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Case Report

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A rare late leptomeningal carcinomatosis from a local advanced squamous cell laryngeal carcinoma after a long-time locoregional tumor control: case report and literature review

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Abstract

Brain metastases in squamous cell carcinomas of the head and neck are extremely rare. More rarely late leptomenengeal metastases (LMMs) manifested after 10 years of laryngeal carcinoma complex treatment are diagnosed. We present a patient with a local advanced well-differentiated laryngeal carcinoma (LC) without metastases in the cervical lymph nodes/pT4 N0 M0 (G1), which was treated in 2011 by total laryngectomy and intensity modulated radiotherapy (IMRT). After 10 years, against the background of the laryngeal tumor control, two brain metastases (BMs) occur, followed by leptomeningeal carcinomatosis (LMC).

Against the background of this rare clinical case and literary review, we focus on the necessary radiotherapy in late BMs, followed by leptomengial carcinomatosis. The prognosis for such distant brain incidents is extremely unfavorable. In a small number of late BMs near the ventricles, the prevention of LMC requires a whole brain radiotherapy (WBRT), followed by overdose by IMRT or radiosurgery (RS). Due to the rare cases of late cerebral and leptomenengeal metastases in head and neck squamous cell carcinomas (HNSCC), there are still no prospective studies to determine optimal complex treatment.

Keywords: Laryngeal Cancer, Brain Metastases, Leptomeningeal Carcinomatosis, Intensity Modulated Radiotherapy, Radiosurgery, Re-Irradiation.

Introduction

Brain metastases (BMs) are one of the most common neurologic complications of cancer [1]. The cumulative incidence from BMs after 5 years was estimated at 16.3% in patients with lung carcinoma, 9.8% in patients with renal carcinoma, 7.4% in patients with melanoma, 5.0% in patients with breast carcinoma, and 1.2% in patients with colorectal carcinoma [2]. The incidence from distant metastases (DM) of laryngeal cancer (LC) was 3.21%, of which 62.6% lung metastases and less than 4% BMs with poor prognosis [3,4]. Head and neck cancer has rarely been reported to be a cause of leptomeningeal carcinomatosis (LMC) [5-8]. In 2003 Stephen R Thompson et al. claim to have described the first case of a patient with LMC, arising from a laryngeal squamous cell carcinoma [9]. In this article, we present a 70-year-old man with a diagnosed in 2011 local advanced laryngeal carcinoma/T4N0M0, treated complexly with a total laryngectomy and intensity modulated radiotherapy (IMRT). After 10 years, against the background of the laryngeal tumor control, two brain metastases occur, followed by leptomeningeal carcinomatosis.

Clinical Case

We present a 70-year-old man with a long history of smoking more than one box of cigarettes a day. In 2011, he was diagnosed with locally advanced laryngeal carcinoma/T4 N0 M0. The histological result estimates a well-differentiated (G1) squamous cell carcinoma (SCC) with extracellular keratin formation. Radical laryngectomy with post-operative intensity modulated radiotherapy (IMRT) by the VMAT method in the area of the tumor bed and cervical lymph nodes bilaterally up to total dose (TD) 60 Gy was performed (Figure 1). By 2019 he conducted regular inspections. In January 2021, due to headache, a brain CT with venous contrast were performed and two brain metastases (cystic with perifocal edema and size 27 mm/16 mm and periventricular near the left front horn of lateral ventricles with a diameter of 14 mm) were identified (Figure 2). The local status on the part of the laryngeal bed and cervical lymph nodes bilaterally, did not show the presence of local or regional relapse. The blood count with biochemical indicators was normal, which excluded hematologic malignancies. Positron emission tomography (PET/CT) of the whole body does not take into account pathological metabolic activity (Figure 3)

and thus reject the presence of other primary solid tumors that cause hematogenous BMs. In March 2021 radiosurgery (RS) in the area of both brain metastases with a single dose fraction 15 Gy were conducted (Figure 4). 2 months later, due to the seizure symptoms, a MRI demonstrated multiple sub and supratentorial leptomeningeal metastases (Figure 5 and 6). We have judged re-irradiation in the whole brain in two brain hemispheres up to TD 34 Gy and in the cerebellum up to TD 46Gy with DD 2Gy (Figure 7). Currently, the patient conducts this second irradiation, covered with antiedematous and antiinflammatory therapy. After 4 months of re-irradiation, the patient died as a result of neurological complications.

