Case Report

Management of a Case of Recurrent Cutaneous Adenoid Cystic Carcinoma of the Scalp with Radiation Therapy

Ajinkya Gupte[1], Purwa Jaiswal[2], Amol Kakade[3], Prasad Raj Dandekar[4]

From [1]Fellow (Precision Radiation Oncology), [2]Trainee, [3]Consultant, [4]Consultant and Head, Department of Radiation Oncology, Sir H.N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India

ABSTRACT

Primary cutaneous adenoid cystic carcinoma (PCACC) is a rare tumor originating within the skin, typically presenting as a solid, gradually enlarging nodule or mass. We report a unique case of recurrent PCACC of the scalp in a 90-year-old male, initially diagnosed in 2010 and managed with surgical excision. Despite initial treatment, the lesion recurred twice, necessitating re-irradiation due to ineligibility for surgical resection at the second recurrence. We discuss the treatment modalities and outcomes of this case, highlighting the importance of a multidisciplinary approach in managing rare malignancies. Our case underscores the feasibility and efficacy of radiotherapy as a palliative treatment option for recurrent PCACC, particularly in patients unsuitable for surgical intervention.

Key words: Adenoid cystic carcinoma, Cutaneous, Recurrent, Re-irradiation, Scalp

Adenoid cystic carcinoma (ACC) is typically identified as a malignant tumor originating in both major and minor salivary glands. It represents about 1% of all head-and-neck malignancies. Despite its rarity, ACC is the most prevalent tumor in the minor salivary glands and the second most common in the major salivary glands, making up around 10–20% of all salivary gland tumors overall [1]. However, it occasionally emerges from unusual locations, particularly those with mucous glands, such as the respiratory tract, external auditory canal, breast, lacrimal gland, uterus, vulva, cervix, prostate, thymus, skin, and esophagus [2,3]. Primary cutaneous ACC (PCACC) originates directly within the skin and requires distinction from metastasis from other primary origins or the direct spread of ACC from a salivary gland to the skin [4]. It represents a rare condition that follows a gradual yet steadily advancing course. It rarely extends to lymph nodes or distant metastatic sites. The aggressive infiltration of the tumor into the reticular dermis and subcutaneous tissue, often accompanied by frequent perineural invasion, may provide insights into the substantial recurrence rates, which can reach up to 50% [3,5]. While surgery has traditionally served as the primary treatment for initial cases, the therapeutic approaches for recurrent cases remain relatively uncharted.

In this report, we present a unique case involving recurrent ACC of the scalp, which was managed using radiation therapy during two separate episodes of recurrence. This case is reported to highlight the challenges and efficacy of radiotherapy as a palliative treatment option for recurrent PCACC, particularly in elderly patients unsuitable for surgical intervention. Given the rarity of PCACC and the high recurrence rates, documenting the management and outcomes in such cases is crucial to expanding our understanding and optimizing treatment strategies.

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CASE PRESENTATION

In August 2023, a 90-year-old male presented with pain in the scalp posterior to the previously treated region. Clinical examination revealed two small, tender, and bleeding lesions. Subsequent magnetic resonance imaging (MRI) brain showed two well-circumscribed ovoid-shaped rim-enhancing collections in the soft tissues of the scalp, measuring 10 × 6 mm and 7 × 5 mm (Fig. 1). The patient's medical history is notable for multiple prior malignancies and treatments. Initially, in 2004, he presented with a longstanding scalp swelling, which was confirmed as benign hemangioendothelioma on biopsy. In 2010, the swelling rapidly enlarged and became painful. A biopsy at that time confirmed ACC of the scalp. He underwent wide local excision with skin grafting, and a post-operative whole-body positron emission tomography-computed tomography (PET-CT) scan showed no residual or focal enhancing lesions. However, recurrence in 2011 necessitated another surgery, with a biopsy again confirming ACC. In 2018, the patient was diagnosed with high-grade papillary urothelial cancer

Correspondence to: Prasad Raj Dandekar, Consultant and Head, Department of Radiation Oncology, Sir H.N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India. E-mail: drprasadraj@yahoo.com

of the urinary bladder. He received BCG treatment, with follow-up scans and cystoscopy showing disease control. In 2020, the patient experienced a rapid increase in the size of the scalp swelling, now with associated bloody discharge. Upon presentation, he exhibited substantial bleeding from the scalp lesion, necessitating multiple daily dressings. MRI brain with venography revealed a large intraosseous mass (6.6 × 4.9 × 3.6 cm) at the midline skull vault, eroding both the inner and outer tables, extending through the vault's thickness, and involving the soft tissues of the scalp and cranial cavity (Fig. 2). A whole-body PET-CT scan indicated a heterogeneously enhancing, metabolically active soft-tissue lesion in the high parietal region of the scalp. This lesion had completely destroyed the underlying parietal bone, with invasion into the superior sagittal sinus.

