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Teaching Case

Intensity Modulated Radiation Therapy for Syringomatous Carcinoma of the Face: A Case Report

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Introduction

Sweat gland carcinomas are extremely rare tumors. The age-adjusted incidence rate of cutaneous appendageal carcinomas, including sweat gland carcinomas, is 5.1 per 1 million person-years.[1] The main treatment method is wide local excision and lymph node dissection, and chemotherapy and radiation therapy have limited roles.[2]

Syringomatous carcinoma is a rare malignant skin appendageal tumor that arises from the sweat glands.[3] Syringomatous carcinoma occurs as a slow growing, locally destructive, firm, and poorly demarcated nodule or plaque and is located predominantly on the face or scalp.[4] In this report, we describe the case of a patient with syringomatous carcinoma of the face who received intensity modulated radiation therapy (IMRT). The patient provided written consent to report the details of her case, including images.

Case Report

The patient was a 79-year-old Japanese woman. In 2006, she noticed a hardening of the skin on both cheeks. In February 2015, her entire face began to swell. The swelling progressively worsened, until April 2015 when the patient had difficulty to open her eyes. With these complaints, she visited our hospital in June 2016.

On physical examination, she presented with board-like induration of the face, which extended from the cheek on either side to the nose (Fig 1). A head and neck magnetic resonance imaging scan revealed a subcutaneous mass with contrast enhancement that extended from both cheeks to the nose (Fig 2). A histopathologic examination of skin biopsy specimens of the left cheek revealed evidence of adenocarcinoma that extended from the subcutaneous fat layer to the facial muscles. Some clear 2-layer structures like sweat ducts were observed (Fig 3). Based on these findings, the tumor was diagnosed as syringomatous carcinoma. The tumor infiltrated the superficial facial muscles and was classified per the TNM classification system of skin cancer (Union for International Cancer Control, 8th edition, 2017) as T3N0M0. Radiation therapy was selected as a treatment because surgery would have necessitated excisions of wide areas of the face.

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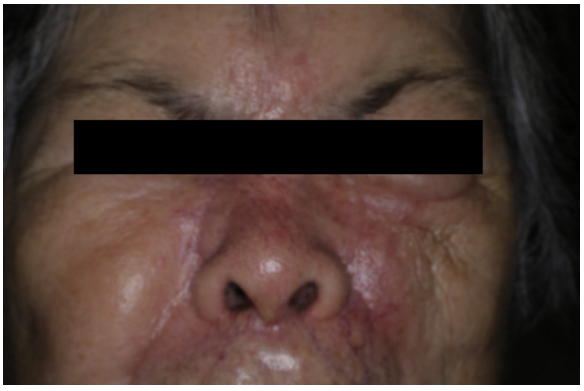

Figure 1 Clinical photograph of the patient (June 2016).

In the radiation therapy planning, the patient's eyeballs, lenses, optic nerves, optic chiasma, oral cavity, brain, brainstem, spinal cord, middle ears, and mandible were contoured as organs at risk (OARs). The gross tumor volume was defined as the macroscopic tumor detected on computed tomography and magnetic resonance imaging scans. A margin of 2 cm was drawn around the gross tumor volume to define the clinical target volume. The planning target volume was defined by addition of a margin of 5 mm to the clinical target volume (Fig 4A). IMRT was delivered with seven intensity modulated beams of 6 MV photons (Fig 4B). A 1 cm bolus was used throughout the entire treatment to ensure sufficient subcutaneous doses to the subcutaneous tissues, and a total dose of 60 Gy in 30 fractions was prescribed to the median of the planning target volume. The dose distribution chart is shown in Figure 4C through F. For dose prescription, we considered the tolerance doses of each OAR. The D_{mean} of the left lens was 35.3 Gy, which was higher than dose constraints of 10 Gy. The doses to all other OARs were within the respective dose constraints.

