Case report

Locally advanced basal cell carcinoma with complete response and long-term follow-up with vismodegib therapy

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Basal cell carcinoma (BCC) is the most common skin malignancy. For locally advanced or metastatic cases not amenable to surgery or radiotherapy, Hedgehog pathway inhibitors represent an effective treatment option. A 50-year-old female, previously treated with surgery, radiotherapy, and chemotherapy, presented with recurrent BCC invading the mastoid bone and dura. The tumor was deemed unresectable, and neoadjuvant carboplatin-docetaxel showed minimal benefit. Vismodegib 150 mg daily was initiated, resulting in significant clinical and radiological regression. Sustained disease control has been achieved for five years without major toxicity. This case highlights the durable efficacy of vismodegib in aggressive, locally advanced BCC and supports its use as a valuable therapeutic strategy when conventional modalities are not feasible.

Key words: basal cell carcinoma, vismodegib, Hedgehog pathway inhibitor.

Introduction

Basal cell carcinoma (BCC) is a common type of skin cancer originating from the epidermis and its appendages [1]. Environmental, phenotypic, and genetic factors contribute to the development of BCC. Approximately 70% of BCCs are located in the facial region due to the influence of solar radiation, while about 15% are found on the trunk. Alterations in several tumor suppressor genes and proto-oncogenes have been implicated in the pathogenesis of BCC [2]. In approximately 90% of cases, BCC development is associated with genetic alterations leading to the hyperactivation of the Hedgehog (HH) protein family signaling pathway. In mammals, there are three HH ligands: Sonic hedgehog (SHH), Indian hedgehog, and Desert hedgehog. Among these, SHH is the most extensively studied ligand. Hedgehog pathway inhibitors targeting this protein family are utilized in the treatment of basal cell carcinoma. The primary treatment modality for BCC is surgery. However, in high-risk cases where surgery is contraindicated or impractical, radiotherapy is prioritized as the primary therapeutic alternative [3]. In cases where surgical treatment is not viable, and in patients with locally advanced or metastatic basal cell carcinoma, therapeutic options include radiotherapy, systemic chemotherapy, and HH pathway inhibitors. In this case, vismodegib therapy was initiated for a patient with BCC involving brain invasion, and a sustained therapeutic response has been observed over a five-year follow-up period.

Case report

A 50-year-old female patient presented to the plastic surgery clinic approximately 15 years ago with a mass she had observed behind her ear. Histopathological evaluation following a biopsy confirmed a diagnosis

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of BCC (Figure 1), and the lesion behind her ear was excised. However, due to the detection of tumor involvement at the surgical margins, the patient underwent adjuvant radiotherapy in combination with cisplatin-based chemotherapy. After completing these treatments, she was placed under follow-up. After a 10-year disease-free interval, the patient presented with similar complaints. Recurrence was suspected, and a subsequent biopsy confirmed the presence of BCC. Imaging studies revealed findings consistent with a mass lesion causing lytic invasion of the mastoid bone, localized on the right side of the neck, anterior and posterior to the ear canal. The case was reviewed in a multidisciplinary tumor board, and the patient was deemed inoperable in her current condition. As part of neoadjuvant therapy, the patient received two cycles of carboplatin (4 AUC) and docetaxel (75 mg/m^2); however, the therapeutic response was suboptimal. Consequently, treatment with vismodegib at a daily dose of 150 mg was initiated. A significant clinical and radiological response was observed (Figures 2–4). ECOG performance status was 1 at baseline and improved to 0–1 during follow-up. Retrospective DLQI assessment indicated minimal impairment. The pa-

