LETTER TO THE EDITOR

WILEY

Intrahospital COVID-19 infection outbreak management: Keep calm and carry on

SARS coronavirus 2 disease (COVID-19) in patients with hematological malignancies showed worse outcomes compared to both the general population with COVID-19 and hematologic patients without COVID-19.^{1,2} This high mortality rate underlines the need and urgency of protecting patients, as well as the healthcare team. Here we describe our experience with the emergence of a nosocomial COVID-19 infection outbreak.

ASST Grande Ospedale Metropolitano Niguarda is a large community hospital in Milan, comprehensive of two oncohematological departments (high and low intensity of care [IOC]) and a bone marrow transplant (BMT) center.

High-IOC and BMT units account for 18 and 6 single rooms respectively, equipped with high efficiency particulate air (HEPA) filters and negative pressure. Low-IOC unit consists of six double rooms, settled in a larger multidisciplinary department. Here, 25 nurses and 3 medical doctors (MDs) are permanently employed; 24 additional MDs carry out medical on-call service.

Between 1 March and 1 June 2020, 99 hospitalizations in 75 patients were recorded in the low-IOC unit.

The first case of COVID-19 was diagnosed on 10 April by RT-PCR nasopharyngeal swab (NPS). A nurse who had worked using personal protective equipment (PPE) and without showing symptoms in the previous days, was tested due to the occurrence at home of fever and cough.

All the 12 patients who were hospitalized in that moment were therefore screened with NPS on 11 April, and 4 of them resulted positive for COVID-19.

As of the 25 March negative NPS was required before hospital admission,³ therefore, it is reasonable to believe that all contagions occurred during the hospitalization.

Following the detection of the intra-unit spread, between 1 March and 1 June serial testing on 75 hospitalized patients led to the detection of 19 contagions (25.3%). Median age of infected patients was 66 years (range: 28–85).

Patients characteristics and outcomes of positive cases at the time of intrahospital outbreak are reported in Table 1. Overall, 16 of 19 patients (84.2%) were symptomatic and 11 (57.9%) presented with interstitial pneumonia. In two additional cases (10.5%), despite severe respiratory distress, chest CT scan was not performed due to rapid deterioration of clinical conditions. Moreover, in two patients

the infection caused familiar spread, leading to further hospitalizations.

Seven of nineteen infected patients deceased: in two, death occurred due to the disease progression in presence of asymptomatic/paucisymptomatic COVID-19; in five patients (26.3%) instead, COVID-19 was considered as the main reason of death. Median age of patients with COVID-19-related death was 73 years (range: 65–85).

No COVID-19 positive cases were detected in the high-IOC and transplant units within the same time-period.

The low-IOC unit was closed for 72 h and sanitized. Patients who could not be discharged, were transferred to COVID units or COVID-free departments, based on the NPS result. Once reopened, patients were admitted in single rooms.

In the lack of a specific regional or national regulation at the beginning of the outbreak, asymptomatic healthcare personnel was not routinely screened for COVID-19, but tested only in case of fever and/or respiratory symptoms.

Between 1 March and 1 June, 5 of 27 MDs (18.5%) and 6 of 25 nurses (24%) were diagnosed with symptomatic COVID-19 in the hematologic equip.

All 11 positive healthcare professionals presented with mild symptoms. In one subject, familiar contagion spread led to a case of severe infection needing intensive care unit admission.

Given the high number of contagions, from 3 to 20 June 2020, the whole medical and nursing staff was again serial tested for COVID-19 every 5 days for a total of three swab/person, even in the absence of symptoms. Overall, a total of 179 NPSs (GeneFinder® COVID-19 Plus RealAmp, ELITech) have been performed. All NPSs were negative except for the discover of one asymptomatic case that was promptly isolated and quarantined (leading to a total number of 7/25 of nurses infected, 28%).

With the intention to estimate virus exposure, all the 52 workers underwent serological screening for the detection of anti-N immunoglobulin G (IgG) (ARCHITECT SARS-CoV-2 IgG assay; Abbott).⁴ Anti-N positive subjects were further tested for semiquantitative detection of anti-S1/S2 IgG (LIAISON® SARS-CoV-2 S1/S2 IgG assay; DiaSorin).