A month after completion of the radiation therapy, the facial swelling disappeared and the patient was able to open her eyes again without difficulty. Her activities of

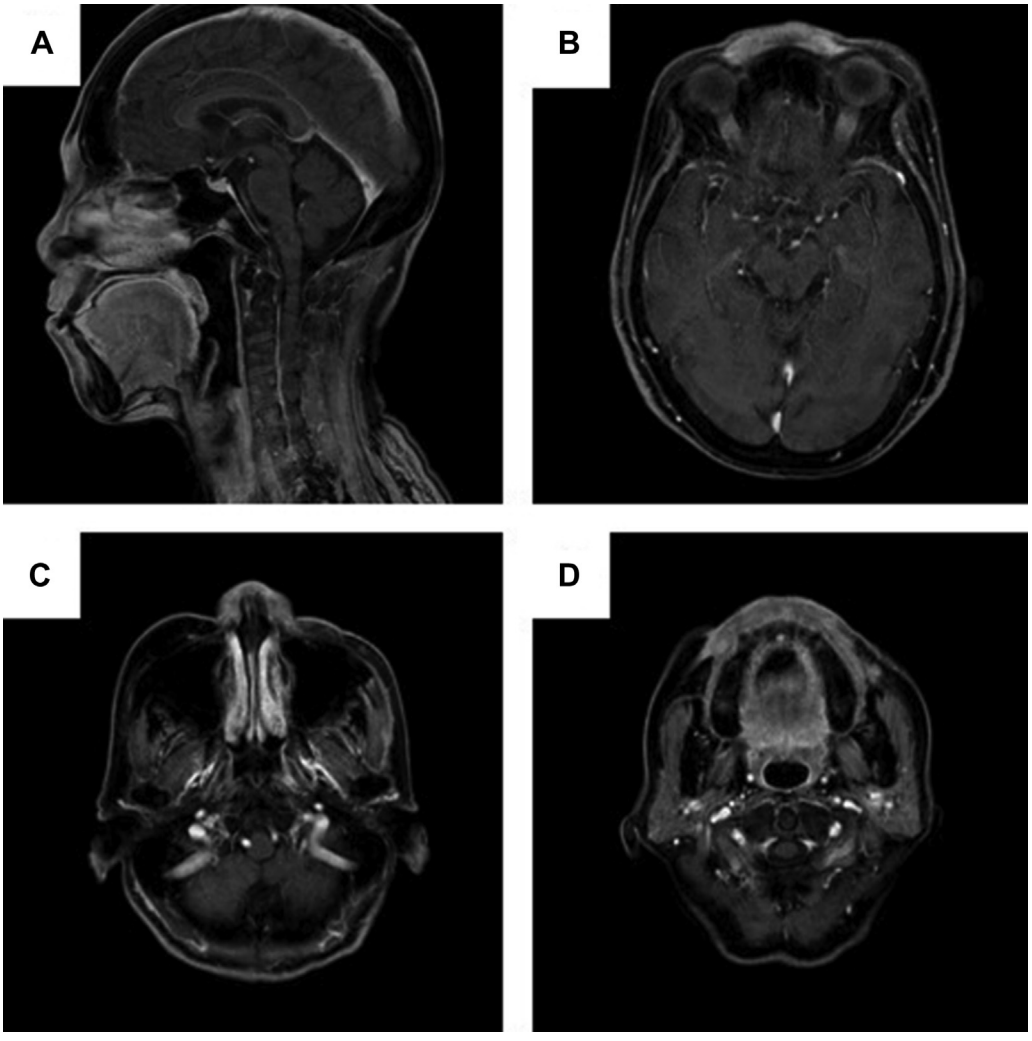

Figure 2 Magnetic resonance imaging scan of the tumor (April 2016, contrast-enhanced T1-weighted images with fat suppression). (A) Sagittal and (B-D) axial views.

