Evolution from hypereosinophilic bronchiolitis to eosinophilic granulomatosis with polyangiitis following COVID-19: a case report

Sirs,

COVID-19, the disease caused by severe acute respiratory syndrome (SARS)-CoV-2 infection, has caused over 905,000 deaths worldwide as of September 10, 2020 (https://coronavirus.jhu.edu/map.html). Increasing age, cardiovascular comorbidities, obesity and chronic pulmonary diseases are risk factors for severe COVID-19 (1). However, little information is available regarding COVID-19 and small-vessel systemic vasculitis. Here, we report the case of a patient with hypereosinophilic bronchiolitis in whom COVID-19 was followed by the onset of systemic manifestations corresponding to the development of eosinophilic granulomatosis with polyangiitis (EGPA).

A 59-year-old patient known for HBV chronic infection presented in July 2019 with a late-onset asthma associated with peripheral eosinophilia (2.6 x10^9/L /L) and nasal polyposis. Respiratory function revealed severe airflow obstruction (FEV/FVC 36%, FEV1 0.97L) despite prolonged inhaled corticosteroid therapy. The CT scan showed extensive bronchiolitis features (Fig. 1). Antineutrophilic cytoplasmic antibodies (ANCA) assessed by indirect immunofluorescence, and anti-myeloperoxidase (MPO) and anti-proteinase 3 antibodies measured using antigen-specific fluorimetry assay were all negative. Bronchoalveolar lavage showed 43% eosinophils. There was no extra-respiratory involvement. The patient was diagnosed with hypereosinophilic bronchiolitis (2, 3). He received 1 mg/kg/day of oral prednisone, slowly tapered down to 10 mg/day over 6 months, with a dramatic clinical improvement, and normalisation of lung function, chest CT, and blood count.

In March 2020, while still receiving 10 mg/day of prednisone, he had asthenia and fever. Prednisone was increased to 20 mg/day. The SARS-CoV-2 nasopharyngeal RT-PCR was positive. The patient's condition improved within days.

On day 34 of COVID-19 related first symptoms, while still receiving 20 mg/day of prednisone, he was admitted to intensive care unit with acute respiratory distress associated with low grade fever, wheezes at auscultation, and ground-glass opacities, ill-defined lung consolidation and pansinusitis at CT. Skin examination showed a necrotic purpura on both legs. Eosinophilic count was 6.8 x10^9/L. Repeated nasopharyngeal RT-PCR for SARS-Cov-2 was negative.

