Necrotizing pneumonia and severe COVID-19 in an infant with CR-BSI by methicillin-susceptible Staphylococcus aureus

Giacomo Brisca[1], Silvia Buratti[1], Daniela Pirlo[1], Luca Basso[1], Marta Romanengo[1], Maurizio Miano[1], Alessio Mesini[1], Pietro Salvati[1], Andrea Moscatelli[1], and Elio Castagnola[1]

[1]Istituto Giannina Gaslini

May 25, 2022

Necrotizing pneumonia and severe COVID-19 in an infant with CR-BSI by methicillin-susceptible Staphylococcus aureus

Giacomo Brisca[1], Silvia Buratti[2], Daniela Pirlo[1], Luca Basso[3], Marta Romanengo[1], Maurizio Miano[4], Alessio Mesini[5], Pietro Salvati[6], Andrea Moscatelli[1,2], Elio Castagnola[5].

1. Sub-Intensive Care Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy
2. Neonatal and Pediatric Intensive Care Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy
3. Radiology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy
4. Hematology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy
5. Infectious Disease Unit, IRCCS IstitutoGianninaGaslini, Genoa, Italy
6. Pneumology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy

Corresponding author:

Giacomo Brisca, MD, PhD, Sub-Intensive Care Unit, IRCCS Istituto Giannina Gaslini,

via Gerolamo Gaslini 5, 16147, Genoa (Italy), +3901056362351, fax: +39010382466; giacomo-brisca@gmail.com

ORCID ID: 0000-0001-7992-0181

Conflicts of Interest:the authors declare that there are no conflict of interest

Keywords : pediatric COVID-19, sepsis, MSSA, catheter-related bloodstream infection, necrotizing pneumonia, SARS-CoV-2

Author contributions : GB was responsible for conceptualization, investigation, data curation, editing and final revision. SB critically revised the initial manuscript and contributed to final revision. DP, MR, MM, AM, PS were involved in patient care, data curation, and manuscript editing. LB was responsible for radiological studies and final revision. EC, and AM critically revised and supervised the manuscript.

All authors contributed to the writing of the final manuscript, and approved the final version of the manuscript.

Abbreviated title: Severe pediatric COVID-19 and CR-BSI by MSSA

Informed consent : informed consent was obtained from patient's parents

To the editor:

We describe the clinical course, laboratory and radiological findings and follow-up of a 4-month-old boy who experienced severe COVID-19 pneumonia with necrotizing pneumonia following a catheter-related bloodstream infection (CR-BSI) by methicillin-susceptible Staphylococcus aureus (MSSA).

He presented to the Emergency Department with a 3-days history of high fever and cough. Since his birth, he had been followed by Hematologists for the occurrence of severe thrombocytopenia, responding to intravenous immunoglobulin (IVIG) administration, associated with neutropenia and hypo-regenerative anemia successfully treated with weekly erythropoietin administration. Diagnostic work-up revealed a postnatal cytomegalovirus infection. Whole Exome Sequencing analysis resulted negative.

A central venous catheter (CVC) had been placed since the age of 2 months for periodic blood tests and erythropoietin treatment.

His last full blood count 10 days before admission was normal (WBC 6270/mm^3, Hb 10,5 g/dl, platelets 213000/mm^3).

At clinical examination he was dehydrated and irritable, with moderate respiratory distress and oxygen saturation of 90% in room air. Chest X-ray demonstrated bilateral peribronchovasal thickening and C reactive protein was increased **(Table 1)** .

Reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 on nasopharyngeal swab sample tested positive in both child and his mother.

High flow nasal cannula (HFNC) and empiric antibiotic therapy with vancomycin and piperacillinetazobactam were started and mild clinical improvement was noticed in the 2 following days.

On day 3 blood cultures turned positive for MSSA and the CVC was removed. Echocardiography did not detect any endocavitary thrombus or bacterial vegetation. Antibiotic therapy was shifted to daptomycin.

On day 4 fever relapsed and increased irritability with nuchal rigidity was noted. Lumbar puncture was performed showing pleocytosis (200 cells/μL, prevalence of lymphomononuclear cells), normal glucose (64 mg/dl) and elevated protein levels (364 mg/dl). RT-PCR for viruses and bacteria resulted negative, as well as cerebrospinal fluid culture. Brain MRI did not detect any pathological findings.

