An “Older Old” Woman with Large Squamous Cell Carcinoma of the Nasal Pyramid: Excellent Response to Ultra-Hypofractionated Radiation Therapy

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Simple Summary: We present a case study of a very elderly patient with locally advanced skin cancer within the head and neck region for whom surgical intervention was excluded. The patient was treated with a tailored exclusive radiotherapy approach, with a favourable clinical outcome. The case presentation is followed by a concise review of the literature on hypofractionated radiation therapy in the elderly.

Abstract: A 98-year-old patient with cognitive impairment and a history of squamous cell carcinoma of the nasal pyramid was referred to the radiation oncology department of our institution’s hospital given that surgery was not recommended. The lesion was sized 6 × 6 cm, ulcerated, and bleeding; was significantly impairing the patient’s health-related quality of life, causing pain; and was not responsive to analgesics, including opioids. The patient experienced deterioration of her general conditions, with a Karnofsky performance status of 40. A single radiotherapy (RT) fraction was delivered on a weekly basis for 3 weeks, up to a total dose of 21 Gy, using a VMAT technique (7 Gy/fraction). The patient was given three fractions of radiotherapy, during which she received continuous assistance due to episodes of mental disorientation and an altered sense of consciousness. One month after the conclusion of the treatment, the patient exhibited a nearly complete clinical response, with full pain relief and an improved health-related quality of life. This favourable clinical outcome was maintained for a period of four months following the conclusion of RT. A brief review was performed on the role of hypofractionated radiation therapy in elderly patients with locally advanced skin cancer of the head and neck region.

Keywords: elderly; hypofractionation; radiotherapy; head and neck squamous cell carcinoma

1. Introduction

Cutaneous squamous cell carcinoma (cSCC) malignancies of the head and neck region predominantly affect the geriatric population [1,2].

It is widely acknowledged that the traditional clinical oncological guidelines may not always be applicable in the case of elderly patients.

Therefore, clinicians need to consider several factors when determining the most appropriate treatment strategy for these patients. In fact, it is evident that elderly patients must be considered in their entirety [3]. In order to classify older patients with cancer into
homogeneous patient groups, the subcategories “younger old” (65–70 years) and “older old” (>80 years) have been introduced [4].

The optimal treatment choice should consider different factors, including not only a patient’s general clinical condition, usual medications, and neuro-cognitive abilities but also the support given by family members, the presence of a caregiver, the possibility of transporting the patient from home to a radiation facility, and the need for hospitalisation [5].

The case of a 98-year-old patient presenting with cutaneous squamous cell carcinoma of the head and neck is discussed with a brief report on the modalities of radiation therapy in “older old” patients.

2. Presentation of the Case

The patient underwent surgical excision of a basal cell neoplasm located within her nasal pyramid in 2016 when she was aged 91 without further postoperative treatments due to her advanced age and frailty. The patient had been experiencing a progressive cognitive decline for approximately five years.

In the summer of 2023, the lesion locally relapsed and exhibited accelerated growth, accompanied by clinical symptoms.

At the beginning of 2024, the lesion was sized 6 × 6 cm, ulcerated, bleeding, impaired her health-related quality of life due to pain, and was not responsive to non-steroidal anti-inflammatory drugs, which were initially used, nor to subsequent opioids. We used the Control, Autonomy, Self-Realization, and Pleasure scale with 12 items (CASP-12) to assess her health-related quality of life (initial CASP-12 score: 4/12) [6,7]. Poor pain management and subsequently limitations in simple activities were the main reasons for this score. The patient initially reported a pain intensity of 8/10 according to the NRS. This pain was initially managed with 2–3 g of paracetamol per day. Successively, combinations with opioids were employed.

Furthermore, the patient’s age and risk of deterioration in neurological status represented significant challenges for pain therapists in the effective management of the condition.

The lesion rapidly extended to the inner canthus of the left eye, resulting in inability for her to lift her eyelid (Figure 1).