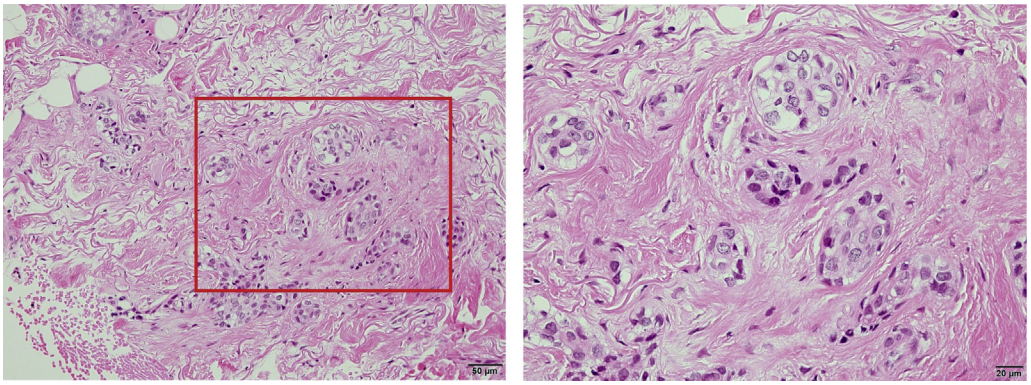

Figure 3 Photomicrograph of the tumor cells (hematoxylin and eosin stain).

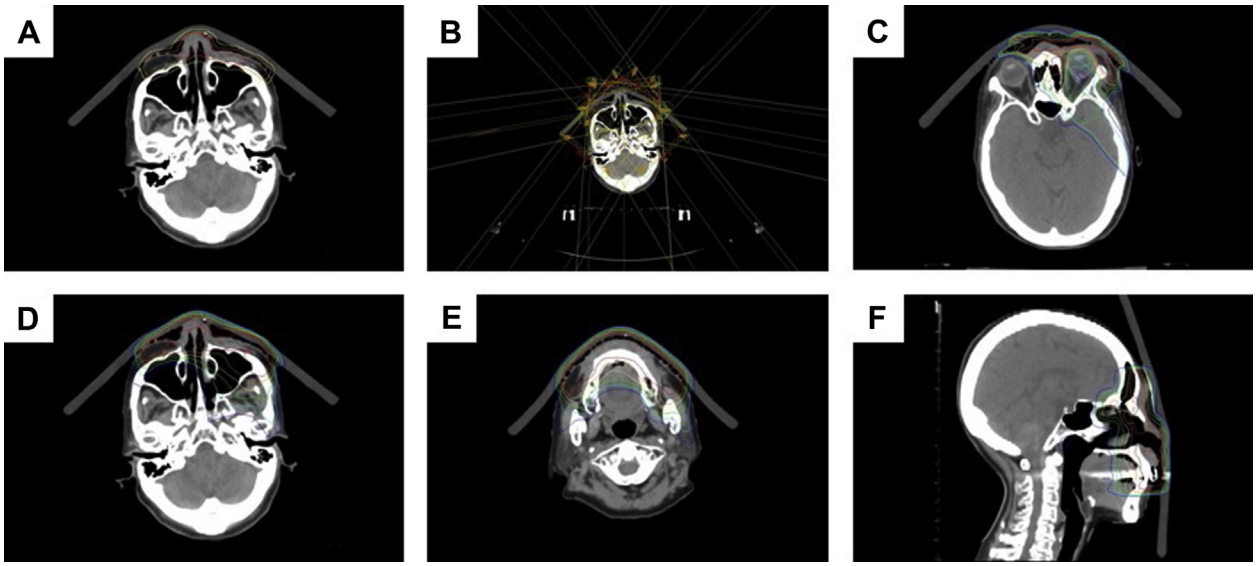

Figure 4 Details of radiation therapy. (A) Contouring (red line: gross tumor volume; orange line: clinical target volume; yellow line: planning target volume), (B) layout of the 7 photon beams, and (C-F) dose distribution of the photon intensity modulated radiation therapy (red line:100% = 60 Gy; orange line: 90%; yellow line: 80%; green line: 70%; light blue line: 60%; blue line: 50%).

daily living improved, and she was able to enjoy her hobby of field work, which she had been unable to do before treatment.