Due to the patient's ineligibility for surgical resection, radiation therapy was initiated. A total dose of 40 Gy was administered in 16 fractions, followed by a boost of 10 Gy in 4 fractions using the volumetric modulated arc therapy technique (Fig. 3). The patient tolerated the radiotherapy well, experiencing neither skin toxicities nor exacerbation of pain. The primary clinical symptom of bleeding from the lesion completely resolved following the treatment. A follow-up CT brain venogram in July 2021 revealed a marked reduction in the lesion size, from 6.6 × 4.9 × 3.6 cm to 3.9 × 1.4 × 1.4 cm, along with decreased infiltrative thrombosis (from 2.2 cm to 1.7 cm). In January 2022, the patient was diagnosed with carcinoma of the prostate, with an initial pre-treatment prostate-specific antigen of 15.7 ng/mL and biopsy revealing a prostatic acinar adenocarcinoma with a Gleason Score of 5+4=9. A whole-body prostate-specific membrane antigen PET-CT scan performed as part of the staging for the prostate cancer showed complete resolution of the previously treated scalp lesion but revealed a new metabolically active nodule in the anterior cut edge of the right parietal bone (Fig. 4). The patient was advised to undergo hormone therapy alone in view of his age and comorbidities.

Considering the August 2023 presentation with pain and bleeding scalp lesions, the patient was scheduled for re-irradiation, with a planned dose of 39 Gy in 13 fractions utilizing the three-dimensional conformal radiation therapy (3DCRT) technique to avoid low dose spill to the brain parenchyma (Fig. 5). He did not develop any skin toxicities, exacerbation of pain, or treatment interruptions during irradiation. Following radiotherapy, clinical examination, and MRI evaluation 3 months post-therapy indicated no observable change in the size of the lesion (Figs. 6 and 7). On follow-up 3-month post-re-irradiation, the patient experienced only Grade 1 skin toxicity.

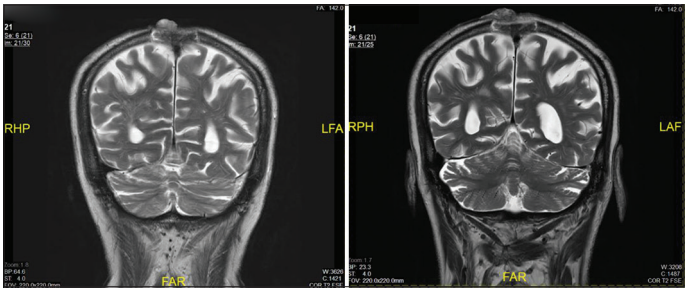

Figure 1: Magnetic resonance imaging brain at 2nd recurrence

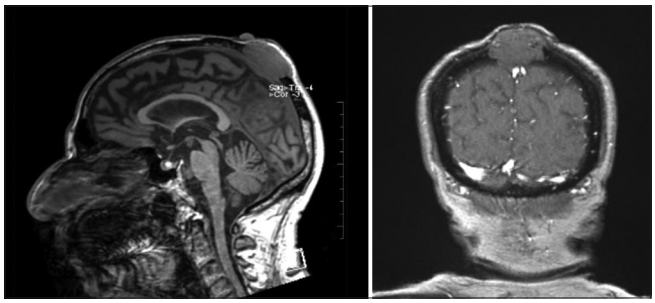

Figure 2: Magnetic resonance imaging brain with venography at 1st recurrence

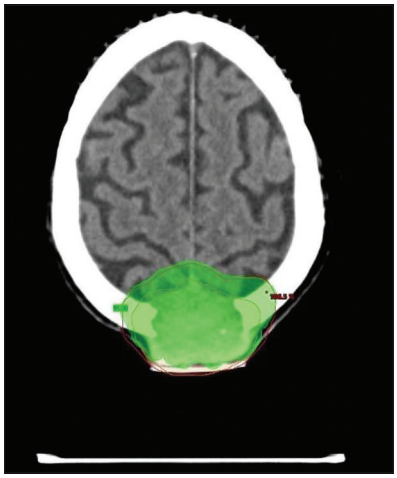

Figure 3: Visual representation of the 1st radiotherapy plan using volumetric-modulated arc therapy technique depicting the dose distribution throughout the treatment area

