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Teaching Case

High-resolution, ultrasound-guided, high-dose-rate, surface brachytherapy for basal cell carcinoma of the skin: A case report

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Introduction

Nonmelanomatous skin cancer (NMSC) is the most common type of malignancy, and radiation therapy (RT) is an excellent alternative treatment for patients who are medically inoperable or refuse surgery.[1,2] High-dose-rate (HDR) surface brachytherapy (BT) can spare adjacent and deeper normal tissue from radiation doses while delivering a larger radiation dose to skin cancers.[3,4] Therefore, surface BT is especially suitable for patients who have lesions that are located in sensitive anatomic regions such as the scalp, eyes, or nose.[3,4] Ultrasound guidance is needed typically for tumor localization during BT for prostate and cervical cancers, but its use for NMSC treatment is uncommon.[5,6] Here, we report on the first case, to our knowledge, in which 3-dimensional, high-resolution ultrasound guidance is used during iridium-based BT for NMSC.

Case report

A 78-year-old male patient presented to the radiation oncology clinic with basal cell carcinoma on the right lateral nasal tip in April 2017. The lesion was initially identified during a routine visit with a dermatologist in January 2017, and the patient estimated that the lesion had existed for approximately a year. The untreated lesion is shown in Figure 1A. In February 2017, biopsy test results revealed nodular basal cell carcinoma. The patient noted heavy bleeding after the biopsy, but had an otherwise uneventful recovery. The patient denied feeling any pain, numbness, tingling, or bleeding at the time of the consultation. A physical examination did not show any abnormality, other than an 8-mm lesion on the right side of the nose.

In terms of oncologic history, the patient had been diagnosed previously with multiple myeloma and bladder cancer. The multiple myeloma was diagnosed in 2012 and treated with an autologous stem cell transplant in 2014. However, progression with hypercellular (60%) marrow was noted on the basis of the bone marrow biopsy test results of June 2016. The patient's multiple myeloma was on observation only at the time, but he had been heavily treated with systemic therapies before presenting with skin cancer. He was also severely thrombocytopenic at the time, and there was a reluctance by the medical oncologist to refer the patient for surgery or RT. With electron beam radiation, there was a concern that radiation

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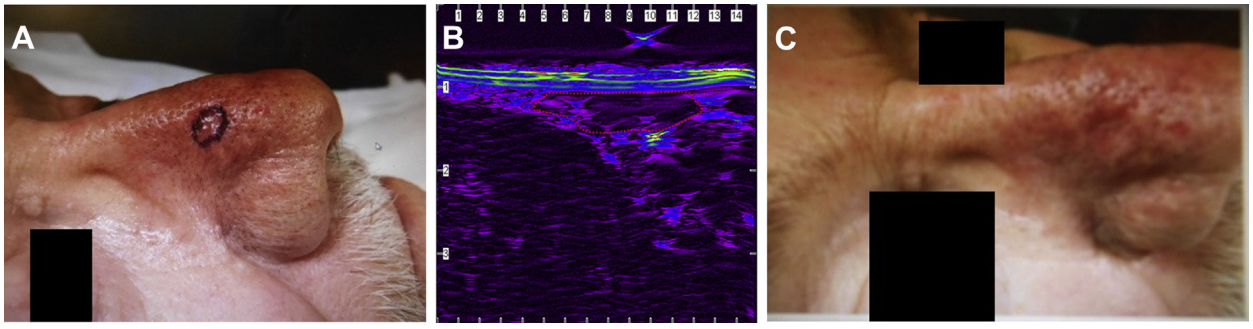

Figure 1 (A) Appearance of the lesion before treatment; (B) 2-dimensional ultrasound image of the lesion; and (C) appearance of the lesion 1 week after treatment completion.

could worsen the thrombocytopenia and cause more epistaxis. The patient's pre-RT platelet count was 39,000/μL. He also had high-grade T1 bladder cancer with carcinoma in situ that was treated with mitomycin. The patient was scheduled to receive Bacillus Calmette-Guerin treatment.

The patient was offered hypofractionated HDR BT to a superficial depth to minimize collateral scatter to the surrounding anatomic structures (minimize collateral scatter to bone marrow) and limit exposure to internal structures within the nostril (limit risk for epistaxis). A high-resolution ultrasound was used to better localize the treatment field before treatment planning. Specifically, the depth and size of the basal cell carcinoma lesion, as measured with a 35-MHz probe of the ultrasound equipment, were used to select the right-size BT applicator. Ultrasound images have a 7.5-μm vertical resolution and the lesion can be clearly identified in these high-resolution images. The tumor measurements on the basis of the ultrasound imaging were 8 mm × 4.5 mm, with a maximum depth of 0.85 mm (Fig 1B). A total of 36 Gy was delivered in 6 fractions with 6 Gy per fraction, as prescribed to the standard 3-mm depth using a Leipzig 2-cm applicator.

