Favourable outcome of coronavirus disease 2019 in a 1-year-old girl with acute myeloid leukaemia and severe treatment-induced immunosuppression

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic outbreak, it has emerged that the clinical course and outcome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is definitely more favourable in children than in adults.[1] Few cases of infection in children with cancer are described; also in these patients, except for one reported case,[2] the disease was largely asymptomatic.[3] Nevertheless, the management of COVID-19 in young patients with comorbidities, particularly cancer, remains a challenge for the clinician; further data are required to optimise the clinical approach to these cases.

A 13-month-old girl with high-risk acute myeloid leukaemia was receiving chemotherapy in our clinic according to the Italian Association of Paediatric Haematology and Oncology Acute Myeloid Leukaemia 2013 protocol [AIEOP LAM 2013, European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) 2014-000652-28]. Routine laboratory evaluation, performed after the third chemotherapy cycle of the induction phase, showed low white-blood-cell (WBC) count (80 cells/μl), haemoglobin (Hb, 79 g/l) and platelets (PLTs, 5000/μl), and mildly increased C-reactive protein (CRP, 1·35 mg/dl, normal values <0·5 mg/dl); therefore, despite good clinical conditions, the patient was admitted to undergo red blood cell and platelet transfusion. As routine evaluation before admission, the patient and her caregivers were tested for SARS-CoV-2. Reverse transcriptase polymerase chain reaction (RT-PCR) testing for SARS-CoV-2 from nasal and pharyngeal swab was positive in both the patient and her parents. Specific isolation precautions[4] were applied, and she was transferred to the paediatric ward in a negative-pressure room in the infectious-diseases-dedicated area. Stool infectious testing (including rotavirus, adenovirus, *C. difficile* and cultures) performed after development of mild diarrhoea and vomiting, were negative, whereas faecal testing for SARS-CoV-2 by RT-PCR was positive. On day 3, she developed fever (39·3 °C), with increased CRP (5·4 mg/dl) and a chest X-ray showed bilateral reticular markings consistent with SARS-CoV-2 infection (Fig 1). Anti-microbial and anti-fungal empirical treatment for neutropenic fever was started with piperacillin-tazobactam and fluconazole. No microbial growth was detected in blood cultures. At that time, no guidelines were available for SARS-CoV-2 infection management in children. However, according to a Consensus Statement of the Italian Paediatric Infectious Diseases Society,[5] treatment with hydroxychloroquine was started. On day 4, lopinavir/ritonavir was added, due to a CRP increase (6·72 mg/dl) and the persistence of fever (up to 39·8 °C). At 2 days later, following persistent fever (39·6 °C) and further CRP increase (7·2 mg/dl), teicoplanin was started, and additional compassionate use of anti-viral therapy with remdesivir was considered. In the following days her clinical condition improved, with resolution of fever (day 9) and normalisation of CRP values (day 10); therefore, remdesivir was deemed unnecessary, and therapy was gradually de-escalated, discontinuing hydroxychloroquine (at day 11), then lopinavir/ritonavir (at day 12) and teicoplanin (at day 14) (Fig 2). The patient's condition remained stable, with negative infectious markers and undetectable viral plasma load at day 16 (Fig 2). Nasal swabs for SARS-CoV-2 were positive on several samplings during the entire 18-day course (Fig 2). A chest X-ray taken before discharge showed no significant modification from baseline examination. No oxygen administration was ever required. Additional laboratory investigations, including cytokines [interleukin (IL)-1β, IL-6, IL-10 and tumour necrosis factor (TNF)α] and cardiac enzymes, were normal; lactate dehydrogenase slightly increased (up to 401 iu/l at day 13), whereas ferritin values showed moderate elevation from day 9 (Fig 2).