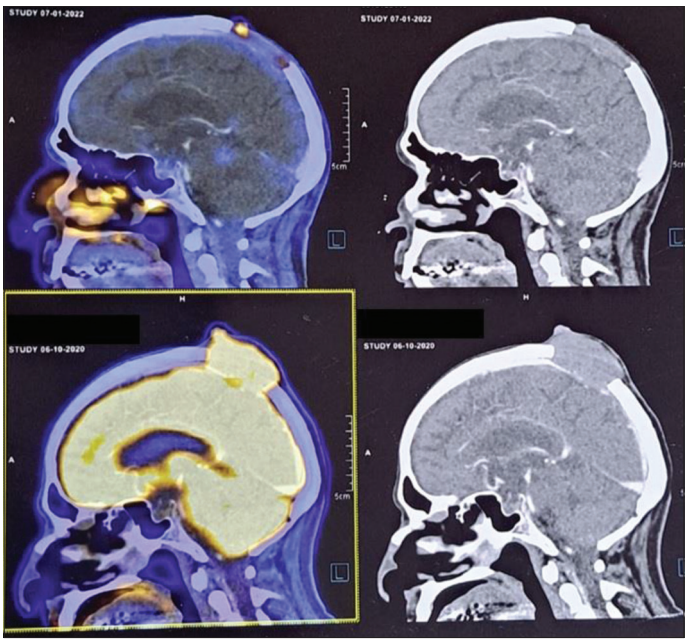

Figure 4: Whole body prostate-specific membrane antigen positron emission tomography-computed tomography done as part of staging carcinoma prostate. The bottom row illustrates pre-radiotherapy status, whereas the top row displays post-radiotherapy status indicating the response to radiation therapy

DISCUSSION

PCACC of the scalp is rare and was first reported by Boggio in 1975 [6]. Dores *et al*. in their population-based study with the highest yearly incidence rate per million population was observed in cases located on the face, head, or neck (0.16). This is followed by a lower incidence rate on the trunk (0.04) and extremities (0.02). Among cases located on the face, head, or neck, the majority were identified on the scalp and neck (33.6%), followed by the external ear (29.8%), face (23%), eyelid (8.6%), and lip (4.8%) [7]. PCACC frequently manifests in individuals during their sixth decade of life, with an average age of around 58 years, and exhibits a higher incidence among females, with a female-to-male ratio of 3 to 2 [8].

The underlying cause of PCACC remains uncertain, but it is likely driven by somatic mutations. However, the specific patterns of somatic mutations in PCACC have not been thoroughly investigated. As a result, a significant number of PCACC cases exhibit the fusion gene MYB-NFIB or demonstrate elevated levels of MYB as indicated by immunohistochemistry, implying a potential shared developmental pathway between salivary gland ACC and PCACC [9,10].

The diagnosis of PCACC relies predominantly on the examination of histological features, as there are no distinct clinical indicators for this tumor. PCACC has occasionally been misdiagnosed as metastatic lesions. Clinically, PCACC presents with a differential diagnosis that includes adenoid basal cell carcinoma and mucinous carcinoma. These entities can be distinguished through histological examination and immunohistochemistry [11]. Comprehensive clinical and radiological assessment is essential to search for indications of primary disease elsewhere, particularly in the salivary glands [12].

PCACC is characterized as a low-grade, less aggressive malignancy, and it exhibits a more favorable prognosis when compared to salivary ACC, which tends to display more aggressive behavior. While PCACC does exhibit a notable degree of local invasiveness, with most cases remaining localized within the skin, only a limited number of instances involving distant metastasis have been documented, typically affecting the lungs and regional lymph nodes [5,13]. Perineural invasion is a frequent occurrence, observed in 76% of PCACC patients, and it is linked to a recurrence rate of 46%, which is notably higher than the 22% recurrence rate observed in patients who do not exhibit perineural invasion [8]. Cutaneous ACC typically manifests as a solid, gradually enlarging, poorly outlined nodule, or mass, which can be without symptoms or may cause discomfort, itching, and subsequent hair loss [14].

The primary approach to treatment is surgical intervention, specifically with the aim of achieving tumor-free margins, which is considered the preferred treatment. The extent of surgical resection depends on tumor size, location, and proximity to critical structures. In cases where complete excision is feasible without compromising functional or cosmetic outcomes, wide local excision is preferred to ensure clear margins and reduce the risk of local recurrence. Discontinuous perineural involvement may produce false-negative margins leading to inadequate resection [3,4]. The role of Mohs surgery in preventing local recurrence has not been well established [15]. Resection of regional lymph nodes is generally not recommended in cases of PCACC without clinical evidence of lymph node metastases [6,16].

