

Therapeutic Radiosurgery Results In Late Solitary Metachronous Lung Metastases From Locally Advanced Laryngeal Carcinoma– A Case Report

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1. Abstract

The present article reports the case of 71 -year -old man with late solitary metachronous lung metastases from locally advanced squamous cell laryngeal carcinoma. A total laryngectomy with bilateral selective lymph node dissection, followed by Intensity modulated radiotherapy (IMRT) in the tumor bed with the bilaterally cervical lymph nodes was completed. Year and three months after the completion of postoperative IMRT, a solitary right lung metastasis, followed after another year by a metachronic solitary left lung metastasis was reported. We are pleased to present the therapeutic result after the Hypofractionated Stereotactic Radiosurgery (HFRS) and Radiosurgery (RS) with respect to the two solitary metachroneus pulmonary metastases. Thanks to the complex treatment, we have achieved a 3.5 year survival rate in a patient with a local advanced laryngeal carcinoma with subsequent late solitary metachroneus pulmonary metastases.

2. Intraduction

Laryngeal cancer is the second most common cancer of the upper aerodigestive tract [1]. The chemo-radiotherapy (Ch-RT) has become increasingly popular as a treatment modality for advanced laryngeal cancer [2,3]. New and optimized treatment methods increase locoregional progression-free survival (LPFS) and disease-free survival (DFS) in patients with advanced head and neck carcinomas and thereby overall survival (OS) in the short-term follow-up [4–7]. The published incidence of DM in a subgroup of patients with stage IV disease was even as high as 55% [8]. Laryngeal cancer commonly spreads via direct extension to adjacent

structures through metastasis to regional cervical lymph nodes. Distant metastases (DM), however, are not commonly observed in laryngeal malignancies [9,10]. The leading site for DM were the lungs, followed by the skeletal system [11,12]. We present a clinical case of a 71 -year -old man with a local advanced laryngeal carcinoma, in which, after a total laryngectomy and postoperative intensity modulated radiotherapy (IMRT), local tumor control (LTC) has been achieved, but after one year and three months, a solitary pulmonary metastasis, followed after another year by a metachronic solitary left lung metastasis was manifested.

3. Case Report

The 71 -year -old man presents in the otolaryngeal department on 18.02.2019 with changes in the voice dating back several years ago and ulceration of the skin above the larynx. Local status from the laryngoscopy - laryngeal tumor, infiltrating the left vestibular folds, ventricle, true vocal cord and descending subchordally and on the level of the glottis with an infiltration and carcinomatosis of the skin. Biopsy was performed with a histological result well differentiated squamous cell (G1) laryngeal carcinoma. No dissemination on the preoperative thoracic CT was found. Intraoperative local status on 07.03.2019 - After U-shaped incision of the neck by widening the incision in the area of the breakthrough process in the midline and excising the skin with carcinomatosis together with subcutaneous tissue and platysma, a total laryngectomy with bilateral selective lymph node dissection was completed. Histopathological result – Larynx - well differentiated G1 laryngeal squamous cell carcinoma, developed at the base of verrucous squamous cell

carcinoma; 10 left cervical lymph nodes from II,III,IV and V level without metastases; 5 right-cervical lymph nodes from IIA, IIB and III level without metastases. The laryngeal squamous cell carcinoma was staged pT4a pN0 M0. The oncology committee discussed that a postoperative radiation treatment was required, which we performed in the period April-May 2019. Intensity modulated radiotherapy (IMRT) by VMAT method in the laryngeal bed up to total dose (TD) 60 Gy in 30 fractions with daily dose (DD) 2 Gy, and in the bilaterally cervical lymph nodes, levels II-V – up to total dose 51.6 Gy with daily dose 1.72 Gy was carried out (Figure 1). On a follow-up PET-CT scan/ September 2019 no recurrence and metastasis was reported (Figure 2). One year and 3 months after the IMRT, a follow-up PET-CT scan / August 2020 a single right lung metabolically active lesion up to 11mm, SUVmax - 5,6