On day 18, routine laboratory testing further improved (WBC 2080 cells/μl with 48% neutrophils, Hb 112 g/l, PLTs

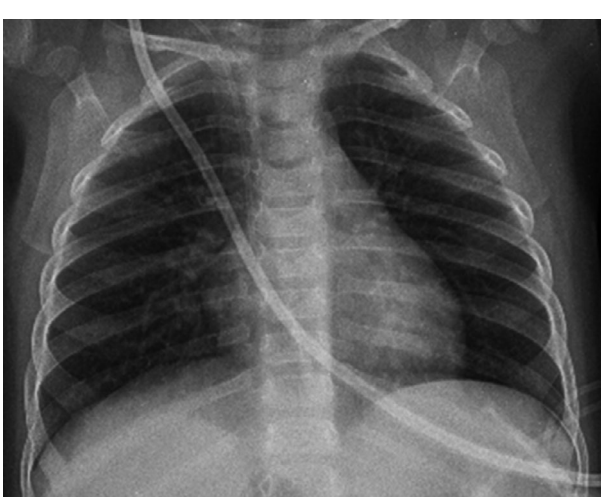

Fig 1. Chest X-ray performed on day 3, showing bilateral increased reticular markings consistent with SARS-CoV-2 infection.

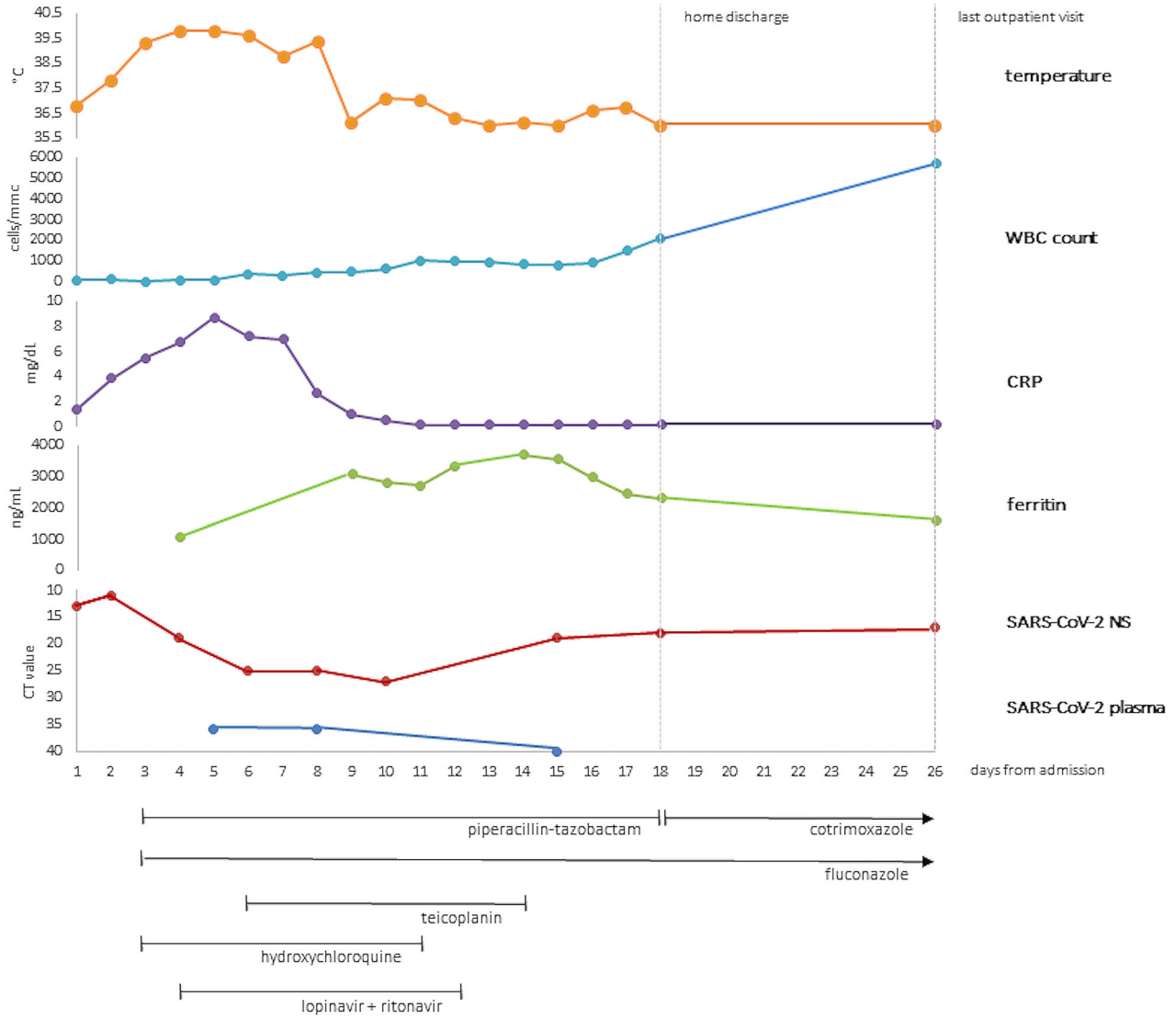

Fig 2. Visual summary including clinical-laboratory findings and treatments. Abbreviations: CT, cycles threshold; WBC, white blood cells; CRP, C-reactive protein; NS, nasal swab.

297 000/μl, negative CRP), and she was finally discharged, despite persistent positivity for SARS-CoV-2 at nasal swab, with oral prophylactic anti-microbial therapy.

During the last outpatient evaluation on day 26, she presented in good clinical condition, afebrile, with normal values of WBC (5650 cells/μl with 50% neutrophils), Hb (129 g/l) and PLT (301 000/μl) counts. The nasal swab for SARS-CoV-2 was still positive, whereas the rectal swab was negative. No seroconversion was observed, although immunoglobulin levels were low during the disease course (at day 3: IgG, 258 mg/dl; IgA, 18·7 mg/dl; and IgM, 7 mg/dl).

A summary of the main clinical and laboratory findings is reported in Fig 2, together with the treatment outline.

Out of the 170 patients followed at our haemato-oncology clinic tested in the last 2 months, SARS-CoV-2 infection was detected at the molecular level (nasal swab) in four cases. In three of them, however, an asymptomatic or mild disease course did not require any treatment. Conversely, the patient we describe here presented with febrile neutropenia and was therefore hospitalised. It was not clear on admission whether her symptoms were COVID-19-related or not. However, chest X-ray findings and the lack of evidences for other pathogens suggested symptomatic SARS-CoV-2 infection. Despite poor clinical evidence of efficacy, early anti-viral therapy was started. As a matter of fact, we were worried about the severe immunosuppression, which could have favoured viral dissemination, and thereafter about a potential inflammatory response during the immune reconstitution period. Despite being at high potential risk of severe SARS-CoV-2 infection, the patient did not experience any respiratory complication and was discharged without clinical sequelae.