The acute adverse events were oral mucositis (grade 2; Common Terminology Criteria for Adverse Events, version 5.0), cheilitis (grade 2), oral pain (grade 2), and radiation dermatitis (grade 2). The late adverse events were periodontal disease (grade 3), left cataract (grade 2), transient left periorbital edema (grade 1), and telangiectasia, especially around the nose (grade 1). Cataract and periorbital edema and discharge of the left eye were observed 4 months after radiation therapy. In March 2018, the patient noticed bleeding from the mouth, and an oral examination revealed a defect of the right upper gum with exposure of a necrotic maxilla. These findings were within the irradiation field, and we made the diagnosis of periodontal disease.

The patient remained recurrence-free until the 18-month follow-up visit after treatment completion (Fig 5). Eventually, in July 2018, subcutaneous induration measuring up to 26 mm appeared near the right corner of the mouth, which had received a dose of approximately 60 Gy during the previous radiation therapy. The patient stopped visiting our hospital after August 2018; therefore, the progress of the tumor thereafter is unknown.

Discussion

The treatment of first choice for sweat gland carcinomas is surgery, but few reports exist about definitive radiation therapy for these cancers. A summary of cases of sweat gland carcinoma treated with definitive radiation therapy in the last 3 decades is shown in Table 1. Herein, we defined sweat gland carcinoma as a cutaneous tumor, as mentioned in a review of malignant sweat gland tumors by Ahn et al.[12] Among the 8 cases listed in Table 1, 4

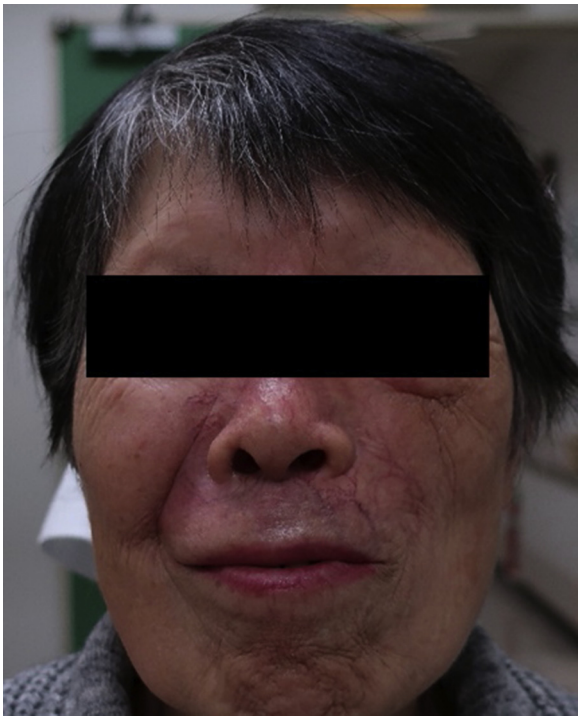

Figure 5 Clinical photograph of the patient after treatment (January 2018).

cases (50%) remained recurrence-free until the end of the follow-up period. Definitive radiation therapy for sweat gland carcinoma can also be deemed effective for the local control in some cases. Therefore, we believe that definitive radiation therapy for sweat gland carcinoma is a potentially valid treatment alternative for cases in which surgery is expected to be difficult.

In our case report, IMRT was used as the radiotherapeutic modality to treat syringomatous carcinoma. IMRT has the ability to deliver high doses of radiation to the tumor target with very high precision while minimizing the dose received by the surrounding normal tissues.[13] For the case of squamous cell carcinoma of the head and neck, randomized studies have demonstrated that IMRT is associated with a reduced incidence of side effects (particularly xerostomia) compared with 3-dimensional conformal radiation therapy (CRT).[14] Some previous case reports exist[8,15] of facial skin cancer treated with IMRT, but to the best of our knowledge, there are no other reports on the use of IMRT to treat syringomatous carcinoma.