Antibiotic therapy was implemented with ceftriaxone and co-trimoxazole – trimethoprim.

The following day the child developed acute respiratory failure. Emergency intubation and mechanical ventilation were required. High frequency oscillatory ventilation was started with high parameters (MAP 20 cm H2O, amplitude 60, frequency 10 Htz, FiO2 0.6) and a PaO_2/FiO_2 ratio of 100. Chest X-ray showed low lung volumes, interstitial thickening associated to bilateral granular opacities and air bronchograms, supporting a diagnosis of acute respiratory distress syndrome (ARDS). Milrinone was started for severe peripheral vasoconstriction and lactic acidosis with stable hemodynamic parameters. Inotropic support was not necessary during the acute phase and metabolic and respiratory acidosis resolved with intensive care support. A marked increase of ferritin, triglyceridemia and lactic dehydrogenase with decrease of platelets count were observed**(Table 1)** . Echocardiography confirmed normal bilateral ventricular function. Treatment with high dose steroids (intravenous methylprednisolone 30 mg/kg for 5 days with subsequent tapering) plus IVIG (2 g/kg) was administered in suspicion of macrophage activation syndrome (MAS). In the following days the fever disappeared, inflammatory markers decreased **(Table 1)** , and it was possible to reduce the respiratory support to PC-AC with intermediate parameters and lower FiO2 (0.45).

On day 15, a new chest X-ray showed increased lung volumes with persistent bilateral lung opacities of the lower lobes and a cavitary lesion within right lower field. Computed Tomography (CT) confirmed bilateral ground glass of lower lobes with a large cavitary lesion within right lower lobe (**Figure 1a**).

On day 18 the child was extubated and placed in HFNC.

On day 42 the antibiotic therapy was stopped, and on day 59 the child was discharged without the need for respiratory support.

At follow-up, he appeared in good general condition. Chest CT was repeated at 3-6-12 months showing a progressive reduction of ground glass and complete resolution of cavitary lesion (**Figure 1 b-d**). Last blood tests showed a normal full blood count **(Table 1)** .

Discussion :

Since the beginning of the COVID-19 pandemic, it was evident that pediatric clinical manifestations were milder, compared to adult patients.

Nevertheless, severe acute COVID-19 complicated by life-threatening conditions, like ARDS and multiple organ failure, has been reported in children, particularly in those affected by underlying respiratory, neurological, or immune disorders[1].

However, definitive data about the risk factors related to clinical outcomes in children are not available.

The presence of secondary infections or co-infections is a recognized factor affecting mortality in adults[2], although it has received inadequate attention among children with COVID-19. In particular, data on CR-BSI during COVID-19 are lacking.

Bloodstream infections are the second most common secondary infection in critically ill COVID-19 patients, following ventilator-assisted pneumonia, with incidences ranging from 3.4 to 50%[3].

Buetti et al. found that COVID-19 pneumonia patients had a higher risk of developing ICU bloodstream infections compared to patients who were critically ill without COVID-19 infection and that Staphylococcus aureus was identified in 7.7% of cases[4].

Some of these cases led to necrotizing pneumonia, likely induced by Panton–Valentine leukocidin (PVL) secreting MSSA.

When Staphylococcus aureus is detected as the cause of pneumonia, especially with an underlying influenza-like infection, such as SARS-CoV-2, it is usually associated with severe disease, potentially leading to pulmonary necrosis, and shock.

Choudhury and colleagues speculated that SARS-CoV-2 infection would have been the possible cause of functional exhaustion of CD4 and CD8 T-cells and persistent cause of MSSA bacteremia[5].

Although in our patient sepsis by MSSA was likely facilitated by SARS-CoV-2, this association remains an extremely rare condition as very few cases have been reported in children, despite over 20 million infected children and adolescents worldwide.

Usually SARS-CoV-2 infection in children has a benign course and we may have initially underestimated the clinical impact of COVID-19 in determining our patient's clinical worsening.

Nevertheless, COVID-19 pneumonia causes a clinical syndrome that is often difficult to distinguish from bacterial pneumonia and hospitalized patients with COVID-19 may develop a persistent inflammatory syndrome that has overlapping clinical features with bacterial sepsis.

Conclusion:

Our case adds new insights to the evolving scenario of SARS-COV-2 effects in children and the potential severe complications related to bacterial co-infection. Strict surveillance and fine scrutiny of the clinical course of COVID-19 are key to identify additional pathologic factors and adapt the therapeutic strategy.

