COVID-19 Infection Associated With Auto-immune Hemolytic Anemia

Antoine Capes
Université catholique de Louvain
Sarah Bailly
Université catholique de Louvain
Philippe Hantson (philippe.hantson@uclouvain.be)
Université catholique de Louvain
Ludovic Gerard
Université catholique de Louvain
Pierre-François Laterre
Université catholique de Louvain

Short Report

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Abstract

A 62-y-old man developed Covid-19 infection. Fourteen days after the first respiratory symptoms, he presented biological signs of hemolysis with cold agglutinins 1/16384. Other causes of auto-immune hemolytic anemia (infectious, hematological,…) were excluded.

Full Text

A 62-year-old man with a medical past history of arterial hypertension and heavy smoking was ongoing radio-chemotherapy for an oropharyngeal squamous cell carcinoma (cT3N0M0). Three days after the first cisplatin injection, the patient started a dry cough without fever. A nasopharyngeal swab was positive for Covid-19 (tested by PCR). A week later, he presented a marked asthenia and was referred to the emergency room. Physical examination showed fever and mild dyspnea, with a low oxygen saturation on room air. The patient was perfectly conscious and there was no evidence of motor deficit. Chest X-ray showed bilateral lung infiltrates. The laboratory examination results were as follows: white blood cell count (WBC) 6,620/µL, lymphocyte count 500/µL (Nl:800-5000), normal neutrophil count, platelet count 101, 000/µL (Nl: 150,000-450,000), hemoglobin 12g/dL (Nl: 13.3-16.7), CRP 45mg/L (Nl: <5), normal serum creatinine, LDH 307 IU/L (Nl: <250), bilirubin 0.7mg/dL (Nl: <1.2).

Fourteen days after the first respiratory symptoms, he was transferred to the intensive care unit (ICU) and orotracheal intubation was required soon after admission. Anemia also deteriorated progressively with a rise of LDH level. On day 16, the patient developed acrocyanosis. Laboratory tests showed : lymphocyte count 120/µL, normal neutrophil count, platelet count 145,000/µL, hemoglobin 6.9g/dl, LDH 726 IU/L, reticulocyte count 40, 000/µL (Nl: 30,000-100,000) raising to 231,000/µL 10 days later, potassium 6.78 mmol/L (Nl: 3.5-5), haptoglobin 0.13g/L (Nl: 0.3-2), CRP 335mg/L, normal creatinine, bilirubin 1.3mg/dL. Blood smear showed numerous red blood cell agglutination, schizocytes <1%. Direct Coombs test was positive for C3b, negative for IgG. Cold agglutinins were positive (titer 1/16384), anti-I (titer 1/1024). Antinuclear antibodies were positive (titer 1/160), ENA screening negative, antiphospholipid negative. A multiplex PCR testing performed on tracheal aspiration was negative for *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Chlamydia pneumoniae, Adenovirus and Influenza*. Serology testing was negative for HBV, HCV, HIV, while IgG antibodies were found for EBV and CMV, and IgM and IgG antibodies for *Mycoplasma pneumoniae*. Leucocytes immunophenotyping performed on peripheral blood showed lymphopenia without evidence of clonality. There was an oligoclonal pattern of gammaglobulins at serum protein electrophoresis; light chains kappa/lambda ratio was normal. The patient received 8 units of red packet cells over one week. At 6-week follow-up, the patient is slowly recovering from respiratory failure.

While the main target of Covid-19 remains the lung, with respiratory failure and acute respiratory distress syndrome for the most severe cases, extra-pulmonary complications are now increasingly reported. Among auto-immune manifestations, auto-immune hemolytic anemia (AIHA) is an usual finding. Auto-immune hemolytic anemia (with warm or cold antibodies) was recently described in 7 patients with

Covid-19 disease [1,2]. The delay between Covid-19 and hemolytic manifestations ranged from 4 to 13 days. Four patients had indolent B lymphoid malignancy either already known or discovered at the time of hemolytic episode. The chronological sequence in our case suggests that Covid-19 was the causal factor for AIHA. Temporal events and exclusion of other potential causes support this hypothesis. Indeed, our patient had a history of oropharyngeal carcinoma which is not usually considered as a triggering factor for auto-immune hemolytic anemia. The interpretation of *Mycoplasma pneumonia* serology should also be extremely careful, as IgM antibodies do not mandatory indicate a recent infection [3]. In our case, PCR testing was negative on the sputum and there was no significant increase in IgG antibody titer over time. Among other hematological complications of Covid-19 infection, auto-immune thrombocytopenia and antiphospholipid syndrome were also described, but not present in our observation [1,4-5].

Declarations

Consent: An informed consent was obtained from the relatives.

Conflict of interest: The authors have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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