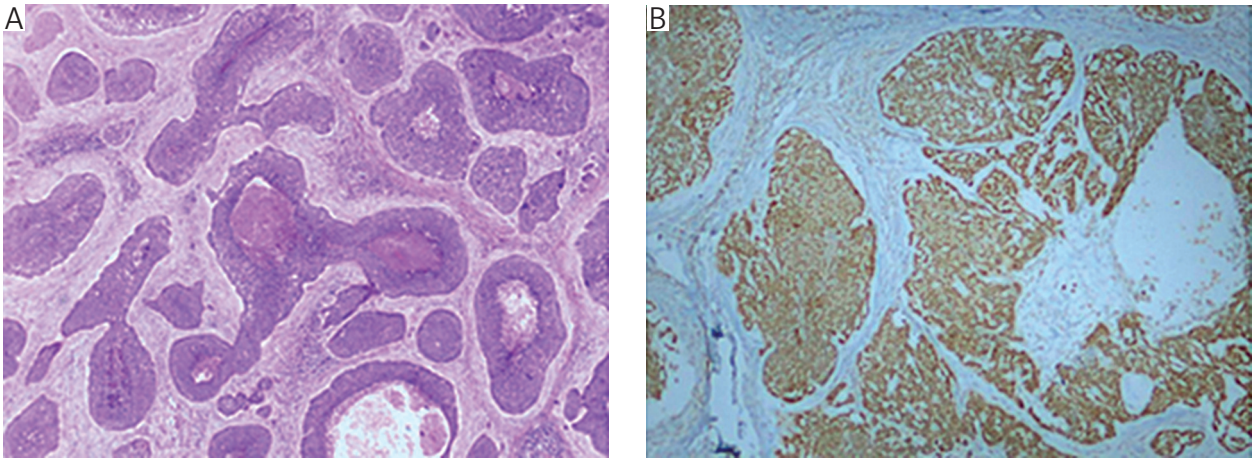

Figure 1. A tumor characterized by basaloid cell islands with fibroblastic stroma and central comedo necrosis
Staining with hematoxylin-eosin – magnification 20× and staining with p63 – magnification 20×.

Figure 2. The patient before vismodegib therapy and after vismodegib therapy for five years

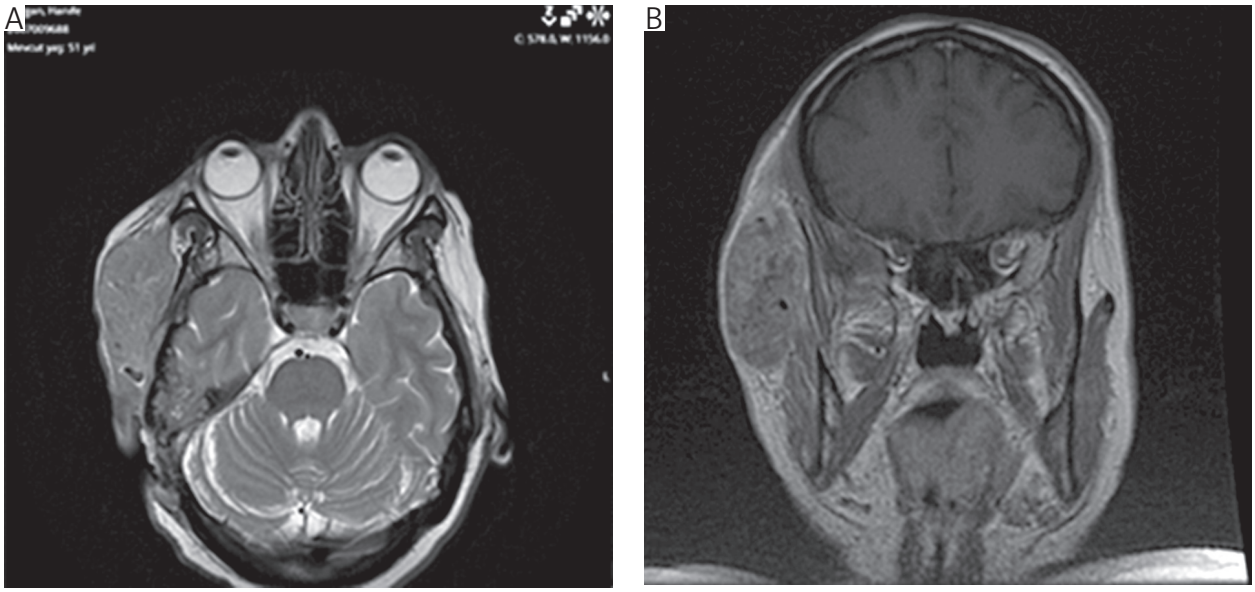

Figure 3. Axial and coronal sections of magnetic resonance imaging performed before vismodegib therapy, May 2019

