisms, such as cytotoxic T lymphocytes, which may cause CNS-lesions. In fact, in our case, we show that sustained aggressive cytotoxic behavior may persist over time and may be associated with the vascular/CNS damage shortly after the infection. Thus, investigating CNS-implications, as well as characterizing persistent antiviral immune responses may be helpful for the early diagnosis of neurovascular/neurodegenerative events related to COVID-19.