SARS COV-2 infection in post-induction AML pediatric patient: A case report

Fernanda O Mota[1], Ana Virgínia L de Sousa[1], Adriana M P S Silva[2], Dafne C Bourguignon da Silva[3], Orlei R Araújo[3], Fabianne A M C Carlesse[4]

[1]Pediatric Oncology Department, GRAACC/IOP/UNIFESP, Grupo de Apoio ao Adolescente e à Criança com Câncer (GRAACC), Instituto de Oncologia Pediátrica (IOP), Sao Paulo Federal University (UNIFESP), São Paulo, Brazil

[2] Infection Control Committee GRAACC/IOP/UNIFESP, Grupo de Apoio ao Adolescente e à Criança com Câncer (GRAACC), Instituto de Oncologia Pediátrica (IOP), Sao Paulo Federal University (UNIFESP), São Paulo, Brazil

[3]Intensive Care Unit, GRAACC/IOP/UNIFESP, Grupo de Apoio ao Adolescente e à Criança com Câncer (GRAACC), Instituto de Oncologia Pediátrica (IOP), Sao Paulo Federal University (UNIFESP), São Paulo, Brazil

[4]Infection Control Committee GRAACC/IOP/UNIFESP, and Pediatric Department, UNIFESP, Grupo de Apoio ao Adolescente e à Criança com Câncer (GRAACC), Instituto de Oncologia Pediátrica (IOP), Sao Paulo Federal University (UNIFESP), São Paulo, Brazil.

Hospital

Instituto de Oncologia Pediátrica

Parceria técnico-científica

UNIFESP

Universidade Federal de São Paulo

1933

Introduction

Since 2020 the world has been experiencing a pandemic due to the new coronavirus – the SARS-CoV-2. Its presentation is described as a spectrum, with the severity usually associated with comorbidities and immunosuppression, the evolution is related to cytokine storm. Pediatric patients have atypical course, severe infections are rare and usually presented as multisystem inflammatory syndrome (MIS-C). There are few descriptions about pediatric oncology patients, with great a fraction of good outcome.

Aim

We describe a case of a child previously diagnosed with acute myeloid leukemia (AML) evolving with severe SARS-CoV-2 infection after induction therapy.

Methods

Retrospective report case. Data was collected from the patient's medical record from a Brazilian institution

Results

5-year-old male patient, diagnosed with AML on July 8th 2020, after presenting petechiae for 3 months, was immediately admitted on hospital to further investigation and treatment. Bone marrow analysis concluded he presented AML M2 subtype (FAB), without recurrent cytogenetic abnormalities. He started induction therapy on July 14th 2020, according to AML BFM 2004 protocol (cytarabine, idarrubicin and etoposide), receiving high dose chemotherapy. After 4 days he presented febrile neutropenia (1300 neutrophils, dropping), without complications. He started receiving cefepime, later vancomycin, amikacin and metronidazole were associated. Despite antibiotic therapy, he maintained fever for 5 days and evolved with cutaneous rash. Bacterial and fungal searches were negative. On day 4 of antibiotics he had remission of fever for 4 days, but then he presented it again on day 10 (38,5°C). It was associated with worsening of cutaneous lesions (Figure 1), cough and diarrhea.

