



Acute myeloid leukemia

Impact of COVID-19 on the treatment of acute myeloid leukemia

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Infections represent the major complication in the management of different hematologic malignancies, and particularly during seasonal outbreaks, respiratory infections can substantially impair the final outcome [1]. Induction and, at less extent, high-dose consolidation chemotherapy in patients with acute myeloid leukemia (AML) cause severe and prolonged granulocytopenia with increased risk of severe infections, particularly of bacterial or fungal origin [2]. Respiratory virus infections can also occur, particularly during seasonal outbreaks, but their clinical impact in AML has been generally considered as less relevant [3]. Covid-19 is now affecting more than two million people around the world and causes illnesses ranging from the common cold to more severe diseases mimicking the Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS) [4]. Therefore, an increasing number of patients with different hematologic malignancies, including AML, is expected to present with concomitant Covid-19 either at diagnosis or during disease course. Detection of SARS-CoV-2 positivity resulting in high risk of respiratory failure, may raise difficulties in administering optimal treatment for the underlying disease, including delay, need for dose reduction and drug-drug interactions. In spite of a number of reports focusing on Covid-19 and cancer [5], only two items were found by imputing AML and COVID-19 in the NCBI Pub Med, one referring to favorable outcome of a 1-year-old girl [6], the second suggesting rule for the management of AML and MDS in the time of Covid-19 [7]; this does not mean that a number of patients with AML were not found with concomitant positivity and/or symptoms due to the virus. He et al. [8] reported on hospitalised patients with haematological

cancers resulted SARS-COV-2 positive, describing a more severe disease and a higher case fatality rate. However, no specific mention was done about AML patients who are at higher risk of infections compared to other hematological cancers.

Here we describe clinical characteristics and treatment outcome of ten consecutive COVID-19 patients with AML, managed at two hematologic institutions in Northern Italy, a geographical area markedly hit by Covid-19 with the highest number of cases in the country.

From 1 to March 31 2020, 101 patients affected by hematological malignancies, including 10 AML cases (Table 1), were found SARS-CoV-2-positive by nasopharyngeal swab. Median age was 60 (range: 31–69), M/F ratio was 5/5. Two patients were observed at diagnosis, six in complete remission (CR), and two in relapse. According to European Leukemia Net (ELN) criteria [9], five patients had favorable-, three intermediate-, and one high-risk AML. One had acute promyelocytic leukemia (APL). Treatment for Covid-19 depended on the policy of the center and included to different options which are currently available [10]. At presentation, respiratory symptoms were absent in two patients, while mild without oxygen need in five. Three patients needed oxygen supplementation by nasal mask. During the course of infection, seven patients experienced rapid worsening of respiratory function, six requiring non-invasive and one mechanical ventilation.

Overall, Covid-19 required hematological treatment modifications in seven symptomatic patients: one died early before any treatment; three discontinued therapy (venetoclax plus azacytidine, venetoclax plus enasidenib in two relapsed patients) and high-dose cytosine-arabioside as first consolidation in one CR patient. All-trans-retinoic-acid and arsenic trioxide doses were reduced in the APL patient. Consolidation therapy was delayed in one patient in CR1. Three asymptomatic patients continued their therapeutic program. Five patients (50%) died after a median of 8 days (range 5–26). Death was Covid-19 related in all cases. Our series demonstrate that Covid-19 infection has a substantial impact on AML patient survival as well as on the possibility

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Table 1 Characteristics and outcome of 10 Covid-19 positive patients.

UPN	Age	SEX (M/F)	ELN risk score	Disease phase	Symptoms at admission	Treatment of respiratory failure	Anti viral treatment	Covid due treatment changes	Time to severe respiratory failure (days)	Outcome of infection (R/I/S/P)	Outcome (A/D)	Survival from COVID (days)
1	31	M	Int, trisomy 21, WT1 mutation	CR1	Yes, no oxygen	No oxygen	Symptomatic	Delay		R	Alive	42
2	45	M	Int, (trisomy 8), DNMT3A, RUNX1, IDH2, ETV6 mutations	REL	Yes, no oxygen	intubation	Kaletra/chloroquine	Discontinuation	7	P	Dead	26
3	64	M	Fav, NPM1mutation	Onset	Oxygen need	NIV	Kaletra/chloroquine/tocilizumab	Palliation	7	P	Dead	6
4	61	F	APL, intermediate risk	Onset	Oxygen need	NIV	Kaletra/ chloroquine	Dose reduction		R	Alive	37
5	65	M	Fav, NPM1mutation	CR1	Oxygen need	NIV	Kaletra/chloroquine/tocilizumab	Consolidation program not completed		P	Dead	5
6	61	F	Fav, RUNX1-RUNX1T1	CR1	No	NIV	Azitromicin/chloroquine	Discontinuation	3	P	Dead	15
7	69	F	Fav, NPM1mutation	REL	Yes, no oxygen	NIV	Azitromicin/chloroquine	Discontinuation	2	P	Dead	8
8	56	F	High, FLT3/ITD mutation	CR1	Yes, no oxygen	NIV	Azitromicin/chloroquine + hyperimmune plasma	No	6	S	Alive	15
9	60	F	Fav, NPM1mutation	CR1	Yes, no oxygen	No oxygen	Azitromicin	No	-	I	Alive	26
10	48	M	Int, no mutations	CR1	No	No oxygen	No treatment	No	-	R	Alive	30

Disease Phase: CR complete remission, REL Relapse.

Treatment of respiratory failure: NIV non invasive ventilation.

Outcome of infection: resolved (R), improved (I), stable (S), progressed (P).

of receiving optimal planned treatment. Finally, we suggest to manage COVID-19 AML patients by hematologists in strict collaboration with pneumologists and intensivists in dedicated units. Alternatively, a single room with negative pressure in the hematology ward can be considered.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest. FF analyzed data and wrote the paper. PZ, ER, and EB collected and analyzed data. GR critically reviewed the paper and gave final approval.

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