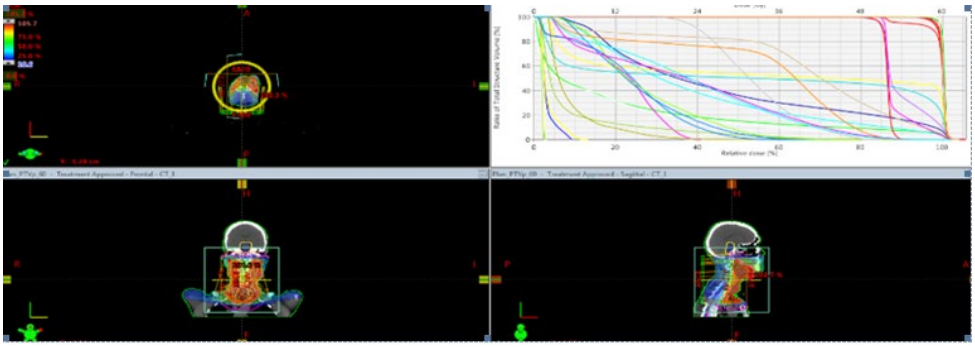

Figure 1: Postoperative intensity modulated radiotherapy by the VMAT method in the area of the tumor bed and cervical lymph nodes bilaterallyup to total dose 60 Gy.

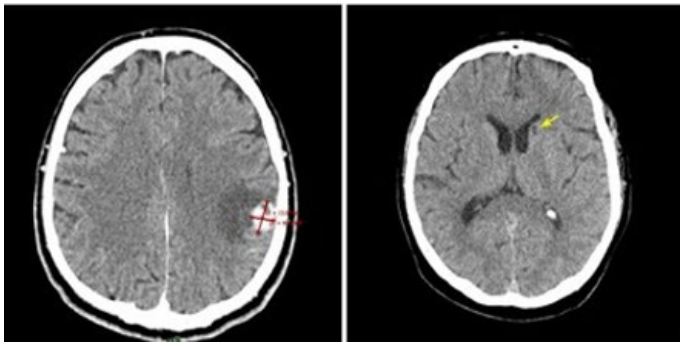

Figure 2: The Brain CT/January 2021 with venous contrast visualize two brain metastases-cystic with perifocal edema and size 27 mm/16 mm and periventricular near the left front horn of lateral ventricles with a diameter of 14 mm.

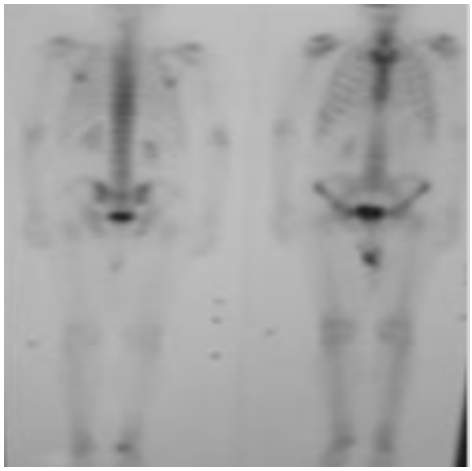

Figure 3: Positron emission tomography (PET/CT)/February 2021 were normal with no evidence of visceral metastasis.

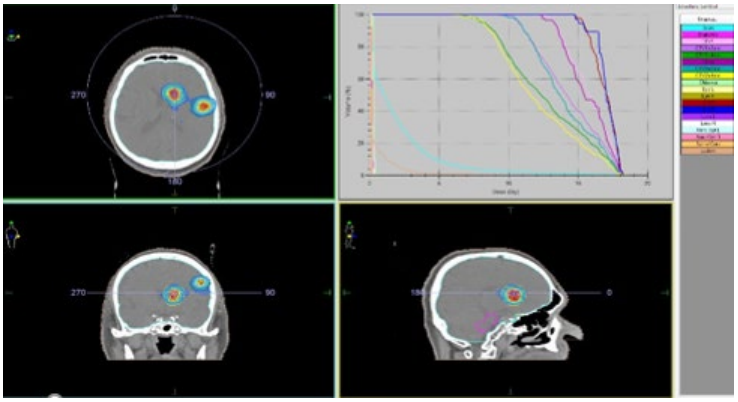

Figure 4: Radiosurgery/March 2021 by the VMAT method in the area of both brain metastases with a single dose fraction15 Gy.

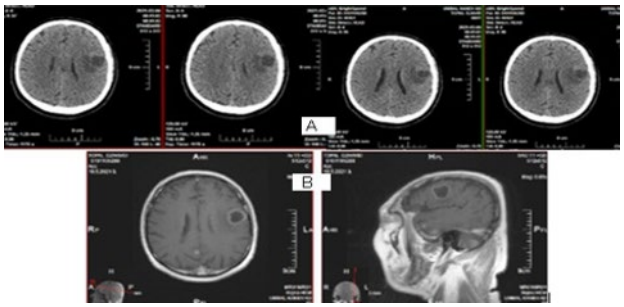

Figure 5: The CT и MRT images of the both brain metastases in left brain hemisphere after 2 months of completion of RS with a single dose fraction 15 Gy.