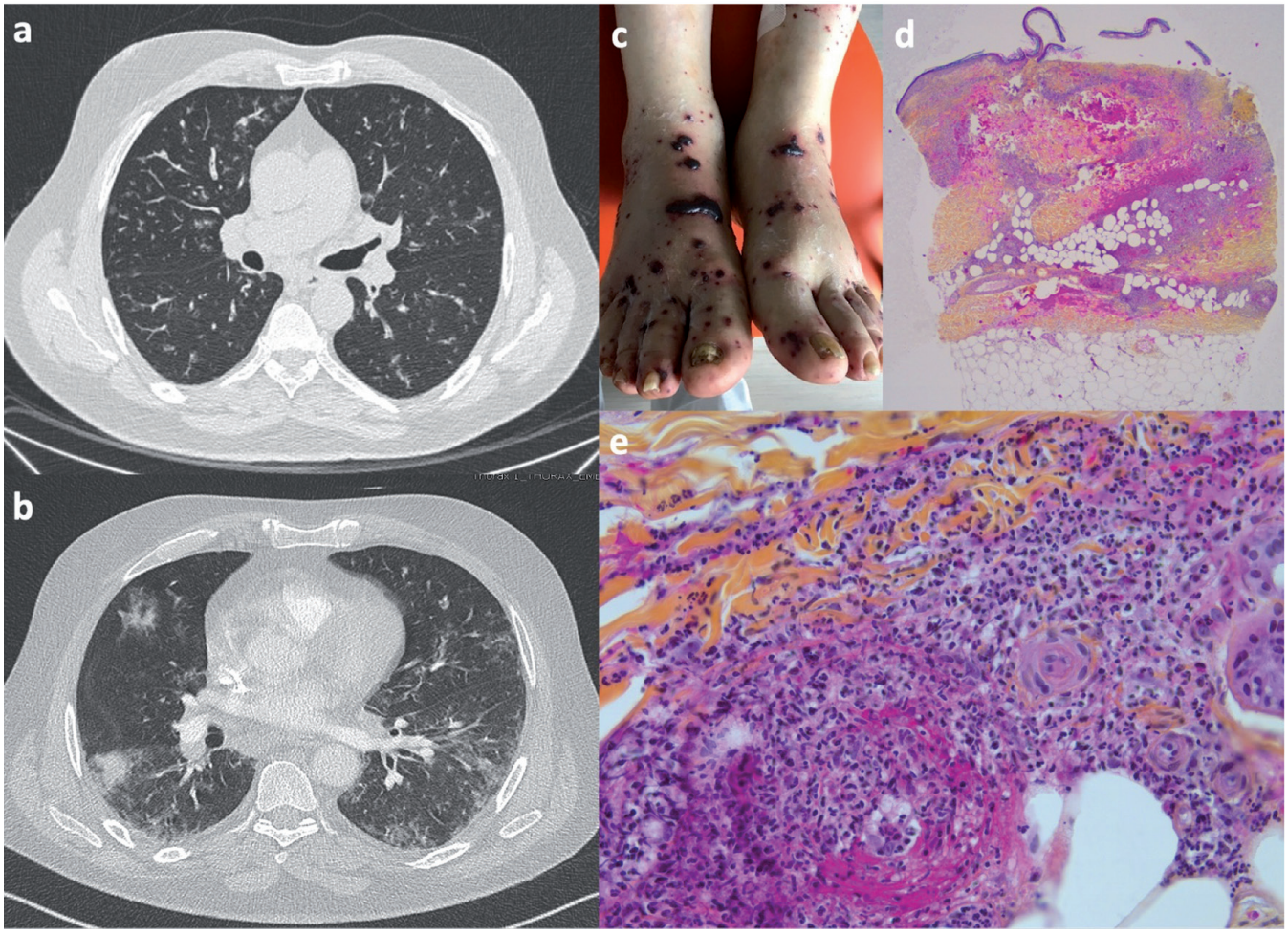

Fig. 1. a. Chest CT scan in July 2019 showing extensive branching opacities suggesting bronchiolitis at diagnosis. **b**. Chest CT in April 2020 showing branching opacities, ill-defined consolidation and ground glass opacities at the time of EGPA flare. **c**. Necrotic purpura on both legs concomitant to panel b. **d.** Skin biopsy (Haematoxyline Eosine Saffron, x 2.5, at day 35 of COVID-19 related first symptoms), showing epidermal detachment due to vascular frailty, microthrombi within small capillaries, and perivascular infiltration of derma and hypodermis by inflammatory cells. **e**. Skin biopsy (Haematoxyline Eosine Saffron, x40) showing leucocytoclastic and necrotising vasculitis with microthrombi and eosinophilic infiltrate. There was no sign of cytopathic viral effect. SARS-CoV-2 RT-PCR performed on the haemorrhagic liquid from purpuric bullae was negative.

Neurological, renal or cardiac involvement was ruled out. ANCAs were now strongly positive by indirect immunofluorescence, with anti-MPO specificity by fluorimetry assay. Cutaneous biopsy revealed leucocytoclastic and necrotising vasculitis with microthrombi. The diagnosis of EGPA was made (4). The patient received supplemental oxygen, broad spectrum antibiotics, nebulised bronchodilators and a pulse of 1g intravenous methylprednisolone, followed by 1 mg/kg/day oral prednisone and azathioprine, with favourable outcome.

In this patient, COVID-19 was shortly followed by the onset of systemic vasculitis. Manifestations changed from ANCA-negative hypereosinophilic bronchiolitis to MPO-ANCA-positive EGPA with new-onset of systemic involvement (necrotic purpura), despite the increase of glucocorticoids dose. Hypereosinophilic bronchiolitis can be a feature of EGPA (3), and it cannot be excluded that our patient already had smoldering EGPA. Although a causative link cannot be demonstrated, the chronology of events suggests a potential role of the viral infection in the dramatic change in phenotype and onset of the vasculitis.

Whether and how SARS-CoV-2 can affect the evolution of systemic vasculitis is not known. Dexamethasone has recently been demonstrated to be beneficial in subjects hospitalised for COVID-19 and requiring mechanical ventilation or oxygen supplementation (5). In patients with systemic small-vessel vasculitis (6), large-vessel vasculitis (7) or other systemic diseases (8, 9), ongoing treatment with glucocorticoids and rituximab might limit the cytokine storm and delay the clinical worsening of COVID-19 (6, 8). Conversely, glucocorticoids might decrease viral clearance. As SARS-Cov-2 can infect endothelial cells (10), we speculate that it might have triggered the onset of the systemic vasculitis in our patient, similar to reports of Kawasaki-like vasculitis (11). Although eosinophil count rose dramatically, there is currently no data to support a direct effect of SARS-Cov-2 on eosinophils.

Our observation supports the general recommendation of a close follow-up of patients at risk of systemic vasculitis even controlled by therapy, and who present COVID-19.

This retrospective case report complies with the declaration of Helsinki. The patient received information attesting his unrestricted rights to ask for the deletion of his data and signed an inform consent for publication. French law does not require ethic committee for retrospective clinical case report. However, no database was used.

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