Instead of conventional fractionation, the hypofractionated course was offered in consideration of the patient's poor prognosis associated with his advanced multiple myeloma. The radiation dose was delivered twice per week (Monday and Thursday) using Iridium-192. The RT was administered in June 2017 over a 3-week period. The setup of the BT treatment is shown in Figure 2. During treatment, a 2 × 2 inch rolled gauze was placed in

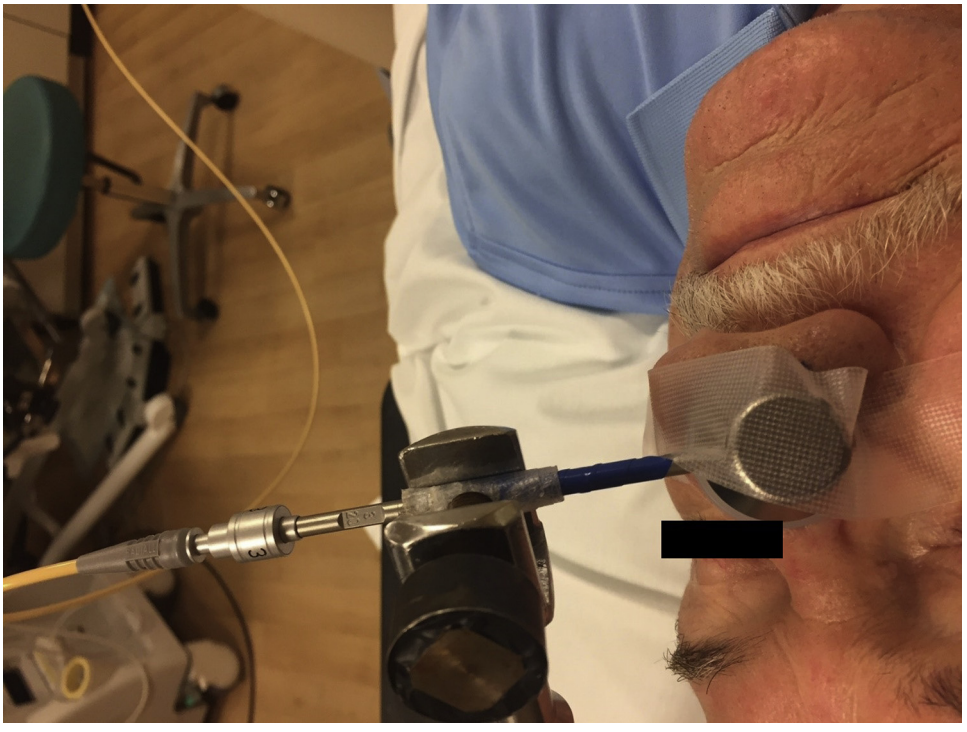

Figure 2 Setup of the field during ultrasound-guided, high-dose-rate brachytherapy.

between the nasal septum and right nasal ala to protect the nasal septum from the radiation dose.

With regard to treatment complications, the patient experienced light epistaxis for 4 days after treatment completion, but no further events were reported. His post-RT platelet count remained largely unchanged at 45,000/μL. Figure 1C shows the lesion 1 week after treatment completion. Unfortunately, the patient passed away from progressively worsening anemia that lead to cardiac arrest (complication from his longstanding multiple myeloma and myelodysplastic syndrome) 4 months after treatment. At the time of his death, there was no evidence of local disease recurrence within the irradiated area, and the treated lesion remained stable.

Discussion

We report on a case in which we successfully treated NMSC with surface BT under high-resolution ultrasound guidance, which was used for lesion localization in this patient and reduction of scatter dose to bone marrow because of the patient's multiple myeloma. To our knowledge, this is the first study to report on the use of ultrasound guidance in iridium-based surface BT for NMSC, and provides reassurance to oncologists that HDR does not significantly affect bone marrow.