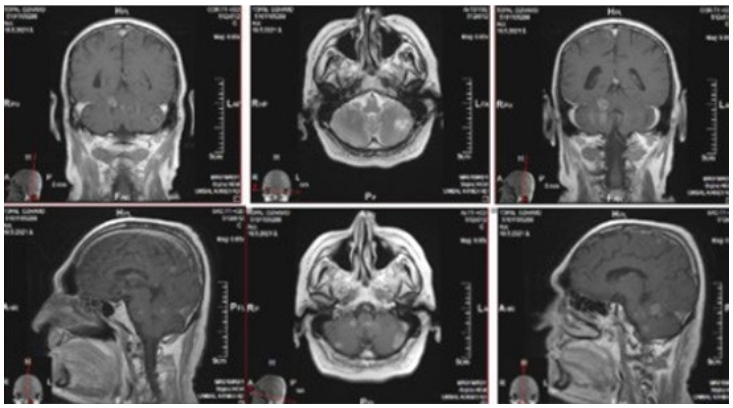

Figure 6: MRI with multiple sub and supratentorial leptomeningeal metastases (abnormal leptomeningeal contrast enhancement) after 2 months of completion of RS with a single dose fraction 15 Gy.

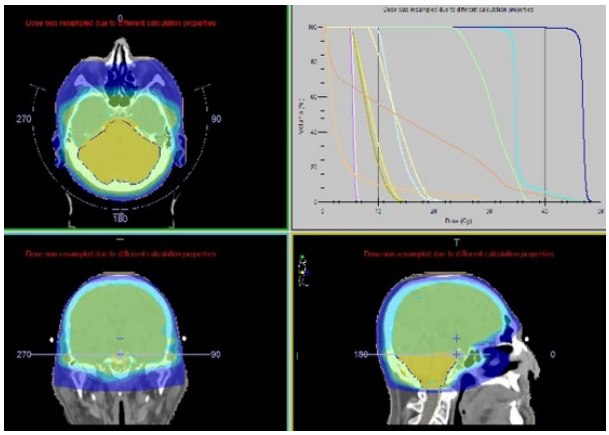

Figure 7: The whole brain re-irradiation by the VMAT method in the area of the two brain hemispheres up to TD 34 Gy and in the cerebellum up to TD 46Gy with DD 2Gy.

Discussion

The incidence of clinically detected distant metastases from head and neck squamous cell carcinoma (HNSCC) ranges from 9% to 11% [10], and from 2% to 8% are located in the brain [11]. Incidents of brain metastases (BMs) increase with the availability of improved imaging techniques which aid early diagnosis, and effective systemic treatment regimens which prolong life, thus allowing cancer to disseminate to the brain [1]. Although BMs are most commonly seen in advanced lung cancer, breast cancer, and melanoma [12], they are a rare sequela of HNSCC, occurring in less than 1% of all reported cases [13-15]. The human papilloma virus (HPV)-related SCC of the oral cavity and oropharynx has been demonstrated to have unique properties and a distinct pattern of metastasis [16]. Laryngeal cancer commonly spreads via direct extension to adjacent structures through metastasis to regional cervical lymph nodes [17]. In our clinical case, it is a local advanced LC with the coverage of the three laryngeal floors and with the infiltration of the laryngeal thyroid cartilage, but due to its well cellular differentiation (G1), there are no lymphatic metastases in the cervical lymph nodes. After the tatal laryngectomy and the intensity modulated radiotherapy (IMRT) (Figure 1), local tumor control is achieved for 11 years when the two brain metastases are proven (Figure 2). The fact that intracranial metastases seem to be more frequent in tumors originating in the supraglottic area or with supraglottic involvement could be explained by a higher vascularization of the supraglottic region compared with the glottis [13]. Distant spreading from laryngeal carcinoma is sustained by hematogenous dissemination or perineural invasion [18]. Vertebral and paravertebral metastases (particularly from breast and lung cancers) as well as head and neck cancers may spread centripetally along peripheral or cranial nerves [19] via the endoneural/perineural route or along coassociated lymphatics or veins [20] gaining access through the dural and arachnoidal sleeves of nerve roots (spinal roots, cranial nerves) and subsequently into the subarachnoid space. The HNSCC BMs that arise from hematogenous spread are a distinct entity [21]. Leptomeningeal carcinomatosis (LMC) is a relatively common and lethal complication caused by a variety of cancers, and is reported to occur in 1%-8% of patients with malignancies [22,23]. Leptomeningeal metastases (LMMs), a lethal complication of certain cancers, is the metastatic tumor cell invasion of the leptomeninges (arachnoid and pia mater) of the meninx and arachnoid spaces [24]. Hematogenous spread to the arachnoid via the arterial circulation, is probably the most common route of metastasis resulting in LMMs, but appears less common in solid tumors compared with hematological malignancies [19,20]. Although any cancer can metastasize to the leptomeninges, breast cancer (12-35%), lung cancer (10-26%), melanoma (5-25%), gastrointestinal cancer (4-14%), and cancers of unknown primary (1-7%) are the most common causes of solid-tumor-related LMMs [25-27]. Frequency of leptomeningeal metastatic involvement from LMC is 1%-2% [8,24]. Interesting in our clinical case is the appearance of two late brain metastases after 10 years of the LC primary complex treatment with achievement of locoregional control (Figure 1and 2). PET/CT/February 2021 were normal with no evidence of visceral metastases (Figure 3). Two months after the radiosurgery with single radiation dose of 15 Gy (Figure 4), MRI reported multiple leptomengial brain metastases (Figure 6). The risk of distant metastases (DM) in subjects with head and neck squamous cell carcinoma is influenced by age, site of primary cancer, local and/or regional extension, grading, and achievement of locoregional control [28]. In the clinical case described by Isabelle Pougnet et al. it concerns LMMs after 2 years of the treatment of a well -differentiated spincellular carcinoma of the lip with perineural invasion of the trigeminal nerve within the temporal fossa [29]. One case was reported in 1984: a 70-year-old man who developed a meningeal spread of a SCC of the lower lip associated to an ipsilateral mandible metastasis [30]. In our clinical case, we report late leptomeneal metastases due to well differentiated spinocellular laringeal carcinoma without lymphatic metastasis, without perineural invasion, only with local advanced local status-T4. We believe that this is the only clinical case published in English medical literature with late LMMs, which appeared after 10 years since the primary treatment and achieved a long -time locoregional tumor control.