was found (Figure 3). In September 2020 using Hypofractionated Stereotactic Radiosurgery (HFRS) in 4 fractions with daily dose 12 Gy up to total dose 48Gy to the right lung metastasis was delivered. In October 2020 the patient completes one course of chemotherapy (Ch) with cisplatin and 5-FU. A year later/ August 2021, a control PET-CT reports another solitary left lung metastasis 9.3mm in size and SUV max – 3.6 (Figure 4). In September 2021 using Radiosurgery (RS) the left lung lesion with a single fraction 24 Gy was irradiated. On the follow-up PET-CT scan / January 2022, in the right lung HFRS zone low metabolic activity SUV max 2,7 and in the left lung RS zone pulmonary fibrosis SUV max 2.1 was found (Figure 5). The patient is currently with LTC, without pulmonary symptoms and good quality of life.

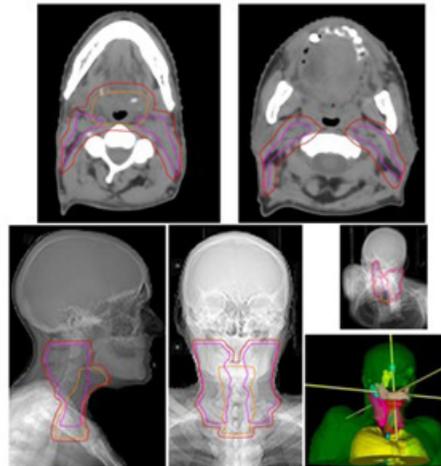


Figure 1. Intensity modulated radiotherapy (IMRT) by VMAT method in the laryngeal bed up to TD 60 Gy in 30 fractions with DD 2 Gy, and in the bilaterally cervical lymph nodes up to TD 51.6 Gy with DD 1.72 Gy.

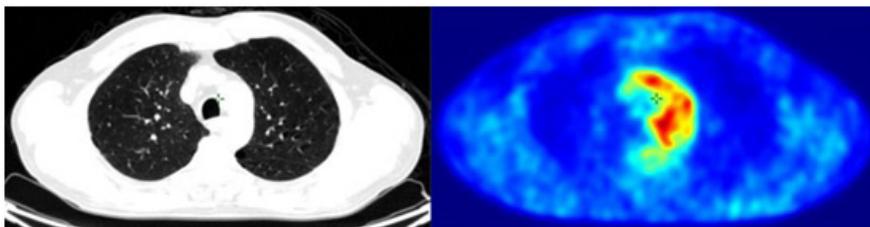


Figure 2: A follow-up PET-CT scan/ September 2019 without recurrences and metastases.

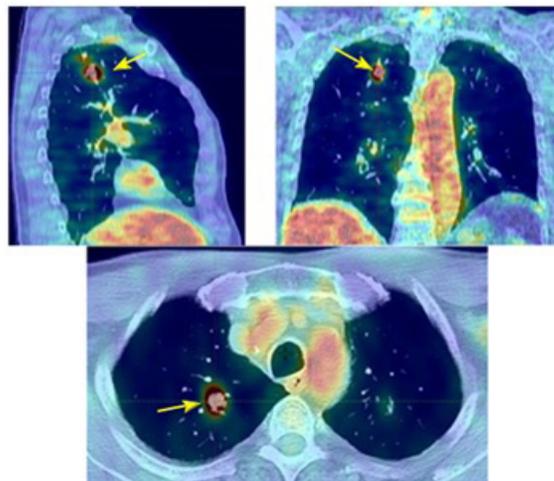


Figure 3: A follow-up PET-CT scan / August 2020 one year and 3 months after the IMRT - a single right lung metabolically active lesion up to 11mm, SUVmax - 5,6. The yellow arrow shows the single right lung metastasis.