Most research studies have combined both PCACC and ACC originating from the salivary glands when investigating the potential benefits of radiation therapy. Advocates for post-operative radiation therapy argue that factors such as advanced

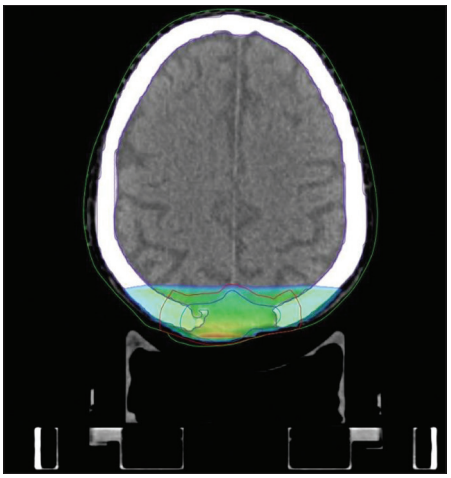

Figure 5: Visual representation of the 2nd radiotherapy plan (re-irradiation) using three-dimensional conformal radiation therapy technique (to reduce low dose spill to brain parenchyma) depicting the dose distribution throughout the treatment area

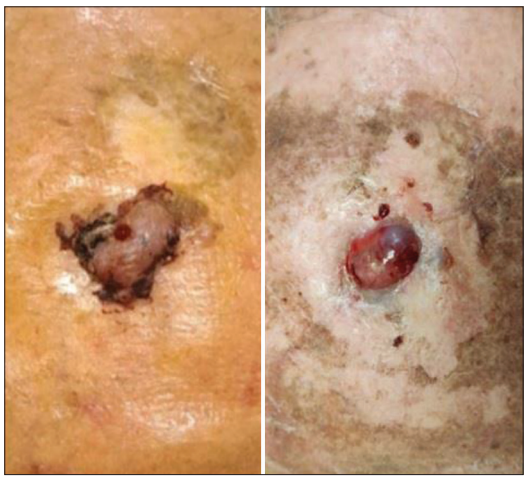

Figure 6: Clinical image displaying the status of the lesion before and after re-irradiation

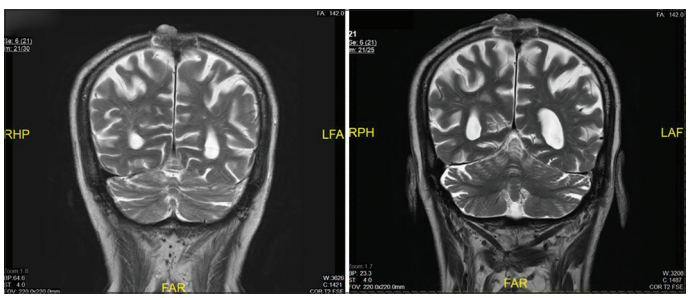

Figure 7: Magnetic resonance imaging brain prior and post-re-irradiation evaluation indicating no observable change in the size of the lesion

T-stage disease, the presence of microscopic positive margins, lymphovascular involvement, and significant nerve involvement have been identified as predictors of local recurrence. As a result, they recommend that the standard of care for ACC of the head and neck should involve a combined treatment approach, starting with surgery followed by radiation therapy administered at doses exceeding 60 Gy [17]. On the contrary, some argue that the factors mentioned earlier are all distinct variables, and there is no disparity in terms of survival, recurrence rates, or the time until recurrence when comparing patients who undergo combined therapy with those who receive surgery alone [14,18]. When patients are considered unsuitable for surgical removal due to their ability to withstand the procedure or due to the presence of locally recurring tumors, palliative radiotherapy has also been employed as an alternative approach [12]. It is imperative to select the appropriate radiation therapy technique based on the disease site. Intensity-modulated radiation therapy (IMRT) has demonstrated effectiveness in achieving uniform and precise dose distributions, enhancing target coverage while minimizing exposure to nearby organs at risk. However, in specific clinical scenarios, such as our case, opting for three-dimensional conformal radiation therapy is prudent during re-irradiation as it aims to mitigate low-dose spillage associated with IMRT, thereby optimizing treatment outcomes while minimizing potential complications.

The role of chemotherapy has not been extensively examined. Nonetheless, the gradual development of pulmonary metastases, if they occur, tends to show a favorable response to a combination of surgical intervention and polychemotherapy treatment [8]. A successful treatment approach for PCACC with pulmonary metastases has involved the use of a combination of cisplatin and fluorouracil chemotherapy [19].

CONCLUSION

Palliative treatment for ACC with radiotherapy is a feasible alternative in some patients and may offer excellent control rates with improved quality of life. In patients without surgical options, palliative radiotherapy may be successfully used. A multidisciplinary evaluation will be critical to decide the most optimal therapeutic approach for the patients.

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