Case Report of Neoadjuvant Use of Vismodegib for Locally Advanced Periorbital Basal Cell Carcinoma: Part I

Lauren Keller, DO, PGY3; Adriana Ros, DO
Palisades Medical Center Dermatology Residency
North Bergen, NJ

Introduction

Basal cell carcinoma accounts for 90% of malignant tumors of the eyelid. Periorbital tumors are most often treated surgically with Mohs micrographic technique, or excision with frozen section determination of margins; these approaches are curative in over 90% of cases. The vast majority of basal cell carcinomas have been found to contain pathogenic alterations within the hedgehog signaling pathway, ultimately resulting in uncontrolled proliferation of tumor cells. The small molecule SMO inhibitor vismodegib, administered orally at a dose of 150 mg once daily, has recently expanded treatment strategies for patients with locally advanced basal cell carcinoma. The duration of treatment in published studies has been until disease progression, unacceptable toxicity, or discontinuation of trial.

Figure 5: After 3 months of treatment

A 64 year old Caucasian male with PMH of scarring disorder and alcoholism was evaluated by the dermatology consult team for a hemorrhagic plaque of the left lateral canthus and periorbital skin. At the time of his initial evaluation, the patient had been admitted to the inpatient psychiatric service. The patient reported that the lesion was a “basal cell,” and he recalled that it had been present for 5 to 7 years. However, due to the patient’s lack of follow up, the lesion was not identified as dry eye. The patient denied changes in vision, and denied restriction of eye movements. He reported that the lesion had slowly enlarged over many years. His primary complaint was that the lesion “stuck” to his eye.

His blood pressure was 170/100, heart rate 72, respiratory rate 14, and temperature 99.8 degrees F. He was noted to have an ulcerative plaque of the left lateral canthus and periorbital skin. The lesion was 3 cm x 2 cm in size, with a mild yellow tint and a well demarcated border. There was noted to be a mild yellow tint and a well demarcated border. There was noted to be a mild yellow tint and a well demarcated border. There was a small amount of peripheral fibrosis around the lesion. The lesion was soft to palpation, and there was no apparent ulceration or erosion. The patient denied pain, tingling, or numbness in the area of the lesion. The patient also denied muscle spasm, decreased taste, and hair loss. The patient denied visual symptoms and difficulty with eye movement. The patient also denied dry eye.

Case Report

After 2 months of treatment with vismodegib, the patient reported a decrease in hemorrhagic episodes and fibrosis. He continued to deny visual symptoms and difficulty with eye movement. The patient also denied muscle spasm, decreased taste, and hair loss. After 3 months of treatment with vismodegib, the patient exhibited improvement in terms of cosmesis and fibrosis. Notably, the patient reported no symptoms of left malar “tightness” as the third month of treatment with vismodegib concluded. On exam, chronic secondary squamous cell carcinoma was noted in the periorbital area, treated with excision with frozen section determination of margins. The patient also reported side effects of muscle cramps and decreased sensation of taste. Recent data from the STEVIE trial, which examined the safety of vismodegib with the secondary endpoint of efficacy, shows a profile consistent with previous studies. STEVIE patients received 150 mg of oral vismodegib on a continuous basis in a 28 day cycle until disease progressed, toxicity became unacceptable, or consent was withdrawn. 468 patients were included in the locally advanced BCC group and 31 patients were within the metastatic BCC group. The median duration of exposure to vismodegib for patients with locally advanced basal cell carcinoma group was 36.3 weeks. Most common side effects were muscle spasm in 64% of patients; alopecia in 62%; dyspnea in 54%; weight loss in 33%. In 9% of patients, muscle spasm led to discontinuation of the drug; 6% discontinued due to dyspnea; 5% discontinued due to weight loss and 4% discontinued due to alopecia. Fortunately, our patient’s symptoms were tolerable and did not necessitate interruption or discontinuation of treatment; however, they did contribute to the decision to facilitate surgical referral following three months of vismodegib.