![Figure 1. Photographs of the patient’s lesion in lateral and frontal views on the day of the first ENT visit.](image-url)

A biopsy was then performed, and the patient was diagnosed with Grade 3 squamous cell carcinoma, according to the WHO classification. A computed tomography (CT) scan of her head and neck region was then acquired for disease assessment and staging. No suspicious adenopathies or metastatic lesions were observed. The case was discussed at the multidisciplinary tumour board, and it was decided that surgical treatment was not appropriate for the patient given her age, clinical condition, and the extent of the tumour. Upon initial examination, the patient showed general deterioration, with a performance status according to the Karnofsky scale of 40 and an Eastern Cooperative Oncology Group (ECOG) performance status of 3 (indicating the requirement for continuous care, provided by family members, and the need for bed rest for more than 12 h per day), in addition to significant facial pain. Furthermore, the
The patient required daily regular medication. In fact, the lesion was ulcerated and prone to bleeding. The presence of poorly controlled pain (NRS score of 8-9/10) was associated with sleep–wake changes, periods of aggressive behaviour, and a progressive deterioration in cognitive function. The patient was frail when assessed with the G8 score [8]. The frailty score was evaluated in conjunction with an onco-geriatrician, who also conducted a comprehensive geriatric assessment and identified the most appropriate pharmacological intervention to balance opioids and non-steroidal drugs.

The multidisciplinary team, including a dedicated medical oncologist, considered the patient unsuitable for chemotherapy due to her age. New systemic agents such as anti-PD-1 or anti-PD-L1 therapy (e.g., cemiplimab) were excluded. In fact, considering her clinical presentation, exclusive radiation therapy with palliative intent was able to be offered to the patient, avoiding the use of chemotherapy or immunotherapy.

A simulation CT scan was performed with a customised thermoplastic mask (Figure 2). Based on a 3D treatment plan, a single RT fraction was delivered each week, with each fraction comprising a dose of 7 Gy up to a total dose of 21 Gy. RT was delivered via the VMAT technique and 6 MV photons (Figure 3).

![CT simulation with personalised thermoplastic mask.](image)

**Figure 2.** CT simulation with personalised thermoplastic mask.

![VMAT treatment plan in axial and sagittal planes.](image)

**Figure 3.** VMAT treatment plan in axial and sagittal planes.

The patient provided written informed consent.

The patient underwent three sessions of RT, during which she received continuous assistance.

Prior to and following each RT session, the patient was administered medication by nursing staff. Additionally, the patient continued to receive ongoing medical therapy for pain management throughout the course of the treatment.

No acute toxicity was reported.

Two months after the completion of the treatment, the patient presented with a nearly complete clinical response (Figure 4).
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Two months after the completion of the treatment, the patient presented with a nearly complete clinical response (Figure 4).

During her most recent clinical consultation, the patient indicated that the intensity of her pain was 2/10 on the Numeric Rating Scale (NRS), with the administration of oral paracetamol (1 g/day).

Since treatment, the patient has gradually reduced her required dosage of analgesic medication. Currently, four months after the end of treatment, she occasionally receives 1 g of paracetamol in the evening before bedtime. The health-related quality of life of the patient (last reported CASP-12 score of 7/12) and the overall functioning of her family has improved. In accordance with her CASP-12 score, there has been a notable improvement in the subjective perception of her age and an enhancement in her social and domestic functioning.

At the present time, there has been a maintained clinical response for 124 days without late toxicity.

3. Discussion

The conventional therapeutic approach to cSCC of the head and neck is surgical excision, followed by adjuvant therapy when indicated.

The elderly are more likely to present with additional medical conditions with a higher perioperative risk. Sometimes, more extensive surgery is needed, such as neck dissection, parotidectomy, lateral temporal bone resection, or major free tissue transfer reconstruction. Elderly patients have a higher chance of developing postoperative complications and more wound-healing disorders [2]. While advanced age is not an absolute contraindication for these surgical procedures, the perioperative risks associated with many comorbidities present in the geriatric population have encouraged the investigation of alternative treatment modalities [9,10]. In this clinical context, RT may be considered a primary treatment option for high-risk cSCC. To date, no prospective randomised trials have been conducted.
to compare the efficacy of RT in terms of local tumour control and patient survival compared to other treatments. Of note, a mean local recurrence rate of 6.4% was reported in a meta-analysis that included 14 observational studies and comprised a total of 1,018 cases of cSCC. [11]. RT is less likely to be recommended in younger patients (below 60 years of age) due to the increased likelihood of potential late toxicity [12]. In fact, the side effects of RT should be considered, and depending on the location of the primary tumour, they may include vision loss, dysphagia (leading to dehydration and malnutrition), skin ulceration, and pain. In addition, conventionally fractionated RT takes place most days of the week for several weeks, and transportation/logistics can be difficult for many frail geriatric patients. The advent of new RT techniques (IMRT and VMAT) has resulted in the sparing of organs at risk, thereby improving patient tolerability and facilitating the management of side effects [13]. Consequently, in elderly patients, RT could be considered a suitable option. To mitigate the negative impact on health-related quality of life, hypofractionated regimens may be employed, which facilitate better patient compliance with treatment.