To date, there is no evidence that in cases of facial skin cancer, IMRT is associated with a reduced incidence of side effects compared with 3-dimensional CRT. However, we hypothesize that IMRT may also be useful to treat

Table 1 Summary of some cases of sweat gland carcinoma treated by definitive radiation therapy (except adjuvant RT) in the last 3 decades

Study first author	Reporting year	Age	Sex	Site	Histologic type	Method	Dose (Gy)	Number of fractions	Chemotherapy	Follow-up (y)	Outcome
Auw-Haedrich[5]	2001	87	M	Right eyelid and right orbital cavity (primary tumor)	Signet ring cell carcinoma of the eccrine sweat gland	Not listed	56	Not listed	None	1.2	NED
Stein[6]	2003	76	F	Right nasal dorsum (primary tumor)	Microcystic adnexal carcinoma	External beam RT	58	Not listed	None	0.5	LR
Yamashita[7]	2008	61	M	Lymph nodes from the left inguinal and internal iliac to the abdominal paraaortic region	Eccrine porocarcinoma	6-MV photons	50.4	28	CDDP+5-FU	0.5	NED
Motta[8]	2009	71	F	Scalp (Local recurrence after surgery and adjuvant RT)	Eccrine mucinous adenocarcinoma	Helical tomotherapy	50	20	None	1	NED
Lalya[9]	2011	68	F	Left parotid area (local recurrence after surgery)	Clear cell hidradenocarcinoma	External beam RT	66*1	33	None	1.25	NED
Pugh[10]	2012	53	F	a. Upper lip (primary tumor) b. Upper lip (local recurrence after RT)	Microcystic adnexal carcinoma	a. 9-MeV electron, followed by low-dose iridium-192 brachytherapy b. 9-MeV electron	a. 63.6†2 b. 64	a. 26 (electron) b. 32	None	a. 4 b. 1.25	a. LR b. NED
Miller[11]	2015	32	M	Bilateral axillary lymph nodes	Apocrine hidradenocarcinoma	External beam RT	50.4	28	CBDCA+PTX	Not listed	PD‡3
Present Report	2019	79	F	Face, mainly in both cheeks and around the nose (primary tumor)	Syringomatous carcinoma	6-MV photons, IMRT	60	30	None	2	LR

Abbreviations: 5-FU = 5-fluorouracil; CBDCA = carboplatin; CDDP = cisplatin; IMRT = intensity modulated radiation therapy; LR = local recurrence; NED = no evidence of disease; PD = progressive disease; PTX = paclitaxel; RT = radiation therapy.

* 66 Gy to the tumor bed, and 50 Gy to the regional lymphatic chains.

† 41.6 Gy(electron) + 22 Gy (brachytherapy).

‡ Clear response at the irradiation site, but multiple metastasis occurred.

sweat gland carcinomas of the face near the OAR in terms of a reduced incidence of adverse events compared with 3-dimensional CRT. This is because facial skin cancer is sometimes located near the OAR, and during radiation therapy, the doses delivered to the OAR may cause adverse events. For example, Auw-Haedrich et al[5] reported on a case of signet ring cell carcinoma of the eccrine sweat glands located at the right eyelid and right orbital cavity that was treated with definitive radiation therapy. The patient became blind in the right eye after radiation therapy. If our case had been treated with 3-dimensional CRT, the doses delivered to the right lens might have exceeded the dose constraint, and adverse events such as right cataract might have occurred. Thus, in cases of syringomatous carcinoma that affect wide areas of the face, we believe that IMRT may be particularly useful.

In this case report, the tumor recurred within 2 years of treatment. The optimal radiation dose for definitive radiation therapy of sweat gland carcinomas is still unknown. However, as shown in Table 1, some cases treated with a total dose of <65 Gy developed local recurrence. In addition, Pugh et al[10] reported on the optimal dose for gross microcystic adnexal adenocarcinoma, which is one of the sweat gland carcinomas. The researchers extrapolated the data reported for squamous cell carcinoma of the head and neck reported in literature, and proposed a dose of 66 Gy to 70 Gy with standard fractionation or a biologically equivalent regimen. When taking all available evidence into consideration, a dose of 60 Gy for definitive radiation therapy of syringomatous carcinoma may be insufficient, and a dose of 66 Gy to 70 Gy with standard fractionation may yield better outcomes.

Conclusions

We report on the case of a 79-year-old female patient with syringomatous carcinoma of the face, who was treated with IMRT, which resulted in temporary palliation. IMRT may be considered as a valid treatment alternative for cases of syringomatous carcinoma in which surgery is difficult to perform, and IMRT may minimize the risk of adverse events.

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