Editorial Commentary

Multidisciplinary approach for rare thoracic tumors during COVID-19 pandemic

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic started in March 2020 (1) and since then it has dramatically changed the diagnostic and therapeutic management of many chronic diseases, including cancer. During the first lockdown, overwhelmed healthcare systems could not guarantee regular access to early cancer diagnosis screening campaigns, as well as to clinical and radiological follow-up of cancer patients, causing a potential diagnostic and therapeutic delay (2), whose effects have been seen in the short-term and may continue to be seen for the next few years. However, life-saving cancer therapies were among the few health services guaranteed, even during the hardest phase of pandemic, as they have been made accessible by implementing effective triage procedures (3).

In this commentary, we describe the peculiar clinical features of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in patients with rare thoracic tumors, including thymic epithelial tumors (TET) and mediastinal germ cell tumors, and focus on the importance of multidisciplinary clinical management of these diseases.

Multidisciplinary treatment for patients with thymic epithelial and mediastinal germ cell tumors and concomitant SARS-Cov-2 infection

The SARS-Cov-2 infection can influence diagnostic and therapeutic choices in cancer patients, which are mostly related to the organs involved by primary/metastatic disease and the specific toxicity expected with administration of anti-cancer treatments. For patients with rare thoracic tumors, the management of COVID-19 and its short- and long-term complications can be particularly challenging.

Mediastinal primary tumors are rare cancers, usually diagnosed in patients between 30 and 50 years old, although they can occur at any age and from any tissue present in the mediastinum. Mediastinal tumor mass can be often asymptomatic for long term; thus incidental diagnosis can frequently occur. In the course of the current pandemic, mediastinal masses were often accidentally identified during evaluation of lung involvement by COVID-19 through imaging methods. This may also generate difficulties in differential diagnosis, as modest dimensional increase of the thymic gland may be due to post-infection hyperplasia (4). In these cases, 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scan showing low tracer uptake can be useful in supporting the diagnostic hypothesis of thymic hyperplasia (5). Mass size may also be indicative, as a reduction in mediastinal masses identified by short-term computed tomography (CT) scan may be another differential criterion between thymic hyperplasia and TET (6).

When patients suffering from mediastinal tumors, who have already been diagnosed and are undergoing treatment, contract SARS-Cov-2 infection, the treatment

of COVID-19 becomes a priority over the anti-tumor treatment. This may lead to interruption or delay of cancer therapies. A survey was conducted among oncologists working at international expertise centers, with the aim of optimizing the management of germ cell tumors during the pandemic and identifying different approaches based on experience of each individual country. This study concluded that chemotherapy should be withheld until the acute phase of COVID-19 has resolved or there are no more respiratory symptoms (7). However, most treatments in oncology cannot be safely postponed for long time, particularly when complete recovery is achievable and delay of treatment can jeopardize its efficacy, such as in the case of germ cell tumors, or when the patient is at immediate risk, due to life-threatening disease. This can happen in patients with large mediastinal masses and severe impairment of cardio-respiratory function. In these cases, it may be reasonable to hold the antineoplastic treatment just until the patient overcomes the acute infectious disease phase and then to proceed with the planned treatment, even with a positive molecular swab (8). In support of this approach, a meta-analysis showed that no viable virus could be isolated from culture beyond day 9 of illness, despite the presence of persistently high viral RNA loads (9). In our opinion, decision-making concerning anticancer treatment (i.e., chemotherapy) and procedures (surgery, radiotherapy) must be closely evaluated against the risks linked to cancer progression and should be evaluated case by case, especially if the interrupted anti-cancer treatments are potentially curative. In addition, the American Society of Clinical Oncology (ASCO) guidelines suggest that specific areas and dedicated personnel should be designated for the treatment of COVID-19 patients and treatment restarted at an isolated infusion center, away from the main infusion center (10).

Regarding the type of treatment of germ cell tumors, the classical schedule including bleomycin, etoposide and cisplatin (BEP) remains a valid option since the omission of bleomycin, due to the risk of respiratory failure and pneumonitis, has no clear indication (7). There are not enough data about the use of immune checkpoint inhibitors (ICIs) during pandemic but this treatment does not appear to be an additional risk factor for severe COVID-19 in patients with cancer (11,12). Moreover, a multicenter observational study showed that the administration of anti-cancer treatment, including chemotherapy, ICIs, and tyrosine kinase inhibitors (TKIs) did not affect survival in patients with COVID-19 (13).

According to our experience, another issue of critical importance in patients with mediastinal tumor and SARS-Cov-2 infection is defining the optimal management of respiratory and cardiovascular symptoms. Mediastinal tumors can cause serious respiratory and cardiovascular complications, due to tumor invasion of the lung, pleura, heart, pericardium and large vessels, with an increased risk of thrombosis or bleeding, to atelectasis due to compressive effect, and to reduced respiratory function due to previous surgery. Moreover, during the first phase of the pandemic a meta-analysis showed that cancer patients are at a higher risk of thromboembolic events and associated complications, such as lung vessel obstructive thrombo-inflammatory syndrome (14). Therefore, cancer patients with SARS-Cov-2 symptomatic infection may need a personalized clinical management, overseen by a multidisciplinary clinical team. This includes close monitoring and re-evaluation of oxygen therapy, with or without high flow and continuous positive airway pressure (CPAP) (15). In addition, anticoagulant thromboprophylaxis with low-molecular-weight heparin (LMWH) or fondaparinux may be recommended (16), but it needs to be carefully evaluated in patients at high risk of bleeding. Further, the management of patients with risk factors for severe COVID-19 (including chronic lung disease, heart failure and active anticancer therapy) changed since the approval of monoclonal antibodies anti SARS-Cov-2 for the treatment of mild cases (17). However, to date, there are no published reports focusing on the use of monoclonal antibodies in patients with rare cancers.

Finally, as vaccine availability has dramatically changed the epidemiology of SARS CoV-2 infection in general population, vaccination is strongly recommended also in cancer patients, according to the European Society of Medical Oncology (ESMO) statements, since it has been shown to be safe and effective in this frail population. For the same reasons, vaccine booster dose should always be considered in cancer patients (18).

Concluding remarks and future prospective

In the current pandemic scenario, cancer-related information like staging, grading, setting of therapy, comorbidities, type of cancer therapy, type of treatment for SARS-Cov-2 infection should be evaluated by a multidisciplinary working team as a key strategy for the management of rare thoracic tumors.

Future research should focus on collecting all the basic characteristics of rare cancer patients with COVID-19,

tumor biology, chemotherapy/radiation-related variables, and the biochemical and inflammatory profile of these patients during infection.

Finally, the limitations in patient hospitalization and access to high expertise centers imposed by COVID-19 pandemic demand the implementation of novel approaches of care, such as telehealth and digital health in oncology. Cross-border teleconsultations by individual healthcare providers within expert tumor networks could be an excellent tool to improve medical education and ultimately clinical outcome of patients with rare tumors during COVID-19 era (19).

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