Don’t Compromise Myeloma Care Due to COVID-19 Pandemic!

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Summary: Patients with active myeloma, especially with earlier stages of the disease, are susceptible to COVID-19 infection and can have adverse outcomes, even in those on first-line treatment. Importantly, myeloma therapy can be safely administered, and optimal control of myeloma is associated with improved outcome.

See related article by Hultcrantz et al., p. 234 (1).

In this issue of Blood Cancer Discovery, Hultcrantz and colleagues report on the clinical features and outcomes of 100 patients with multiple myeloma and COVID-19 infection at five academic centers in New York City, which was the epicenter of the infection in the United States (1). They describe a higher incidence of adverse outcomes in Hispanic/Latinos and African Americans, as well as in patients with higher levels of inflammatory markers and cytokines. Moreover, 29% of hospitalized patients died, highlighting the severity of COVID-19 infection in these patients.

A recent report of COVID-19 infection in 890 patients with cancer in Europe (the European cancer cohort) demonstrated an increased mortality in patients with hematologic malignancies than breast cancer and other solid tumors (2), coupled with other reports documenting inpatient mortality rates of COVID-19 infection in patients with myeloma ranging from 27% to 55%, further highlighting the significance of COVID-19 infection in these patients (3, 4).

An important aspect of COVID-19 infection is the relationship between age and patient outcome. Infection has been reported in a broad age range both in the general population and specifically in patients with cancer, suggesting that age by itself does not significantly affect susceptibility (5). For example, in the VA cohort study with 1,794 patients with cancer with COVID-19 positivity from the U.S. Veteran Affairs database, the prevalence of COVID-19 was similar across all ages (6). Of note, however, higher numbers of older patients with cancer may be diagnosed, as they are tested for COVID-19 more frequently. In the same study, COVID-19–related mortality was strongly associated with age, ranging from 0.23% in patients less than 50 years old to 20.5% in patients older than 80 years (P < 0.001). Although the New York City (NYC) report did not identify age greater than 65 years to be an independent risk factor associated with adverse outcome (1), a larger study of 650 patients with myeloma with COVID-19 infection from the International Myeloma Society (the IMS cohort) did find a relationship between age and mortality, with an estimated probability of death of 17.8%, 31.4%, and 49.3% in patients aged 40, 60, and 80 years, respectively (4). This and other studies in myeloma demonstrate a clear relationship between increasing age and adverse outcome of COVID-19 infection, particularly important since the median age of newly diagnosed patients with myeloma is 71 years.

In the VA cohort, the prevalence of COVID-19 infection in patients with cancer was 15% and 10.9% in African American and Hispanic/Latino patients, respectively, compared with 5.5% in whites (6). Importantly, the rate of hospitalization was 3.5-fold higher in African Americans, but the COVID-19–related mortality was similar between the two populations. Myeloma is more common in African Americans, but the NYC study cannot address the relative incidence of COVID-19 in racial populations; it did demonstrate a higher risk of adverse outcome in African American and Latino populations. Although the development of novel therapies over the last 10 to 15 years has transformed the treatment paradigm in myeloma, the median survival in African Americans has not been prolonged to the same extent as in other patient subgroups. Moreover, a recent AACR FDA Workshop demonstrated low rates of enrollment of African Americans on myeloma clinical trials; however, African American patients treated with novel agents have outcomes similar and even superior to other patient subgroups (7). Whether adverse outcome of COVID-19 infection in African Americans is due to unique susceptibilities, genetic or environmental factors, lack of access to current myeloma therapies, and/or access to intensive and supportive care, including antiviral therapy and ventilatory support for COVID-19 infection, remains unclear.

The adverse outcome of COVID-19 infection has been associated with comorbidities in most studies, including...
in patients with cancer and myeloma; however, the types of comorbidities have been variable. For example, in the
European cancer cohort study, COVID-19 with cognitive impairment and chronic kidney disease was associated
with higher mortality rates (2). The CCC19 study found that individual comorbidities were not statistically signifi-
cant (8), but that the Charlson Score representing general performance status and other comorbidities was correlated
with increased COVID-19-attributable deaths, ranging from 3.1% in patients with Charlson score 0 to 15.0% in
patients with Charlson score ≥5 (P < 0.001; ref. 6). A Spanish cohort study found that at least one comorbidity was
associated with COVID-19 infection in 75% patients with myeloma, as well as in 77% age- and sex-matched noncan-
cer patients (9). In the IMS cohort, multivariate analysis identified renal disease as an independent predictor of
adverse outcome (4). In contrast to these studies, comorbi-
dities including hypertension and diabetes in patients
with myeloma were not associated with adverse outcome of
COVID-19 infection in the NYC cohort.

The impact of cancer treatment in patients with COVID-
19 is variable depending on both type of cancer and therapy
being administered, including its impact on immune and
inflammatory response. For example, within the VA cohort,
provision of chemotherapy, targeted therapy, and immu-
notherapy as well as cancer therapy within 6 months of
the COVID-19 infection was not associated with increased
mortality (6). Similarly, the European cancer cohort con-
firmed that the type of systemic anticancer therapy was
not associated with COVID-19 severity, and, in fact, active
anticancer therapy at the time of COVID-19 was associ-
ated with lower risk of complicated disease (2). Several
reports of myeloma and COVID-19 infection highlight the
importance of not compromising the use of novel therapies
for myeloma, including high-dose therapy and autologous
stem cell transplantation, due to COVID-19 infection. For
example, high-dose therapy and stem cell transplant within
1 year of COVID-19 infection did not portend adverse
patient outcome in the NYC cohort or the IMS cohort.
Most importantly, several reports highlight the need to
achieve disease control in myeloma and not to compromise
primary therapy due to COVID-19 infection. For example,
suboptimal myeloma disease control was associated with
adverse outcome in the IMS report (4). Access to intensive
care unit and ventilatory support varies in the reports of
patients with myeloma with COVID-19 infection and clearly
impacts outcome.

Within patients with myeloma infected with COVID-19,
does immune status impact outcome? Defects in adaptive
and innate immunity, including both cellular and immune
responses, are a hallmark of myeloma. Patients with mye-
IgG <650 mg/dL
5. In the IMS cohort, a higher susceptibility to COVID-19
infection in 75% patients with myeloma in 2019 to 2020 compared with 22% patients overall
diagnosed with myeloma in this timeframe, per Surveillance, Epidemiology, and End Results data (4). It is interesting
to speculate that preserved immune competence in patients
with myeloma allows for the development of cytokine storm
and pulmonary toxicity/acute respiratory distress syndrome
and poor outcome.

This experience is based on “real-world” evidence rather
than prospective clinical observational trials. Nonetheless,
the aggregate experience to date suggests that patients
with myeloma are likely more susceptible to COVID-19 infection
and can have adverse outcomes, even in those on first-line
treatment or not requiring therapy. This highlights the need
for heightened precautions including handwashing, wearing
a mask, social distancing, and avoiding viral exposure in all
patients with these plasma cell disorders and their fami-
lies. Importantly, the emerging data suggest that myeloma
therapy can be safely administered in patients with COVID-
19 infection, and that myeloma disease control portends
improved outcome of COVID-19 infection.

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