Conclusions and Considerations for Further Study

Vismodegib can be safely used in the setting of locally advanced basal cell carcinoma of the orbital region, and may be successful as a neoadjuvant therapy preceding Mohs micrographic surgery. Cost considerations and medication side effects may support a shorter duration of treatment with vismodegib, as part of a treatment approach combined with Mohs micrographic surgery after reduction of tumor is achieved. Available evidence is limited regarding neoadjuvant vismodegib, but current data shows reduced surgical defect size following a minimum of therapy for three months preceding surgical intervention. Treatment with vismodegib may result in the replacement of tumor with fibrosis, which confers a new clinical challenge. As noted, further follow-up is required in this case, as the patient has been referred for surgical evaluation at the time of this writing.

References


Contact

Corresponding author:
Lauren Keller, PGY3
Palisades Medical Center Dermatology Residency
7600 River Road
North Bergen, NJ
730-989-9580
laurentkeller311@gmail.com

Physical Exam Findings

Findings prior to initiation of treatment with vismodegib and during treatment with vismodegib

Discussion

The treatment of basal cell carcinoma involving the eyelid poses challenges both in terms of cosmesis and functional preservation. Optimally, intervention would occur in an early phase of tumor growth, in this case, neglect led to locally advanced disease. Initiation of vismodegib produced clinical resolution in lesions of dimensions and extent of ulceration; however, other considerations arose during the patient’s course of treatment.

Notably, the patient reported symptoms of left malar “tightness” as the third month of treatment with vismodegib concluded. On exam, chronic superficial squamous cell carcinoma was noted in the periorbital area, treated with excision with frozen section determination of margins. Maier et al examined basal cell carcinoma tumors using non-invasive imaging techniques between weeks 9-24 of hedgehog pathway inhibitor therapy, followed by biopsy within 1-7 days of imaging. Histopathologically, pseudocystic structures were identified, with rim of basophilic cells and central density of fibrocytes; in later stages, massive fibrosis was found in place of tumor cells. Maier et al note that basal cell carcinoma that is cleared by hedgehog pathway inhibition may be replaced by scar tissue. The formation of fibrosis in the area of tumor regression may therefore present new clinical challenges, such as contracture in the region.

Our patient also reported side effects of muscle cramps and decreased sensation of taste. Recent data from the STEVIE trial, which examined the safety of vismodegib with the secondary endpoint of efficacy, shows a profile consistent with previous studies. STEVIE patients received 150 mg of oral vismodegib on a continuous basis in a 28 day cycle until disease progressed, toxicity became unacceptable, or consent was withdrawn. 468 patients were included in the locally advanced BCC group and 31 patients were within the metastatic BCC group. The median duration of exposure to vismodegib for patients with locally advanced basal cell carcinoma group was 36.3 weeks. Most common side effects were muscle spasm in 64% of patients; alopecia in 62%; dyspnea in 54%; weight loss in 33%. In 9% of patients, muscle spasm led to discontinuation of the drug; 6% discontinued due to dyspnea; 5% discontinued due to weight loss and 4% discontinued due to alopecia. Fortunately, our patient’s symptoms were tolerable and did not necessitate interruption or discontinuation of treatment; however, they did contribute to the decision to facilitate surgical referral following three months of vismodegib.

Furthermore, cost considerations may favor a combined approach, as we recommended for our patient. Current estimates place the cost of vismodegib at $5700 per month, with the surgical treatment of basal cell carcinoma typically costing $2000 or less. The experience of Alcalay et al, who report two cases of neoadjuvant vismodegib prior to Mohs surgery, indicates successful surgical result following a six month course of treatment with hedgehog pathway inhibitors. Ally et al. in their open-label study of 11 patients treated with vismodegib preceding Mohs technique for basal cell carcinoma, found that the surgical defect size was reduced by 27% in those patients who took vismodegib for three or more months. Therefore, a three month course of treatment followed by prompt Mohs micrographic surgery may result in improved outcomes for patients with cosmetically and functionally sensitive tumors, as well as decrease overall expense of treatment. At the time of this writing, our patient had completed three months of vismodegib therapy and Mohs surgical referral had been placed, but surgical evaluation was not yet completed. The decision to continue vismodegib in the interim was made, since the side effects were not significantly impacting the patient’s quality of life or overall health status.

We await histopathologic findings and final surgical result in order to fully evaluate the success of neoadjuvant vismodegib in this patient’s case.