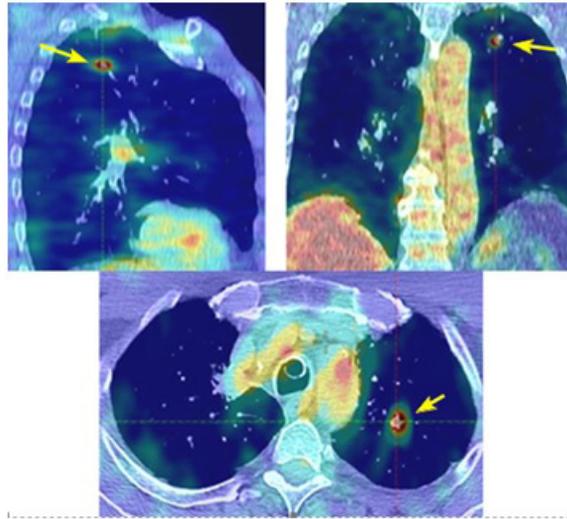
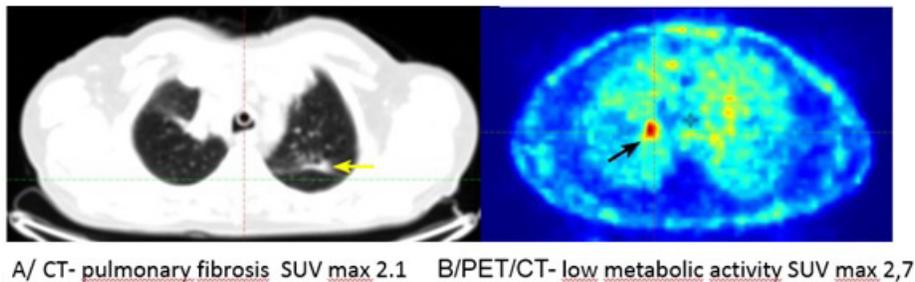


Figure 4. The follow -up PET-CT/ August 2021, after two years and three months from HFRS another solitary left lung metastasis, 9.3 mm in size and SUV max – 3.6. The yellow arrow shows the single left lung metastasis.



A/ CT- pulmonary fibrosis SUV max 2.1 B/PET/CT- low metabolic activity SUV max 2,7

Figure 5. The follow-up PET-CT scan / January 2022- In the right lung HFRS zone low metabolic activity SUV max 2,7 and in the left lung RS zone pulmonary fibrosis SUV max 2.1.

4. Discussion

The term advanced laryngeal cancer generally denotes stage 3 or 4 laryngeal cancers according to the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) staging [13]. T4 classification is attained in tumors with cartilage destruction or extra laryngeal invasion [14]. Although laryngeal cancer represents only 2–5% of all malignancies, it is particularly important to investigate this type of cancer because of its significant effects on the voice, swallowing, and quality of life [15]. The main indications for TL in the practice are (1) failure of either RT or Ch-RT and (2) for management of T4 cancers. All treatment modalities are important. For successful management of advanced head and neck cancer, multimodality treatment is usually necessary [16]. Sanabria et al. recommended that TL be considered for advanced T4 laryngeal cancers in non-academic settings, given that its survival outcomes appear to be better than those for Ch-RT, according to the results of many observational studies [17]. Conventional treatment for advanced laryngeal cancer (T3 and T4) with total laryngectomy (TL), or TL with post-operative radiotherapy (RT), is associated with significant patient disfiguration [18]. The standard of care for advanced laryngeal cancer is either chemo-radiotherapy (Ch-RT) or total laryngectomy [19]. For many years, TL followed by RT was considered the standard treatment

for advanced laryngeal cancer [20]. Dziegielewski et al. reviewed 258 cases of T3 and T4a laryngeal cancer diagnosed between 1998 and 2008 using the Alberta Cancer Registry. They found that patients treated with TL plus RT and/or Ch had longer overall survival (OS) than patients treated with Ch-RT or RT alone [21,22]. Patients treated with TL experienced complications such as loss of voice and decreased social abilities leading to decreased quality of life in various aspects of life [22]. Zhang et al. conducted a SEER database study comparing treatment trends and OS for patients with supraglottic and glottis laryngeal cancer. Whereas they found an increase in the use of RT over time [23]. A study by Gourin et al. on patients with stage IV laryngeal cancers suggested that those with a higher N stage were at a greater risk of death [24]. Combination of TL plus Ch-RT provides superior local tumor control (LTC) and better survival compared to either RT or Ch-RT in patients with advanced laryngeal cancer [25]. The nonsurgical organ preservation approach (Ch-RT) had an independent effect on increasing the probability of recurrence with significant statistical difference, especially in Stage IV laryngeal cancer [19]. Supraglottic and transglottic carcinoma are liable to regional lymph node spread, especially with occult regional lymphatic spread that makes early diagnosis difficult and with much worse prognosis [26]. In our clinical case, it is a local advanced laryngeal carcinoma