All the therapeutic options should be reviewed by a multidisciplinary tumour board to determine the extent and combination of surgery, RT, and systemic therapy [14], if indicated, in each single case.

In our patient, surgery was immediately ruled out due to her general condition. It is also important to note that the patient is an “almost centenarian”.

As we previously indicated, medical oncologists did not recommend systemic treatment or the more recent anti-PD-1 or anti-PD-L1 therapies (e.g., cemiplimab).

A randomised trial published in 2020 demonstrated the efficacy of cemiplimab in patients with locally advanced cSCC. This study included a cohort of 78 patients up to the age of 81 years. Despite the partial or complete local control achieved in 79% of patients, Grade 3–4 treatment-related adverse events occurred in 44% of patients. The median follow-up was very limited in this trial (9.3 months). The most common side effects were hypertension in 8% patients and pneumonia in 5%. Serious treatment-related adverse events were observed in 29% of patients. One case of treatment-related mortality was documented, occurring after the onset of aspiration pneumonia [15].

Given the highlighted side effects and the paucity of studies on “very elderly” patients, a recent position paper has also underlined that cemiplimab can be employed in cases in which surgical and/or RT treatment is not viable or recommended [16]. It is also noteworthy that cemiplimab is available for prescription and reimbursement in Italy for the treatment of adult patients with metastatic or locally advanced cSCC who are not candidates for curative surgery or curative radiotherapy.

In our evaluation, we identified a very elderly female patient who could be offered radiotherapy. In accordance with the standard practice for geriatric patients, the G8 score was employed to assess the patient’s frailty [8]. We evaluated the patient’s limited mobility, the significant pain she experienced, and her inability to maintain a supine treatment position for prolonged periods. In light of the patient’s elevated risk of neurocognitive decline and the counsel of neurologists and onco-geriatricians, it was recommended the duration of her hospitalisation to be shortened. A short course of RT was deemed a safer and more prudent option.

In accordance with the ASTRO guidelines [17], the fractionation of choice in cases of cSCC in a definitive setting is conventional (1.8–2.0 Gy/fx), with a BED10 of 70–93.5. Alternatively, hypofractionation (2.1–5.0 Gy/fx), with a BED10 of 56–88, may be employed. Conventional fractionation is delivered over five days per week, whereas hypofractionation is delivered on a daily basis or two to four times per week. The decision regarding the most appropriate modality and fractionation scheme should be based on both the characteristics of the tumour (e.g., its shape, contour, depth, and location) and considerations regarding normal tissue (proximity to critical structures). A comprehensive examination of the relevant literature indicates that the use of any of the four principal radiation modalities (electrons, brachytherapy, and low-energy and high-energy photons) results in comparable local control and cosmetic outcomes [18–24].
Some case reports have been presented to the scientific community about elderly and hypofractionated RT with electrons or brachytherapy. For example, de Felice presented a case in which electrons and weekly fractionation (8 Gy in a single fraction per week over eight weeks) resulted in an excellent clinical response [25]. Roberson published a paper on the utilisation of brachytherapy with Ir-192 in the treatment of skin lesions, predominantly located in the head and neck regions. Similarly, the results were satisfactory [26]. It is acknowledged that these case reports provide insight but do not offer definitive guidelines for elderly patients.

High-energy therapy with photons is often used to treat more deeply invasive or larger cSCC such as T3/T4 lesions, which typically have a thickness >3 cm, have potential bone and/or cartilage involvement, or are adjacent to critical structures, for which advanced RT techniques would be indicated [27]. It is important to exercise caution when treating periocular and perioral skin with hypofractionated regimens [17]. Compared with standard fractionation, hypofractionation can lead to more late toxicities, skin atrophy, and fibrosis. This may potentially compromise its otherwise optimal functional outcomes. Several other fractionations can be used with the objective of adapting RT treatment to the specific needs of the patient, considering age and other factors. To date, no randomised study has been conducted to define the optimal treatment schedule.