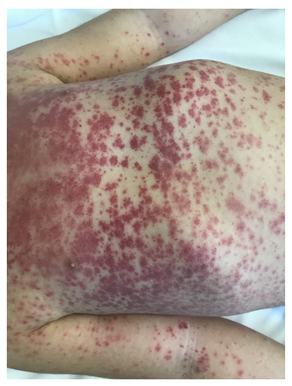

Figure 1- Cutaneous lesions 28/07

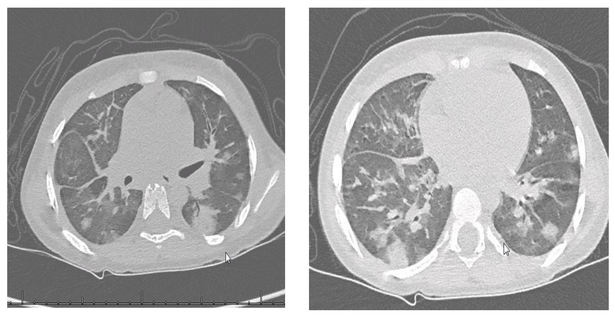

Figure 2- CT scan 29/07

He had elevated inflammatory markers (CRP 124; Fibrinogen 446; D-dimer 1500) and PCR for SARS CoV 2 positive, leading to criteria for MIS-C. He received methylprednisolone (2mg/kg) and immunoglobulin(2mg/kg). He presented acute respiratory distress, which needed intubation – with protective ventilation –, renal failure with continuous hemodyalisis and also myocardic dysfunction, receiving hemodynamic medications, including levosimendan. On August 2nd (4th day after worsening) a single dose of Tocilizumab (8mg/kg) was administrated, an anti IL-6 monoclonal antibody, presenting rapid laboratorial response with drop of inflammatory levels (Figure 4/Table 1). He had no adverse effects from the drug. The patient also received Granulocyte colony-stimulating factor due to its severe neutropenic condition (from 02/08 to 09/08). Anticoagulation had few use because of thrombocytopenia, enoxaparin was only used when platelets level were higher than 50.000. The clinical recover was slower, extubation was proceeded on August 27th (27 days on ventilation). After 2 negative COVID tests (49 days after de 1st positive test), the AML treatment was continued. Although the pause on treatment, he did not present relapse during treatment. His last chemotherapy cycle was on November 26th. He has no sequelae of covid.

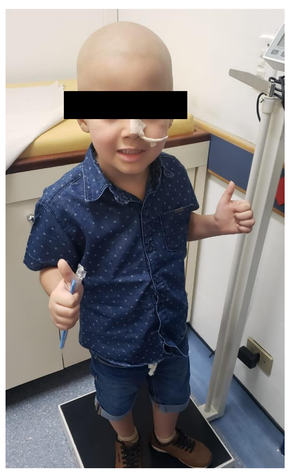

Figure 3- Follow up evaluation on 28/09/2020

Figure 4 –Evolution of WBC and CRP during infection.

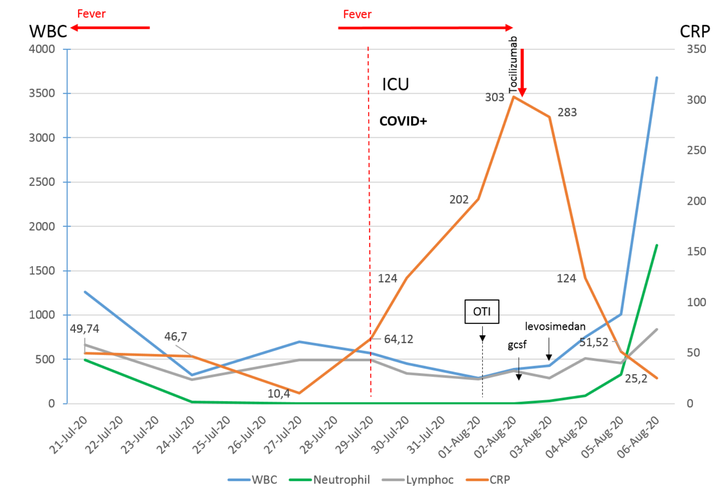

Table 1 – Evolution of platelets and inflammatory markers

Exams	21/07	29/07	30/07	31/07	01/08	02/08	05/08	06/08	07/08	09/08	10/08	12/08
Plat 10^3	20	7,3	33,4				35,3	73,4		107		
Ferritin				1.012	1.278		3.993		3.063			
IL-6				101				187	131		81	
D-dimer				1.500	3.296		5.667	15.814	9.460		7.710	2.840
Fibrino			446		531		240	189	187			

Conclusions

MIS-C is an entity of severe presentation of SARS-COV-2 in children. This case presented an immunocompromised patient infection, who recovered after hard multidisciplinary work. The bases of MIS-C management envolves immune modulation, which indicates the use of glucocorticoids and IVIG. The use of tocilizumab had its importance on downregulating the inflammatory response. As he had severe neutropenia secondary to high dose chemotherapy, due to the severity of infection, GCSF was used to accelerate white blood cells increase, leading to contribute to immune regulation.

References

Pascarella, G., Strumia, A., Piliego, C., Bruno, F., Del Buono, R., Costa, F., Scarlata, S., & Agrò, F. E. (2020). COVID-19 diagnosis and management: a comprehensive review. Journal of internal medicine, 288(2), 192–206

Kakodkar P, Kaka N, Baig MN. A Comprehensive Literature Review on the Clinical Presentation, and Management of the Pandemic Coronavirus Disease 2019 (COVID-19). Cureus. 2020;12(4):e7560.

Boopathi, S at al(2020) Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment, Journal of Biomolecular Structure and Dynamics

Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. BMJ 2020; 368: m1036

Zhou G, Chi C. A model simulation study on effects of intervention measures in Wuhan COVID-19 epidemic. Medrxiv 2020.