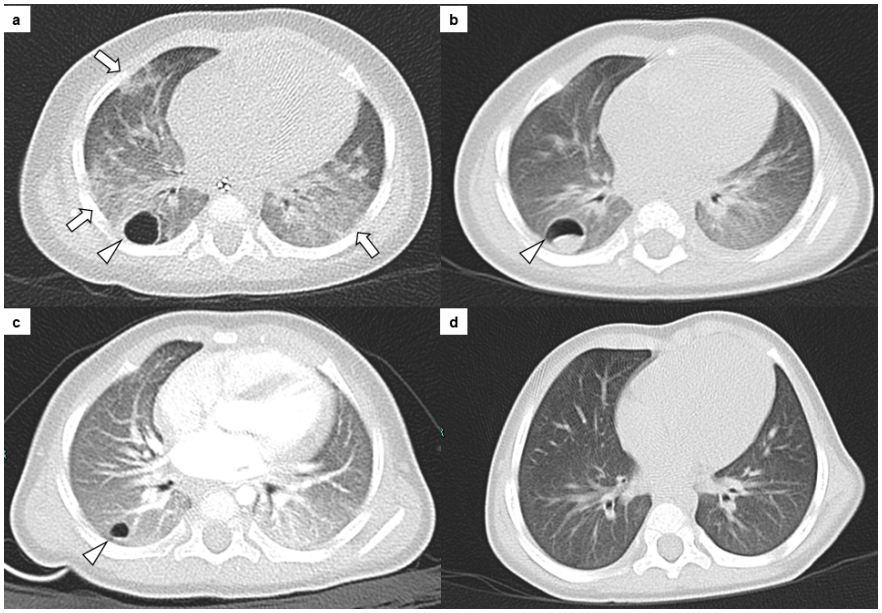
References:

1. Delahoy MJ, Ujamaa D, Whitaker M, O'Halloran A, Anglin O, Burns E, Cummings C, Holstein R, Kambhampati AK, Milucky J, et al; COVID-NET Surveillance Team; COVID-NET Surveillance Team. Hospitalizations Associated with COVID-19 Among Children and Adolescents - COVID-NET, 14 States, March 1, 2020-August 14, 2021. MMWR Morb Mortal Wkly Rep. 2021 Sep 10;70(36):1255-1260. doi: 10.15585/mmwr.mm7036e2. PMID: 34499627; PMCID: PMC8437052.

2. Grasselli G, Cattaneo E, Florio G. Secondary infections in critically ill patients with COVID-19. Crit Care. 2021 Aug 31;25(1):317. doi: 10.1186/s13054-021-03672-9. PMID: 34461962; PMCID: PMC8405344.
3. Omoush SA, Alzyoud JAM. The Prevalence and Impact of Coinfection and Superinfection on the Severity and Outcome of COVID-19 Infection: An Updated Literature Review. Pathogens. 2022 Apr 7;11(4):445. doi: 10.3390/pathogens11040445. PMID: 35456120; PMCID: PMC9027948.
4. Buetti N, Ruckly S, de Montmollin E, Reignier J, Terzi N, Cohen Y, Siami S, Dupuis C, Timsit JF. COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network. Intensive Care Med. 2021 Feb;47(2):180-187. doi: 10.1007/s00134-021-06346-w. Epub 2021 Jan 27. Erratum in: Intensive Care Med. 2021 May;47(5):640. PMID: 33506379; PMCID: PMC7839935.
5. Choudhury I, Han H, Manthani K, Gandhi S, Dabhi R. COVID-19 as a Possible Cause of Functional Exhaustion of CD4 and CD8 T-cells and Persistent Cause of Methicillin-Sensitive Staphylococcus aureus Bacteremia. Cureus. 2020 Jul 4;12(7):e9000. doi: 10.7759/cureus.9000. PMID: 32775080; PMCID: PMC7402531.

Conflicts of Interest: the authors declare that there are no conflict of interest

Funding sources: nothing to declare



Hosted file

Table 1.docx available at https://authorea.com/users/484970/articles/570557-necrotizing-pneumonia-and-severe-covid-19-in-an-infant-with-cr-bsi-by-methicillin-susceptible-staphylococcus-aureus