In patients aged 80–90 years or older, a reduction in the overall treatment duration may be beneficial. In cases where their life expectancy is short and the primary objective is to improve their health-related quality of life, the treatment courses should be shortened. Patients in this phase of life often experience discomfort with transportation and prefer to spend more time at home with loved ones. In these cases, the potential for an increased risk of long-term side effects associated with larger doses per fraction related to late-responding tissues is of lesser consequence. Furthermore, a lower biological equivalent dose of these shorter courses can be employed to further minimise the risk of late side effects [28,29].

Hypofractionation can be proposed as a treatment option for various cancer types, including those affecting the head and neck region. This anatomical region has always been considered a particularly critical site due to the presence of numerous organs at risk [28,30–33]. In all cases, the objective of hypofractionation is to control symptoms, although a favourable clinical response has consistently been observed [34,35].

In cSCC, hypofractionation can be achieved by administering daily RT fractions of 3–4 Gy over a period of 2–3 weeks (40–45 Gy in 10–15 fractions). In elderly patients (>80 years old), a less frequent treatment schedule (1 to 3 times per week) and larger fraction sizes are recommended. These may include 5–7 Gy in 5 to 6 fractions [18,36–39]. In a single series, Chan used a single-session RT treatment with doses of 18–22.5 Gy, which yielded satisfactory outcomes with regard to local control [19]. Nguyen et al. reported a weekly hypofractionation scheme, providing a proof of principle for targeted clinical use. A dose of 8 Gy was delivered on days 0, 7, and 21 [40]. This study served as a reference point for our clinical case. A dose of 7 Gy was selected in lieu of an 8 Gy dose, as the 3D surface and air–tissue interface rendered the dose variability high and overdose a potential risk. Given the tumour’s proximity to the inner eye canthus, conservative fractionation was employed. In the case of our patient, it is important to note that our primary objective was not to achieve a complete response to the disease through RT. Instead, the aim was to mitigate her pain and limit the growth of the tumour towards noble organs such as the eye.

The case study by de Felice [41] is nonetheless interesting. Patients aged over 75, ineligible for surgical intervention but with ECOG scores of 0 or 2, were included in this analysis. This study aimed to investigate the potential role of definitive weekly hypofractionated RT as a curative treatment for older adults with cSCC who are unfit for surgery. A total of 19 older adults with 27 cases of cSCC were included in the study. The patients received definitive weekly hypofractionated RT using electrons. The prescribed dose was 56 Gy in 7 weekly fractions of 8 Gy or 64 Gy in 8 weekly fractions of 8 Gy. No supplemental external beam radiation was allowed. A completed response was observed.
in 70.4% of cases, with a median time to response of 1.1 months. In all cases, bleeding was resolved, and pain was relieved.

Compared to de Felice’s article [41], our patient presented with an ECOG score of 3, indicating greater fragility and complexity of management. However, thanks to the integration and teamwork with nurses and radiation technicians, it was possible to treat the patient with good results. It is acknowledged that the lack of a long-term follow-up represents a limitation of our case study. However, the initial objective was to achieve local control, control of bleeding, and improvement in the patient’s family’s management. These results have been successfully identified, and it is hoped that local control can also be maintained on a long-term basis. The case we presented is particularly notable due to the patient’s extreme fragility, as evidenced by her ECOG score. Similar cases are often treated with a single session of haemostatic therapy or left to receive only supportive care. This case demonstrates that fractionated treatment can be proposed even for these patients, with the option of modifying the treatment plan in accordance with the patient’s and their family’s wishes. The treatment was well tolerated and produced results that exceeded the conventional expectations of palliative care.

A recent systematic review [29] highlighted that hypofractionation does not have a negative impact on acute and late toxicities, even in elderly patients. It is important to note, however, that this review, like the majority of the existing literature in this field, focuses on elderly patients aged 80 and above.

