Inflammatory olfactory neuropathy in two patients with Covid-19

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Case Report

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Abstract

Coronavirus disease 2019 (Covid-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a public health emergency recently, leading to fatal respiratory failure in a number of patients. The clinical manifestation of Covid-19 is manifold, cardio-respiratory symptoms and multiorgan failure being the most critical. Anosmia was reported to be an early symptom in a significant number of Covid-19 patients and is frequently the only symptom without underlying nasal congestion. Here we present neuropathological work-up of olfactory epithelium and associated olfactory nerves from two patients succumbing to Covid-19, one of which was anosmic. We show that SARS-CoV-2 infection is associated with inflammation in the olfactory epithelium and leads to axonal damage in olfactory structures of the CNS - potentially explaining anosmic symptoms.

Main Text

We report two cases of olfactory neuropathy diagnosed at autopsy in patients with severe acute respiratory syndrome due to coronavirus 2 (Sars-CoV-2) infection. One patient experienced anosmia. Information about anosmia was not available in the other patient.

Patient 1, a 70-year-old male and patient 2, a 79-year-old male, both tested positive for Sars-CoV-2. Patient 1 was a renal transplant recipient with coronary artery disease and arterial hypertension. He developed progressive respiratory failure due to coronavirus disease-19-associated (Covid-19) pneumonia and required mechanical ventilation. He was treated with hydroxychloroquine (total 1600mg). Patient 2 was previously diagnosed with severe pulmonary hypertension and was admitted with fever, cough, and increasing dyspnea as well as loss of taste and smell. He was also treated with hydroxychloroquine (total 1600mg); however, he declined invasive treatment. Patient 1 died eight days, patient 2 six days after hospitalization.

Post-mortem histological analysis of the olfactory epithelium in both patients showed prominent leukocytic infiltrates in the lamina propria, and focal atrophy of the mucosa (Figures 1a,g,h,i). There was a slight predominance of CD3⁺ T over CD20⁺ B lymphocytes. Expectedly, olfactory nerve fibers in the lamina propria were negative for myelin basic protein. However, they showed numerous CD68⁺ digestion chambers, suggestive of axonal damage (Figures 1b,i). Scattered intraneural CD45⁺ leukocytes were consistent with an inflammatory neuropathy (Figures 1c,h), the infiltrates comprised both CD4⁺ and CD8⁺ T lymphocytes, CD20 was negative (Figure 1d-e). In patient 1, the olfactory tract showed CD45⁺ infiltrates (Figure 1f), isolated CD45⁺ leukocytes were seen in patient 2. In both cases, the olfactory striae were unremarkable. Both brains showed perivascular leukocytic infiltrates, predominantly in the basal ganglia; patient 2 harbored intravascular microthrombi.

Anosmia is a common symptom in Covid-19 patients ¹. Inflammation of the olfactory system and anosmia have been reported in other viral diseases ² as was age-related atrophy of the olfactory epithelium ³. The observed neuritis is most likely associated with axonal damage, as olfactory fila lack

myelin⁴. Sars-CoV-2-induced damage might be mediated by viral entry through its receptor angiotensin converting enzyme 2 and the transmembrane serine protease 2, which are expressed in non-neural cells of the olfactory epithelium⁵. It is unclear whether the observed inflammatory neuropathy is a result of direct viral damage or is mediated by damage to supporting non-neural cells. Due to the rapidly evolving pandemic, unravelling the neuroinvasive properties of Sars-CoV-2 will have major implications for Covid-19 patients.

Declarations

Consent for autopsy and publication was obtained from next-of-kin in all cases. Case series do not need institutional review board approval according to Swiss legislation.

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Figures

Figure 1

The histological workup of olfactory epithelium. Patient 1 a-f, patient 2 g-i. Olfactory epithelium is depicted in all panels except (f) = olfactory tract. ep = epithelium of olfactory mucosa, N = nerve.