COVID-19, impact on myeloma patients

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To the Editor:

The worldwide COVID-19 pandemic is expected to be a devastating infection in patients with chronic hematological disorders. So far, no data have been reported in multiple myeloma (MM), a disease characterized by a severe humoral and cellular immune deficiency that exposes patients to infectious complications.

In order to assess the impact of COVID-19 in the Belgian MM community, we collected data on the disease by sending questionnaires to 30 different cancer centers. As of April 12, 2020, 20 symptomatic MM patients were confirmed with COVID-19 in 12 out of 20 hospitals that answered the survey (Table 1).

Median age was 68 years (range, 57–83). Twelve patients were male, 8 of African origin (5 North-Africans, 3 Blacks), 14 suffered from cardiovascular or renal comorbidities, 5 from diabetes, and 3 from another neoplasm. Sixteen were under therapy, mainly IMiD-based combinations (n = 13, 81%). Previous ASCT was noted in 8 (median, 7 years), immunoparesis in 6.

The most common initial symptoms were fever (n = 13, 65%), cough (n = 11, 55%), dyspnea (n = 10, 50%), and hypoxemia (SaO2 < 93%) (n = 9, 45%). Diarrhea, skin, joint, or neurological complains were uncommon. Clinical status [1] was considered as mild in 5 (25%), severe in 13 (65%), or critical in 2 (10%), with lung infiltrates reported on imaging in 16 (80%) and multiple organ failure in 1 (5%). Eleven patients presented a grade 4 eosinopenia (64%). Grade 3–4 lymphopenia was common, mostly related to corticosteroids administration.

Hospitalization was required in 18 patients for a median of 12 days (range, 3–32), 5 in ICU with 2 needing mechanical ventilation. Most patients required O2 administration, in addition to antibiotics in 13 (65%), and hydroxychloroquine in 14 (70%), following the Belgian guidelines [2]. No patients received anti-IL6 or other antiviral therapy, since access was restricted to clinical trials. No thromboembolic complications were reported, but most patients were under prophylaxis.

Adverse outcome occurred in 7 patients (median age, 77; range, 58–83). All suffered from either a cardiovascular comorbidity or a secondary cancer, all were under dexamethasone (median monthly dose; 80 mg), and 5 had a progressive disease. In addition, 5 were of African origin. We failed to identify any impact of ISS stage, immunoparesis, and number of previous lines of therapy including ASCT. Time from MM diagnosis to COVID-19 was longer in this group, but not statistically significant. Of note, no post-mortem studies were performed.

Our limited experience of COVID-19 emphasizes the severity of this condition in MM patients, with a high mortality incidence (35%). However, based on these preliminary data, in a country where 800 new MM are diagnosed each year and where 52,000 cases of COVID-19 have been reported so far,
# Table 1: Clinical features and outcomes in multiple myeloma patients