A review of the literature reveals a paucity of studies examining the utilisation of hadrotherapy in the treatment of cSCC [25]. Proton therapy represents a promising avenue for the management of patients with non-melanoma skin cancer, particularly in cases where clinical perineural invasion is present. The utilisation of proton therapy may mitigate the risk of complications in the eye, the cochlea, and proximate brain structures, which frequently receive radiation doses greater than their tolerance threshold. It is important to note that there are a limited number of proton therapy facilities, and patients and their families frequently have to travel considerable distances to access them. Furthermore, the positioning techniques and extended treatment delivery durations may not be appropriate for elderly patients.

The findings of our study indicated that photon hypofractionated regimens do not necessitate hospitalisation and do not carry an increased risk of side effects. Furthermore, a cost–benefit analysis revealed that these regimens have a lower economic impact than more sophisticated therapies or new oncological drugs.

A notable limitation of this case study is the restricted follow-up period. It is acknowledged that the follow-up period is insufficient to provide definitive answers about disease control. Nevertheless, in a patient of 98 years of age, a gain of a few months represents a notable improvement. The objective of our study was to assess the feasibility and tolerability of this fractionation and the improvement in quality of life. This objective was met. It is hoped that the patient will continue to demonstrate a sustained response.

A further significant limitation is the absence of any comparison with similar cases in the literature. It is also noteworthy that the other studies published include participants with head and neck cancers aged over 90 years in their age range, yet no distinct analysis is presented for this age category [38,42].

To the best of our knowledge, this is the only case study in the literature on a 100-year-old patient with a low performance status. It would be beneficial to initiate multicenter comparisons for the treatment of similar patients. An exemplar of a multidisciplinary study is the one proposed by the International Geriatric Radiotherapy Group. Among other objectives, this study will assess the feasibility of radiotherapy treatment in combination with immunotherapy [43].

4. Conclusions

It is not uncommon for curative treatments, such as radiotherapy, to be deemed infeasible in elderly patients.
Our case report and the data from the literature show that in older patients with cSCC, a hypofractionated course of RT may be employed with a high degree of safety, resulting in favourable outcomes with minimal acute or late toxicities. This treatment option can be considered effective, safe, and tolerable. This weekly hypofractionated RT schedule also suggests its potential benefit in terms of health-related quality of life, both for patients and their families. Furthermore, the number of hospital admissions for frail patients is reduced. This case study illustrates the viability of suggesting this form of treatment as an additional option, with beneficial results and considerably favourable financial implications within the context of an analysis of cost-effectiveness. Given the growing demand for treatment in oncological and RT departments, it would be beneficial to define the most appropriate treatments for elderly patients, particularly those over the age of 90. This could be achieved through multicenter collaboration.

**Author Contributions:** Conceptualization, C.P. and P.F.; methodology, C.P.; resources, C.P.; data curation, C.P.; writing—original draft preparation, C.P. and P.F.; writing—review and editing, C.P. and P.F.; supervision, A.G., A.C., M.K. and P.F. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** This study was conducted in accordance with the Declaration of Helsinki. Ethical review and approval were waived for this study because this clinical case was conducted in accordance with the standard clinical procedures employed by our centre, in line with the international clinical guidelines.

**Informed Consent Statement:** The patient provided written consent to participate in the study and for us to publish this paper.

**Data Availability Statement:** The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding authors.

**Acknowledgments:** We thank the patient and her family who participated in the study.

**Conflicts of Interest:** The authors declare no conflicts of interest.

**Abbreviations**

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>RT</td>
<td>radiotherapy</td>
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<td>VMAT</td>
<td>volumetric modulated arc therapy</td>
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<td>cSCC</td>
<td>cutaneous squamous cell carcinoma</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>Gy</td>
<td>Gray</td>
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<td>CT</td>
<td>computed tomography</td>
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<td>ECOG</td>
<td>Eastern Cooperative Oncology Group</td>
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<td>CASP-12</td>
<td>Control, Autonomy, Self-Realization, and Pleasure scale, 12 items</td>
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<td>MV</td>
<td>mega voltage</td>
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<td>IMRT</td>
<td>intensity-modulated radiotherapy</td>
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<td>BED</td>
<td>biological equivalent dose</td>
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<td>ASTRO</td>
<td>American Society for Radiation Oncology</td>
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<td>3D</td>
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<td>NRS</td>
<td>Numeric Rating Scale</td>
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