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Older patients with cancer and febrile neutropenia in the COVID-19 era: A new concern

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Dear Editor,

The correct management of myelosuppressive drugs for older patients with cancer is crucial since the development of febrile neutropenia is a dangerous complication [1]. The main guidelines about this topic consider advanced age as an important risk factor to develop severe complications related to febrile neutropenia. For this reason, they suggest considering the use of granulocyte colony-stimulating factor (G-CSF) to older patients (usually >65 years), even under treatment <20% of the risk of myelosuppression [2].

The therapeutic role of G-CSF in neutropenic cancer patients with fever is controversial, and the results from different data are mixed. Indeed, the administration of G-CSF in cancer patients under febrile neutropenia does not seem to influence mortality. However, it shows a reduction in hospitalization time and a faster recovery of neutrophils count [3]. Both of these factors could be important for older patients because a prolonged neutropenic status and hospitalization could compromise the outcome. In this background, the clinicians, based on the clinical situation, use to consider the administration of G-CSF in older patients with cancer affected by febrile neutropenia.

Nevertheless, the care of older populations with cancer could be compromised by a new infection, provided by a new type of virus and named coronavirus disease 2019 (COVID-19). The mechanism of action of this virus is not clearly understood and it is still under investigation. The central hypothesis is the association among virus replication, over-response of the immune system, and hypercoagulability state, compromising the respiratory function and, in some cases, leading to death [4].

Although this infection could affect individuals of any age, it predominantly occurs in adults and persons with comorbidities, and in particular older adults are more likely to develop severe disease. Recent studies identified older age as a risk factor for high mortality in patients affected by COVID-19 [5,6].

Febrile neutropenia in this setting could represent a harder challenge for the oncologists. Although most of the time, cancer treatments

are suspended under COVID-19, find a cancer patient positive for the infection and under febrile neutropenia could complicate the choice of the best treatment.

A recent case-series, indeed, suggests that the administration of G-CSF for febrile neutropenia in cancer patients affected by COVID-19 could induce respiratory complications and a worsening of the infection course [7]. The reason is not clear, but one hypothesis is that the G-CSF could worsen the over-response by the immune system. Whang H et al., demonstrates that, during bacterial or viral pneumonia, the number of the granulocyte colony-stimulating factor receptors (G-CSFr) increase, because it is involved in the pathogen clearance. Moreover, binding the G-CSFr with a monoclonal antibody, neutrophils count, the protein levels in the bronchoalveolar lavage (BAL), and fluid (a marker of edema) are significantly reduced, decreasing the inflammation, without affecting pathogen clearance [8]. Therefore, a correlation between the administration of G-CSF and a worsening of pneumonia could be more than just a suggestion.

This kind of event could be fatal in this setting, and if true, especially for the older patients, it could change the actual recommendations about the administration of G-CSF as a therapeutic intent.

To avoid the COVID-19 related complications in these patients, testing for COVID-19 all cancer patients with febrile neutropenia, before the G-CSF administration, could be an option. To know the status of every single patient in this scenario could make the difference, considering that, in the experience mentioned above, the outcome was fatal. This is particularly important for the frailer cancer patients, in particular the oldest old.

Starting to think about a potential solution and collect more data about this issue is becoming crucial, as presently COVID-19 is a pandemic likely to last for a while.

Declaration of Competing Interest

The authors declare that there is not conflict of interest.

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