According to previous reports on COVID-19 in adults,[6,7] biochemical predictors of severity and fatal outcome were tested. A slight increase in ferritin was the only feature suggesting a hyperinflammatory state, as that described in adults. Despite our present findings being consistent with previous reports in children, a role of immunosuppression can not be excluded. The only published paediatric case with cancer and an aggressive course, requiring mechanical ventilation, was an 8-year-old child receiving chemotherapy for T-cell acute lymphoblastic leukaemia; in this patient elevated ferritin levels (6417–15 758 ng/ml) were found, while CRP and IL-6 were only mildly increased.[2]

Interestingly, about 1 month after the clinical onset of the disease, the patient's nasal swab remained positive, whereas her rectal swab was negative, diverging from previous reports on longer faecal elimination.[8]

Overall, despite our prudential approach, we found no evidence that the comorbidities presented by our patient influenced in any significant way the disease course; even highly immunocompromised children on anti-cancer therapy may have a favourable outcome. An optimised management of COVID-19 is essential, in order to identify and treat patients with a more severe disease course; nevertheless, the resumption of the oncological treatment should remain among our first priorities.

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Assessing the impact of lockdown: Fresh challenges for the care of haematology patients in the COVID-19 pandemic

Worldwide cases of confirmed COVID-19 are approaching three million, and citizens around the world are experiencing unprecedented changes to their lifestyles due to the measures implemented to slow the spread of the disease.

Patients with haematological cancers have also made dramatic changes to their lives. The UK Government has recommended shielding for a period of at least 12 weeks[1] in order to reduce the risk of exposure to the virus, and this has nurtured a fear of contact with others, and especially with healthcare systems, which are rightly considered as potential sources of infection.

Haematology teams have thus radically altered the way their care is delivered.[2,3] Teleconferencing is now the norm, intervals between blood monitoring have been extended, end of treatment scans have often been omitted, maintenance chemotherapies have been suspended, non-curative chemotherapy and