noma originating in the glottic with a break through the laryngeal cartilage to the skin. Despite the 4th clinical stage, there are no metastases in regional cervical lymph nodes. The lack of pathologically verified lymph metastases was the reason during IMRT to realize a low radiation dose in the bilateral cervical lymph nodes up to TD 51.6 Gy with DD 1.72 Gy (Figure 1). However, after the TL with selective bilateral cervical dissection and IMRT (Fig.2), we achieve a 3,5 year LTC. This clinical case is interesting in that after a year and three months of the complex treatment completion, a follow-up PET/CT reported a solitary right lung metastasis without a local relapse of the primary laryngeal tumor (Figure 3). The finding of a solitary lung nodule in patients with extrathoracic cancers, on the other hand, presents a daunting diagnostic challenge [27-29]. Solitary lung tumors in patients with head and neck squamous cell carcinoma (HNSCC) are generally believed to represent second primary tumors if they occur more than 3 years after treatment of an HNSCC [30]. In the report by Alvi et al. DM developed after a mean time of 15 months and survival was 5 months after diagnosis of DM [31]. Finley et al. reported on their evaluation of surgical resection of pulmonary metastases of head and neck cancer that a resection of a solitary pulmonary metastasis resulted in long-term survival in selected patients [32]. The control PET/CT reported a LTC in the field of primary laryngeal tumor and lack of active metabolic accumulation in other organs, except for the solitary lung metastasis, which is surrounded by pulmonary parenchyma without pathological changes. This has to accept that it is a solitary lung metastasis from laryngeal carcinoma, which requires definitive HFRS. The 2016 National Comprehensive Cancer Network (NCCN) guidelines indicated that the standard treatment for recurrent cancer in a distant organ is chemotherapy, and recommended platinum + 5-Fluorouracil (FU) + Cetuximab as the first-line choice for patients with Performance Status (PS) 0–1 [33]. In our clinical case, after the manifestation of solitary lung metastasis after HFRS, only one course of Ch was performed, without clear why 6 courses Ch were not performed. Year and three months after the completion of postoperative IMRT a solitary right lung metastasis, followed by a metachronic solitary left lung metastasis was reported (Figure 4). Again, it was decided that this second solitary lung metastasis should be treated by radiosurgery. We are pleased to present the therapeutic result after the HFRS and RS with respect to the two solitary metachroneous pulmonary metastases, which is visible at PET/CT since January 2022 (Figure 5). The patient is currently with LTC, without pulmonary symptoms and good quality of life. Thanks to the complex treatment, we have achieved a 3.5 year survival rate in a patient with a local advanced laryngeal carcinoma with subsequent late solitary metachroneous pulmonary metastases.

5. Conclusion

1. Although the case is a locally advanced glottis carcinoma pT4 with a infiltration through the laryngeal cartilage with the cutane-

ous carcinomatosis, there are no cervical lymph node metastases.

2. After the total laryngectomy with bilateral selective lymph node dissection and postoperative IMRT up to total dose 60 Gy, a local tumor control for 3 years and 6 months was achieved.

3. Year and three months after the completion of postoperative IMRT a solitary right lung metastasis, followed by a metachronic solitary left lung metastasis was reported.

4. After HFRS and RS, the last follow-up PET/CT reported a very good therapeutic response - pulmonary fibrosis in the left lung metastasis with low metabolic activity (SUV max 2.1) and SUV max 2,7 in the right lung metastasis.

5. Thanks to the complex treatment, we have achieved a 3.5 year survival rate in a patient with a local advanced laryngeal carcinoma with subsequent late solitary metachroneous pulmonary metastases.

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