|                                | Total (n = 20) | Survivors (n = 13) | Deceased (n = 7) |
|--------------------------------|----------------|--------------------|------------------|
| Median age, year (range)       | 68 (58–83)     | 64 (57–81)         | 77 (58–83)       |
| Male sex, n (%)                | 12 (60)        | 8 (61)             | 4 (57)           |
| Ethnicity, n (%)               |                |                    |                  |
| Caucasian                      | 11 (55)        | 9 (69)             | 2 (28)           |
| African (North-Africans/Blacks)| 5 (25)/3 (15) | 1 (7)/2 (15)       | 4 (57)/1 (14)    |
| Hispanic                       | 1 (5)          | 1 (7)              | 0                |
| Comorbidities, n (%)           |                |                    |                  |
| Cardiovascular and/or renal disease | 14 (70)    | 9 (69)             | 5 (71)           |
| Diabetes mellitus              | 5 (25)         | 2 (15)             | 3 (42)           |
| Other cancer                   | 3 (15)         | 0                  | 3 (42)           |
| Hypogammaglobulinemia          | 6 (30)         | 4 (30)             | 2 (28)           |
| MM characteristics             |                |                    |                  |
| Mean time from MM diagnosis to COVID-19, months| 65            | 57                 | 79               |
| Salmon Durie Ib’ II-III, n/n   | 1/19           | 1/12               | 0/7              |
| ISS stage II-III, n/total n (%)| 8/16 (50)      | 6/11 (54)          | 2/5 (40)         |
| Progressive disease at COVID-19 diagnosis, n (%) | 8 (40)      | 3 (23)             | 5 (71)           |
| Therapy at time of COVID-19, n (%) | 16 (80)   | 11 (85)            | 5 (71)           |
| 1st line—bortezomib/lenalidomide based | 6 (30)   | 5 (38)             | 1 (14)           |
| – no treatment                 | 3 (15)         | 1 (7)              | 2 (28)           |
| 2d line—daratumumab-Rd         | 3 (15)         | 3 (23)             | 0                |
| – no treatment                 | 1 (5)          | 1 (7)              | 0                |
| ≥3d line—pomalidomide/daratumumab based | 8 (40)  | 4 (30)             | 4 (56)           |
| Previous ASCT                  | 8 (40)         | 6 (46)             | 2 (28)           |
| Signs and symptoms, n (%)      |                |                    |                  |
| Fever                          | 13 (65)        | 9 (69)             | 4 (57)           |
| Cough                          | 11 (55)        | 8 (61)             | 3 (42)           |
| Dyspnea                        | 10 (50)        | 8 (51)             | 2 (28)           |
| Hypoxemia (SaO2 < 93%)         | 9 (45)         | 6 (46)             | 3 (42)           |
| Confusion                      | 4 (20)         | 2 (15)             | 2 (28)           |
| Diarrhea                       | 2 (10)         | 0                  | 2 (28)           |
| Multiple organ failure         | 1 (5)          | 0                  | 1 (14)           |
| Clinical status, n (%)         |                |                    |                  |
| Mild                           | 5 (25)         | 4 (31)             | 1 (14)           |
| Severe                         | 13 (65)        | 9 (69)             | 4 (57)           |
| Critical                       | 2 (10)         | 0                  | 2 (28)           |
| Laboratory values              |                |                    |                  |
| Lymphopenia < 1000/mm³, n/total n (%) | 16/17 (94)   | 10/10 (100)        | 6/7 (86)         |
| Eosinopenia < 50/mm³, n/total n (%) | 11/17 (64) | 5/10 (50)          | 6/7 (86)         |
| Thrombocytopenia < 150,000/mm³, n/total n (%) | 9/17 (53) | 4/10 (40)          | 5/7 (71)         |
| Radiological characteristics, n (%) |                |                    |                  |
| Lung infiltrates on chest x-rays or CT | 16 (80)  | 11 (85)            | 5 (71)           |
| Hospitalization, n (%)         | 18 (90)        | 11 (85)            | 7 (100)          |
| Median duration, days (range)  | 12 (3–32)      | 15 (6–32)          | 9 (3–13)         |
| ICU admission, n (%)           | 5 (25)         | 2 (15)             | 3 (42)           |
| Median duration, days (range)  | 6 (3–10)       | 5.5 (4–7)          | 6 (3–10)         |
| Management, n (%)              |                |                    |                  |
| Oxygenotherapy                 | 15 (75)        | 9 (69)             | 6 (86)           |
| Mechanical ventilation         | 2 (10)         | 0                  | 2 (28)           |
| Hydroxychloroquine             | 14 (70)        | 9 (69)             | 5 (71)           |
| Antibiotics                    | 13 (65)        | 9 (69)             | 4 (57)           |
| Anti-IL6, others               | 0              | 0                  | 0                |

ASCT autologous stem cell transplant, ICU intensive care unit, ISS International Staging System, MM multiple myeloma, n number, Rd, lenalidomide-dexamethasone
this complication remains very rare. Age, comorbidities, disease status, and ethnicity may be relevant. Ethnic differences in angiotensin-converting-enzyme-2 expression might play a role, as well as socioeconomic, cultural, or other genetic predisposing factors [3]. Our data support also the need to reduce at least the dexamethasone dosage, as proposed by others [4, 5]. Grade 4 eosinopenia is common [6], a possible landmark feature of COVID-19. Further investigations are mandatory in order to assess the impact of this new viral infection on MM patients.

Authors’ contributions ID, JR, FA, GV, and MCV analyzed the data. ID, JR, and MCV wrote the manuscript. All authors collected the data and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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References

1. Wu J, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72,314 cases from the Chinese Center for Disease Control and Prevention. JAMA 323:1239. https://doi.org/10.1001/jama.2020.2648

2. Van Ierssel S, Dauby N, Bottieau E, Huits R (2020) Interim clinical guidance for adults with suspected or confirmed covid-19 in Belgium. Sciensano; https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_InterimGuidelines_Treatment_ENG.pdf. Accessed 07 Apr 2020

3. Kamlesh K, Awadhesh Kumar S, Manish P, Wasim H (2020) Is ethnicity linked to incidence or outcomes of Covid-19? Br Med J 369:1548

4. Malard F, Mohty M (2020) Management of patients with multiple myeloma during the COVID-19 pandemic. Lancet Haematol. https://doi.org/10.1016/S2352-3026(20)30124-1

5. Rajkumar SV, Cavo M, Mikhail J, Mateos MV, Jackson G, Moreau P, Richardson P, Dhakal B (2020) COVID-19 and multiple myeloma: frequently asked questions, version 1.1, last updated April 23, 2020. American Society of Hematology, Covid-19 resources. https://www.hematology.org/covid-19/covid-19-and-multiple-myeloma. Accessed 23 Apr 2020

6. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, Akdis CA, Gao YD (2020) Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. https://doi.org/10.1111/all.14238.v

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