Gosain, R., Abdou, Y., Singh, A., Rana, N., Puzanov, I., & Ernstoff, M. S. (2020). COVID-19 and Cancer: a Comprehensive Review. Current oncology reports, 22(5), 53.

Azkur, Ahmet Kursat et al. (2020) Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. Allergy, v. 75, n. 7, p. 1564-1581

Tay, M.Z., Poh, C.M., Rénia, L. et al. The trinity of COVID-19: immunity, inflammation and intervention. Nat Rev Immunol 20, 363–374 (2020)

Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: A clinical-therapeutic staging proposal. J Heart Lung Transplant. 2020;39(5):

Shi Y, Wang Y, Shao C, Huang J, Gan J, Huang X, Bucci E, Piacentini M, Ippolito G, Melino G. COVID-19 infection: the perspectives on immune responses. Cell Death Differ. 2020 May;27(5):1451-1454

Safadi, M. A. P., & Silva, C. A. A. D. (2020). The challenging and unpredictable spectrum of COVID-19 in children and adolescents. Revista Paulista de Pediatria, 39.

Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020 Jun;109(6):1088-1095.. Epub 2020 Apr 14.

Nakra, Natasha A., et al. Multi-system inflammatory syndrome in children (MIS-C) following SARS-CoV-2 infection: review of clinical presentation, hypothetical pathogenesis, and proposed management. Children 7.7 (2020): 69

Pereira, M. F. B., Litvinov, N., Farhat, S. C. L., Eisencraft, A. P., Gibelli, M. A. B. C., Carvalho, W. B. D., ... & Fante, A. L. (2020). Severe clinical spectrum with high mortality in pediatric patients with COVID-19 and multisystem inflammatory syndrome. Clinics, 75.

Meirelles, A. F. V., Chaves, C. R. M. D. M., Pereira, C. D., Pacheco, C. A. M. S., Britto, J. A. A. D., Ramos, J. R. D. M., ... & Gomes, M. A. D. S. M. (2020). COVID-19 e Saúde da Criança e do Adolescente.

Sieni, E., Pegoraro, F., Casini, T., Tondo, A., Bortone, B., Moriondo, M., ... & Favre, C. (2020). Favourable outcome of Coronavirus-19 in a 1-year-old girl with acute myeloid leukaemia and severe treatment-induced immunosuppression. British Journal of Haematology.

Flores, V., Miranda, R., Merino, L., González, C., Serrano, C., Solano, M., ... & Cárdenas, A. (2020). SARS-CoV-2 infection in children with febrile neutropenia. Annals of Hematology, 1-2.

Bisogno, G., Provenzi, M., Zama, D., Tondo, A., Meazza, C., Colombini, A., ... & Meneghello, L. (2020). Clinical Characteristics and Outcome of Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Italian Pediatric Oncology Patients: A Study From the Infectious Diseases Working Group of the Associazione Italiana di Oncologia e Ematologia Pediatrica. Journal of the Pediatric Infectious Diseases Society. Puyó, P. V., Moreno, L., de Heredia, C. D., Rivière, J. G., & Palacín, P. S. (2020, August).

Tocilizumab in a child with acute lymphoblastic leukaemia and COVID-19-related cytokine release syndrome. In Anales De Pediatria. Elsevier.

Lee, L. Y., Cazier, J. B., Starkey, T., Briggs, S. E., Arnold, R., Bisht, V., ... & Curley, H. M. (2020). COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. The Lancet Oncology, 21(10), 1309-1316.

Saini, K. S., Tagliamento, M., Lambertini, M., McNally, R., Romano, M., Leone, M., ... & de Azambuja, E. (2020). Mortality in patients with cancer and coronavirus disease 2019: A systematic review and pooled analysis of 52 studies. European Journal of Cancer, 139, 43-50.

Sanchez-Pina, J. M., Rodríguez Rodriguez, M., Castro Quismondo, N., Gil Manso, R., Colmenares, R., Gil Alos, D., ... & Cuellar, C. (2020). Clinical course and risk factors for mortality from COVID-19 in patients with haematological malignancies. European journal of haematology

Zeidan, A. M., Boddu, P. C., Patnaik, M. M., Bewersdorf, J. P., Stahl, M., Rampal, R. K., ... & Roboz, G. J. (2020). Special considerations in the management of adult patients with acute leukaemias and myeloid neoplasms in the COVID-19 era: recommendations from a panel of international experts. The Lancet Haematology.

Acknowledgements

Thanks to all GRACC staff that contributed for the successful recovery of this patient

21st ICHS Symposium on Infections in the Immunocompromised Host

ICHS International Congress on Hospital Infections in Immunocompromised Hosts