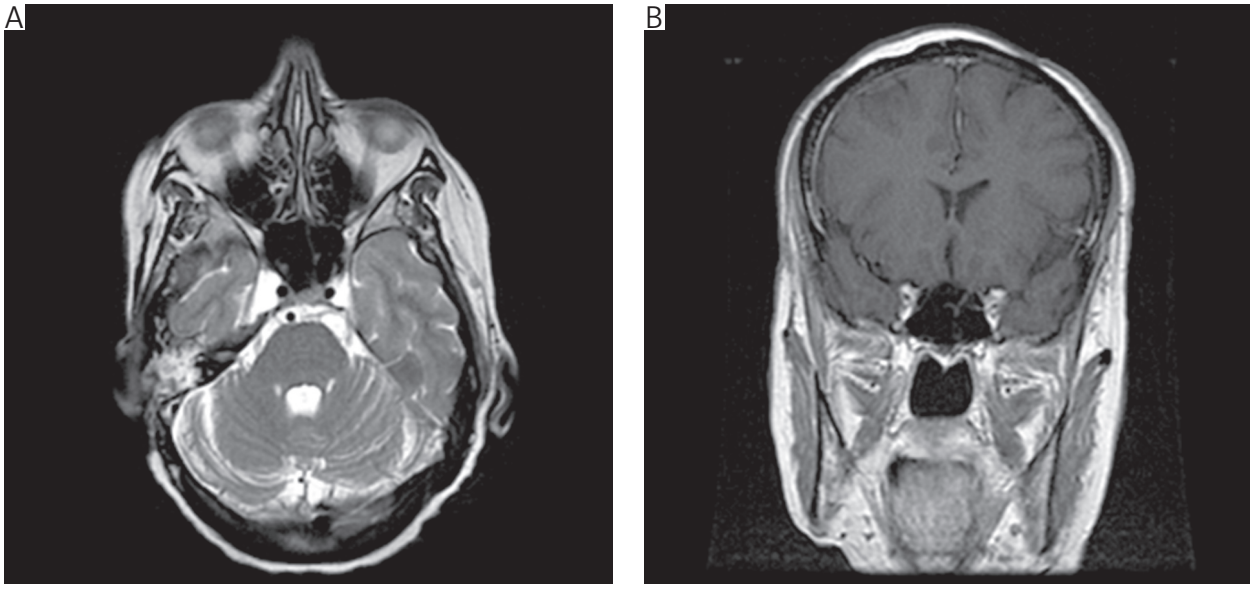

Figure 4. Axial and coronal sections of magnetic resonance imaging performed after vismodegib therapy for 5 years, August 2024

tient has been maintained on vismodegib therapy since 2019, with ongoing follow-up demonstrating sustained efficacy.

Discussion

Surgical intervention is the primary treatment modality for BCC. However, for patients with metastatic or locally advanced BCC who are ineligible for surgery or radiotherapy, the use of a SHH pathway inhibitor represents a therapeutic alternative. Vismodegib, a targeted inhibitor of the SHH signaling pathway, is approved for the management of both locally advanced and metastatic BCC.

The STEVIE trial, encompassing 1,119 cases of locally advanced BCC and 96 cases of metastatic BCC (a total of 1,215 patients), demonstrated an objective response rate of 69% in patients with locally advanced disease and 37% in those with metastatic disease. With a median follow-up duration of 18 months, the median progression-free survival was reported as 13 months for metastatic BCC and 22 months for the overall study population [4].

In an Argentinian cohort study evaluating vismodegib, 63 patients (57 with locally advanced BCC and 2 with metastatic BCC) were analyzed. Partial responses were observed in 36 patients (57%), while 10 patients (16%) achieved complete responses. Adverse events

were reported in 48 patients (76%), with the most commonly observed being muscle spasms and dysgeusia [5].

A 2023 meta-analysis, encompassing 22 studies and 2,384 patients published between 2009 and 2022, evaluated the efficacy and safety of SHH pathway inhibitors. The overall response rate (ORR) across all patients was reported as 64.9%, highlighting that the majority of patients receiving these inhibitors demonstrated partial responses. For vismodegib specifically, the ORR was calculated at 68.5% [6].

The updated BCC guidelines, published in the *European Journal of Cancer* in October 2023, recommend the use of SHH pathway inhibitors in cases of locally advanced or metastatic BCC [7].

In a separate study, patients who had discontinued vismodegib therapy due to disease progression were rechallenged with the drug. The response rate among these patients was found to be 50%, with all responses classified as partial [8].

A systematic review of 37 studies involving 435 patients with periocular BCC reported complete response rates of 20–88%, while the overall response rates were 68–100% [9].

A study assessing visual function in patients with orbital or extensive periocular BCC treated with vismodegib evaluated visual assessment weighted score (VAWS) values. The mean VAWS was 44/50 at baseline, increasing to 46/50 at three months and 47/50 at 12 months. Tumor regression was observed in 56% of patients based on physical examination and in 47% based on imaging studies (computed tomography or magnetic resonance imaging) [10].

Conclusions

In this case, the patient presented with a recurrence localized in the head and neck region 10 years post-initial treatment, with an inoperable lesion invading the dura and bone. Given these findings and the supporting evidence from the aforementioned studies, vismodegib therapy was initiated and has been successfully maintained for five years, demonstrating sustained efficacy.

Disclosures

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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