The oncologic and cosmetic outcomes achieved with electronic BT for NMSC has been excellent. Bhatnagar reported on the outcomes of 122 patients with 171 NMSC lesions treated to 40 Gy in 8 fractions with HDR electronic BT.[7] After a mean follow-up time of 10 months (range, 1-28 months), no local recurrence was noted, no Grade $\geq$3 adverse events were observed, and comesis was excellent for 92.9% and good for 7.1% of patients.

In another series, Paravati et al. investigated the outcomes of 127 patients with 154 NMSC lesions treated with HDR electronic BT to 40 Gy in 8 fractions.[8] After 16.1 months, the overall crude recurrence rate was 1.3%. Grade 3 skin toxicity was observed in 13% of patients, but no grade 4 or 5 toxicities were reported. The cosmetic results were excellent in 94.2% and good in 3.3% of patients.

Tormo et al. demonstrated that, with a longer follow-up period, the outcomes are still excellent.[9] Their series reviewed the outcomes of 32 patients with 45 NMSC lesions treated with the Valencia applicator to 42 Gy in 6 or 7 fractions delivered twice weekly. After a median follow-up time of 47 months, 98% of the lesions were locally controlled, and no grade $\geq$2 late adverse events were observed.

Furthermore, Guix et al. showed that the outcomes achieved with iridium-based BT for NMSC was just as excellent as those with electrons.[10] Their series included 136 patients with either skin basal or squamous cell carcinomas treated to 60 to 65 Gy in 33 to 36 fractions by surface molds and HDR BT with Iridium-192. The actuarial 5-year local control rate was 98%, and no severe complications were reported.

Goyal et al.'s pilot study was the only case series to date in the literature to show the outcomes achieved by using ultrasound guidance in BT for NMSC.[6] In this series, 19 patients with 23 NMSC lesions underwent surface electronic BT, and a 14- or 18-MHz ultrasound device was used to determine lesion depth and lateral extension. The mean depth was 2.1 mm (range, 1.0-3.4 mm), and the mean largest diameter was 8 mm (range, 2.6-20 mm). The radiation dose ranged from 32 to 50 Gy in 8 to 20 fractions. After a median follow-up period of 12 months, neither local failure nor prolonged skin toxicities were reported.

Our study is unique because we used a higher resolution ultrasound probe with more sensitivity at 35 MHz. The use of ultrasound in the management of skin cancers has been recently recognized by several investigators. Wortsman et al. assessed the performance of variable-frequency ultrasound in the evaluation of skin cancers by reviewing diagnostic accuracy in 4338 skin lesions, including both malignant and benign lesions.[11] Ultrasound imaging with variable frequencies (7-16 MHz) was used to characterize all reviewed lesions. With a final pathology report as the gold standard, the pre-ultrasound diagnostic accuracy was 73%, and postultrasound accuracy was 97% ($P < .001$). The ultrasound was concluded to be able to serve as a reliable adjuvant for skin lesion diagnosis, with the caveat that lesions located in the epidermis only or <0.1 mm in depth cannot be detected.

Song et al. also evaluated the correlation between ultrasound and histology findings in the depth of involvement of skin cancers.[12] In the 49 skin cancer lesions of 40 patients, the mean depth was 3.97 $\pm$ 3.15 mm by ultrasound and 4.04 $\pm$ 2.92 mm by histology, with an interclass correlation coefficient of 0.953. Studies such as these demonstrate that ultrasound technology can reliably aid clinicians in diagnosing and localizing skin cancers.

In the current case, an ultrasound was used to guide patient selection and provide reassurance that both the routine standard HDR applicator would adequately cover the peripheral margins of the tumor and standard dosimetry would adequately treat the deep margins of the tumor. This case was not part of a clinical trial; therefore, with little published data on ultrasound-guided HDR, we treated the patient with a routine standard-of-care approach. Future directions should include clinical trials to allow for a reduction in field size, alterations in dosimetry, or treatment depth as a function of ultrasound-guided HDR. In addition, despite the use of HDR BT to reduce the risk of epistaxis, this side effect was not avoided in our patient, who still experienced mild epistaxis for 4 days.

Conclusions

The premature death of the patient in our series precludes long-term follow-up of his treated lesion. However, during the limited follow-up duration, his lesion responded well to treatment, and the cosmetic outcome also was excellent. Because of the success of this experience, we encourage further exploration of ultrasound guidance to treat NMSC in critical locations using BT. Future trials should consider ultrasound-guided HDR, including potential changes in prescribing to different depths and ensuring adequate margins in cases where a clinically evident nodule may be more extensive subdermally.

Acknowledgments

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