Prognostic Factors In Patients with Diagnosed Brain Metastases

Multivariate analysis determined that patient age, performance status, extracranial metastases, radiotherapy and re-craniotomy are independent factors of prolonged survival [31]. From the three strongest prognostic factors (performance status, response to steroids, and evidence of systemic disease) simple identification of favorable and unfavorable subgroups of patients with BMs can be constructed [32]. Major favorable LMMs prognostic factors include excellent performance status, absence of serious fixed neurologic deficits, normal CSF flow scans, and absent or responsive systemic tumour [8]. In our clinical case, the general condition of the patient was good, he was of local tumor control with respect to LC. The only symptoms were neurological with the manifestations of periodic seizures.

Treatment

BMs from laryngeal squamous cell carcinoma (SCC) are rare [33-35], with a reported incidence less than 4% of cases [4], and there are no standardized treatments [36]. The current development of computer-assisted stereotactic navigation and stereotactic radiotherapy may facilitate surgical diagnostic exploration and improve treatment, especially in patients without extracranial disease [13]. Surgery and/or radiochemotherapy increase the survival of these patients [36]. Radiosurgery is effective in single small brain metastases, and in greater, hypofractionated radiosurgery is required. Due to the fact that BMs in LC are extremely rare, we did not assume that they would be followed by leptomenngeal metastases (Figure 6). This made us first to perform radiosurgery with a single radiation dose of 15 Gy, not a whole brain radiotherapy (WBRT) with subsequent overdose/ boost in both metastases. Localization of one of the metastases (near the frontal horn of the left lateral cerebral ventricle) was a signal that leptomengial carcinomatosis was possible. After the already prominent multiple LMMs in the brain, then we decided to perform the WBRT as a re-irradiation after radiosurgery (Figure 7).

Conclusion

Brain metastases in squamous cell carcinomas of the head and neck are extremely rare. More rarely are diagnosed late leptomenengeal metastases manifested after 10 years of laryngeal carcinoma complex treatment. The prognosis for such distant brain incidents is extremely unfavorable. Due to the rare cases of late cerebral and leptomenengeal metastasis in HNSCC, there are still no prospective studies to determine optimal complex treatment. In our clinical case, we present late leptomeneal metastases due to well-differentiated spinocellular laringeal carcinoma without lymphatic metastasis, without perineural invasion, only with local advanced local status/T4. In a small number of late BMs near the ventricles, the prevention of leptomenengeal carcinomatosis requires a whole brain radiotherapy, followed by overdose by IMRT or radiosurgery. We believe that this is the only clinical case published in English medical literature with late LMMs, which appeared after 10 years since the primary treatment and after achieved a long-time locoregional tumor control.

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