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Letter to the editor

Managing locally advanced adenoid cystic carcinoma of the head and neck during the COVID-19 pandemic crisis: Is this the right time for particle therapy?



The rapid worldwide spread of coronavirus disease 2019 (COVID-19) has forced radical changes in everyday life resulting in a massive health, social, and economic global crisis. A strong need for deep revision of clinical practice and health system organization, both in terms of human and structural resources, is therefore emerging [1]. Many hospital accesses and activities have been reduced or re-prioritized, and an unprecedented number of surgical interventions cancelled or deferred, potentially leading to adverse effects for un- or subtreated patients as a ramification of the pandemic [2].

Oncological patients need active and non-deferrable treatments, in order to avoid reduction of their survival probability. Moreover, since they are more susceptible to pathogens [3], it is mandatory to minimize the risk of cross-infection and reduce the time spent in hospitals.

In this scenario, head and neck cancer (HNC) poses unique challenges in many respects. Patients are frequently frail, and at risk for treatment-related complications. In addition, some COVID-19 signs or symptoms can potentially mimic treatment-related toxicity or tumor recurrence. Furthermore, increasing evidence has emerged that otolaryngologists and head and neck surgeons are at high risk of infection during diagnostic and therapeutic procedures [4]. Certain HNCs (oral cavity cancer, advanced laryngeal cancer, salivary gland carcinoma) are typically managed by surgeons, and there is almost complete lack of level I evidence supporting the use of alternative radiation-based protocols [5]. HNC management requires a highly specialized (web-based) multidisciplinary team aimed to evaluate surgical risks and alternative therapeutic options, balancing the risks related to HNC progression and COVID-19 infection and/or complications [6].

Radiotherapy (RT) plays an essential role in management of HNCs, both in radical and postoperative settings. Therefore, RT departments have to continue their activity, although re-organized, to face the pandemic challenge. Recently, the American Society of Radiation Oncology and the European Society for Radiotherapy and Oncology published recommendations for treatment of HNC, suggesting radical and postoperative RT for involved margins with higher priority compared to adjuvant RT for minor risk factors. Moreover, use of more hypofractionated RT schedules is encouraged (applying concomitant chemotherapy only with conventional or mildly hypofractionated RT of ≤ 2.4 Gy/fraction) [7,8]. Although these recommendations referred specifically to squamous cell carcinoma of the upper aerodigestive tract, it is our opinion that they should be extended even to rare HNC, including adenoid cystic carcinoma (ACC).

ACC represents approximately 10% of all salivary gland tumors, and 1% of HNC [9], with an annual incidence of 3–4.5 cases per million people. The gold standard treatment is surgery followed by postoperative RT in presence of risk factors e.g. advanced tumor stages, positive or close surgical margins, perineural, lymphovascular, and bone invasion [10,11].

ACC represents a major challenge for radiation oncologists, not only

for its well-known radio-resistance requiring high RT-doses, but also given the frequently horseshoe-shaped target volume and proximity to highly radiosensitive structures of the head and neck (HN). Indeed, locally advanced diseases, in particular when developing in minor salivary glands of paranasal sinuses, can infiltrate the skull base, either directly or via perineural spread. In these cases, radical resection is extremely challenging, often requiring multi-specialty ablative and reconstructive approach, potentially prolonging surgical time and causing high patient morbidity. Generally, a tumor deemed non-resectable is treated with definitive RT [12].

In this regard, high-linear energy transfer carbon ions radiotherapy (CIRT) has recently entered the clinical practice. Particle therapy (PT) enables dose-escalation due to specific ions physical properties (allowing highly conformal dose distributions) and offers superior relative biological effectiveness by at least a 2–3-fold factor in comparison to photons.

There is some evidence that ACC may benefit from CIRT in terms of local control (LC), overall survival (OS) and safety, even in R2, inoperable cases or recurrences [13–24].

The largest experience in salivary gland tumours management by CIRT is from Japan with treatment delivered with hypofractionated protocols of 16 fractions over 4 weeks [14]. A subanalysis of the clinical results of 289 unresectable or R2 ACC patients treated in the 4 CIRT Japanese facilities from 2003 to 2014 has been recently published, showing a 2- and 5-year LC rates of 88% and 68%, and a 2- and 5-year OS of 94% and 74%, respectively, and a tolerable toxicity profile [19]. Although data are very promising, longer follow-up is needed.

At the National Center for Oncological Hadrontherapy (CNAO) in Italy, exclusive CIRT is administered with the same hypofractionated schedule used in Japan. Our preliminary data about unresectable and R2 ACC patients (2-year LC and OS rates of 81% and 85%, respectively) are encouraging [25]. Promising findings have been also confirmed by the Heidelberg Ion-Beam Therapy Center (HIT) in Germany, exploring the combination of Intensity Modulated RT and dose escalated carbon ion boost [22]. Interestingly, a recent study on 227 sinonasal ACC patients showed no significant difference in LC for patients treated postoperatively (R2 in 63% of cases) or definitively after biopsy only (3 year LC rates of 82% and 79%, respectively), with a more favourable late toxicity profile in the latter [23].

Radical CIRT might be proposed as upfront strategy in the majority of cases of inoperable or operable but locally advanced ACC, deemed to be at risk of R2 after surgery. This approach could potentially avoid long term hospitalization often required after extensive surgery. Furthermore, the hypofractionated CIRT schedule might help in reducing hospital accesses compared to conventional RT [26], minimizing travelling and risks related to SARS-COV-2 exposure both for patients and hospital staff.

European facilities are few and only a limited number of patients

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might possibly be considered for CIRT. ACC is a rare disease that might benefit from this particular treatment and therefore patients selection must be aimed to guarantee adequate access to treatment, especially in the new pandemic scenario requiring health resources re-organization and optimization. CNAO has been so far in full operation ensuring treatment with both protons and carbon ions beams since the begin of Covid outbreak in late February 2020.

We felt useful to remind to the oncological HN community about this option of cure that besides having promising evidence in literature, meets the temporary and the future medical needs of our patients.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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