without being able to ascertain a causal connection with the infection. Our intent is to make readers aware of the observed skin symptoms, and we strive to collect additional cases to construct a clearer picture of COVID-19's potential skin manifestations.

Case 1: A 74-year-old Wuhan man presented with fever (100.4 F), dry cough and fatigue. A CT scan of the lung showed ground-glass changes. The throat swab was positive for COVID-19 nucleic acid. Treatment included hydroxychloroquine, lopinavir/ritonavir, thymosin and methylprednisolone. The rash appeared on the 12th day after admission. In physical examination, the patient had diffuse, irregular shaped, partially confluent weals throughout the body (Fig. 1). The patient was diagnosed with COVID-19 pneumonia and secondary urticaria of undetermined aetiology.

Case 2: A 65-year-old subfebrile (98.6 F) Wuhan woman had dry cough, fatigue and diarrhoea (four times a day). A CT scan showed bilateral ground-glass changes,[6] which is the primary tool for Covid-19 diagnosis in the epidemic area. Swabs did not detect SARS-CoV-2. One day after admission, we observed multiple, disseminated, variable size, erythematous patches throughout the body, which faded on pressure. Few patches were confluent (Fig. 2). We considered the symptoms as unspecific viral rash due to COVID-19 and included as differential diagnosis a drug eruption due to the antineoplastic drug ruxolitinib.

Taken together, we observed in 2 COVID-19 patients one unspecific, potentially viral rash and one case of urticaria. Unfortunately, we lack biopsies, which were deplorably not taken due to prioritizing emergency measures and patient isolation. Apart from our observation, no other skin symptoms have been observed in COVID-19 patients, but secondary rashes due to drug treatment and the like are to be expected. We postulate that in some cases, COVID-19 may have cutaneous symptoms, e.g. viral exanthema that may pass unnoticed for being asymptomatic, rapidly evolving and/or self-limited. We urge colleagues caring for COVID-19 patients to examine the skin as a potential site of viral pathologic changes.

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Conflict of Interest

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'We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work'.

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COVID-19 in a melanoma patient under treatment with checkpoint inhibition

Editor,

SARS-CoV-2 poses new challenges in all aspects of health care.[1] Patients with pre-existing cardiovascular conditions are at higher risk of developing severe symptoms and worse outcome.[2] Data also suggest that patients with cancer are particularly vulnerable,[2,3] but differences between tumour entities and cancer treatments may exist. Little is known how cancer treatment engaging immune checkpoints affects the course of COVID-19.

We present the case of a 47-year-old woman contracting COVID-19 while being under adjuvant immunotherapy with the PD1-antagonist nivolumab for fully resected stage IV melanoma. The patient was first diagnosed with metastatic melanoma in August 2019 and started adjuvant immunotherapy with nivolumab 480 mg i.v. every 4 weeks in November 2019. No side effects were noted. One week after receiving anti-PD-1 treatment on March 12th 2020, the patient reported symptoms of an upper respiratory tract infection (sore throat, cough, headache), followed by 3 days of fever (max. 39.4°C). PCR-testing for SARS-CoV-2 was positive on March 23 (Fig. 1).

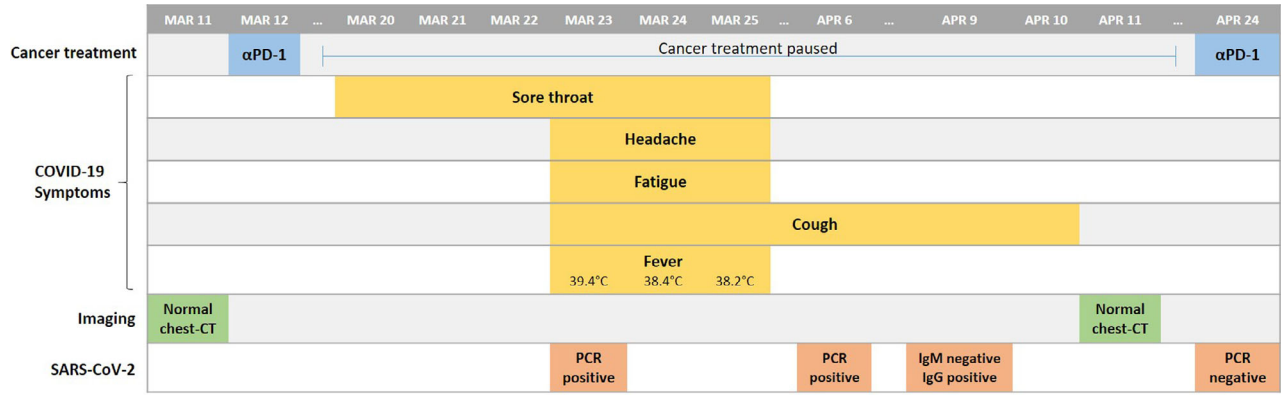

Figure 1 Timeline of the COVID-19 disease course, cancer treatment, imaging results and SARS-CoV-2 tests.

The patient did not develop any severe respiratory symptoms like dyspnoea or drop in oxygen saturation throughout the course of the disease; fever resolved spontaneously within 3 days. No treatment for COVID-19 was required; however, checkpoint inhibition was paused as a precautionary measure.[4] Two weeks after the first onset of COVID-19 symptoms, SARS-CoV-2-IgG antibodies were detected suggesting (at least) partial immunity. Extensive laboratory tests, including analyses of T-cell sub-populations were all within normal range. A thoracic CT scan 3 weeks after onset of symptoms did not show any lung pathologies nor immune-therapy associated alterations.

Checkpoint inhibition (CPI) has revolutionized melanoma treatment by reengaging exhausted T cells boosting cancer cell elimination. Yet, CPI is a two-edged sword: while the reactivation of antitumour immunity has proved successful therapeutically, immune-related adverse events (irAE) particularly CPI-induced pneumonitis may be life threatening. Similarly, a well-orchestrated and balanced T-cell response most likely determines the course of viral infections including COVID-19.[5] First data indicate that persisting viral infections cause T-cell cytopenia and the exhaustion of T cells responsible for the development of more severe symptoms.[6] It remains an open question; however, if checkpoint blockade may positively affect COVID-19 disease course leading to a stronger antiviral, adaptive immune response, or on the contrary may cause a pro-inflammatory phenotype leading to access tissue damage.[6,7]

Our melanoma patient receiving adjuvant PD-1 treatment had mild to moderate COVID-19 symptoms, has now fully recovered and remains tumour free.

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LETTERS TO THE EDITOR

Health insurance claim- and prescription record-based algorithms as a population-based method for eczema ascertainment

Editor

Eczema (atopic eczema) is a common, chronic and recurrent inflammatory skin disease affecting 10–15% of the population.[1,2] A limited Canadian study based on a small survey sample reported that the annual cost of eczema is $CAD 1.4 billion