Notably, cumulative anti-S1/S2 IgG seroprevalence on 5092 healthcare workers screened in the whole Niguarda Hospital was 7.6% (95% confidence interval: 6.9%–8.3%).⁵

ID	Age	Sex	Diagnosis	Disease status	NPS	Symptoms	Outcome	Comments
#1	66	М	BL	First line	Positive	F/RS	Alive	
#2	28	F	DLBCL	R/R	Positive	IP	Alive	2C
#3	62	F	DLBCL	R/R	Positive	No	Alive	
#4	69	F	PTCL	First line	Positive	IP	Death (PD)	4C
#5	79	М	DLBCL	First line	Positive	F/RS	Alive	
#6	62	М	DLBCL	First line	Positive	IP	Alive	
#7	85	М	DLBCL	R/R	Positive	IP	Death (COVID)	
#8	59	М	DLBCL	First line	Positive	IP	Alive	
#9	49	F	DLBCL	First line	Positive	IP	Alive	
#10	63	F	FL	First line	Positive	IP	Alive	
#11	69	М	HD	R/R	Positive	IP	Alive	11C
#12	78	М	HD	R/R	Positive	No	Alive	
#13	55	F	MM	First line	Positive	IP	Alive	
#14	65	М	MCL	First line	Positive	IP	Death (COVID)	
#15	70	М	PTCL	R/R	Positive	No	Death (PD)	
#16	69	F	DLBCL	R/R	Positive	F/RS	Death (COVID + PD)	16C
#17	54	М	MM	R/R	Positive	F/RS	Alive	
#18	79	М	ITP	First line	Positive	IP	Death (COVID)	
#19	73	М	MM	R/R	Positive	F/RS	Death (COVID + PD)	19C

 TABLE 1
 Characteristics and outcomes of COVID-19 positive patients

Note: 2C: Delay in chemotherapy administration. Delay in CART infusion. Risk of death for disease progression. 4C: Familiar spread. Husband hospitalized (IP). 11C: Familiar spread. Wife hospitalized (IP). 16C, 19C: No chest CT scan was performed due to rapid deterioration of clinical conditions.

Abbreviations: BL, Burkitt lymphoma; DLBCL, diffuse large B-cell lymphoma; F, female; F, fever; FL, follicular lymphoma; HD, Hodgkin disease; IP, interstitial pneumonia; ITP, immune thrombocytopenic purpura; M, male; MCL, mantle cell lymphoma; MM, multiple myeloma; NPS, nasopharyngeal swab; PD, progressive disease; PTCL, peripheral T-cell lymphoma; R/R, relapsed/refractory; RS, respiratory symptoms.

Right now, all patients need to perform NPS within 48 h before the hospitalization and all rooms are routinely sanitized following COVID-19 sanitization protocol at discharge.⁶

Healthcare personnel undergoes COVID-19 screening with NPS every 2 weeks.

As per our experience, in case of nosocomial COVID-19 outbreak, some pragmatic measures should be adopted:

- Personnel training to the proper use of personal protective equipment;
- Serial COVID-19 testing of all patients and healthcare workers;
- · Hospital admission of patients with recent negative NPS only;
- Isolation and quarantine of positive cases/transfer to specific COVID-19 departments;
- Tracing and isolation of contacts;
- Avoid external visits to hospitalized patients;
- In case of uncontrolled spread despite the adoption of all the above measures, temporary closure of the department for sanitization; screening of the whole staff, then allow the admission in single rooms of patients with negative NPS.

The high mortality rate seen in our series (26.3%), is comparable to that reported in other Italian hematologic centers^{1,2} and must lead us to adopt clear prevention strategies.

The presence of HEPA filters, together with single room and negative pressure, could have contributed to the absence of COVID-19 contagion in high-IOC and transplant departments.

Our experience dramatically demonstrates how hospitalworkers protection is crucial to counter the contagion. Healthcare personnel can represent a vehicle for the infection. In the present report, virus spread occurred during the incubation period in an asymptomatic staff member who correctly used PPE. The lack of a prompt testing of the healthcare team allowed COVID-19 contagion to perpetuate.

Strict surveillance through serial NPS testing, even in the absence of symptoms, is essential to prevent an unconscious virus spread and at the same time, to protect healthcare workers.

The application of these simple measures allows early detection of new cases and rapid start of contact tracing that, waiting for a mass vaccination, still remain the main strategies to contain the current ongoing pandemic wave.

CONFLICT OF INTEREST

The authors declare no conflict of interests.

AUTHOR CONTRIBUTION

Roberto Cairoli designed the manuscript. Roberto Cairoli, Daniela A. Campisi, and Massimo Puoti revised the final version. Federica Di Ruscio, Maria L. Pioltelli, and Emanuele Ravano revised the data. Anna M. Frustaci, Maria L. Pioltelli, and Emanuele Ravano wrote the paper.

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