Multiple drugs

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Lethal COVID-19 and lack of efficacy: case report

A 3.5-year-old girl died after developing lethal COVID-19 respiratory infection during treatment with prednisolone and methotrexate for an unclassified autoinflammatory disease. Additionally, she exhibited lack of efficacy during treatment with levosimendan, dobutamine, milrinone, norepinephrine and vasopressin for arterial hypotension [*routes not stated*].

The girl, who had an unclassified autoinflammatory disease, diagnosed at the age of six months was admitted. Ten months prior to admission (at the age of 3.5 years), she started receiving treatment with prednisolone 0.16 mg/kg/day and methotrexate 12.5 mg/m^2/week. Five days prior to admission, she had runny nose and fever. On day 2 of the illness, she attended routine follow-up for methotrexate treatment monitoring, and received a dose of methotrexate. At night, she developed fever up to 39°C. At the time of presentation to outpatient clinic on the next day, she had no fever, and was diagnosed with nonspecific viral infection. On day 5, the fever had subsided. However, she had become anxious, and distressed by loud noises. After two hours, the she developed a tonic-clonic seizure, which stopped spontaneously after five minutes. Consequently, she was admitted to hospital. Upon admission, she was diagnosed to be in an afebrile postictal state with signs of an acute upper airway infection. She had no clinical signs of meningitis. Haematological tests revealed an increased CRP, leukopenia, anaemia and thrombocytopenia. Biochemical examination showed normal creatinine and transaminases. During five to eleven hours following admission, she developed several tonic-clonic seizures. The seizures responded to phenobarbital and unspecified benzodiazepines. Nine hours following admission, native emergency CT scan showed no evidence of brain oedema or intracranial haemorrhage. She underwent a lumbar puncture, which revealed pleocytosis, increased levels of protein and lactate, and a normal glucose level. At 90 minutes following lumbar puncture, she developed an acute heart failure. Following cardiopulmonary resuscitation for 15 minutes, sufficient cardiopulmonary function resumed. She received repeat doses of epinephrine [adrenaline]. She remained unconscious. Unspecified instrumental diagnostics revealed evidence of cardiac insufficiency, diminished electrical activity of the brain and bilateral pneumonic infiltrations. Findings of laboratory investigations were consistent with the diagnosis of disseminated intravascular coagulation and metabolic acidosis. Creatinine and transaminase levels were elevated. She was transferred to paediatric ICU.

The girl received plasma [fresh frozen plasma], antithrombin III and vitamin K. Her core body temperature was 34°C. An amplitude integrated electroencephalography (aEEG) showed a burst suppression and flat trace pattern, which remained unchanged despite warming. Chest x-ray revealed bilateral pneumonic infiltrations. Aspiration pneumonia was suspected, and she was treated with ampicillin. A non-contrast chest CT revealed extensive bilateral airspace consolidations, ground glass opacities secondary to pneumonia, and small bilateral pleural effusions. At that time-point, throat swabs were taken for SARS-CoV-2 testing as her father reported contact with a SARS-CoV-2 positive patient. Two days following hospital admission, she developed signs of multiorgan failure and respiratory distress syndrome. She developed arterial hypotension, for which she received levosimendan 0.2 µg/kg/min, dobutamine 15 µg/kg/min, milrinone 0.7 µg/kg/min, norepinephrine maximum 0.4 µg/kg/min and vasopressin maximum 1.3 mIU/kg/min along with volume replacement. However, no improvement was noted. A repeat cranial CT scan showed findings compatible with a thrombosis of the dural sinus and venous infarction. SARS-CoV-2 test showed positive result. She was comatosed, with a Glasgow Coma Scale (GCS) of 3, and had fixed, isocoric pupils. Despite continued intensive care management, she died of multi-organ failure 62h following admission.

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