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Case Report

Synergistic Effect of Concurrent Radiotherapy with Adjuvant Vismodegib on Aggressive Intracranial and Orbital Invasion with Basal Cell Carcinoma of Scalp

Bahram Eshraghi and Babak Masoomian*

Oculoplastic and Ocular Oncology Service, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran

***Corresponding Author:** Babak Masoomian, Oculoplastic and Ocular Oncology Service, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract

The purpose of this study is to report a case with visual loss eye secondary to intracranial and orbital spreading of scalp Basal cell carcinoma (BCC) in which provided amazing response to combination of radiotherapy and oral Vismodegib. A 69-years-old man 3 years after invasive scalp BCC excisional biopsy and radiotherapy presented with a gradual decrease in his vision, proptosis and limited ocular motilities in his left eye. Magnetic resonance imaging revealed 360 encircle thickening with soft tissue enhancement around left orbital apex and whole cavity. Orbital biopsy showed subperiostal extension of BCC that was extended to frontal bone. Two weeks after surgery the patient's left eye vision dropped quickly to the level of light perception. He underwent stereotactic radiotherapy adjuvant with 150 mg daily oral Vismodegib at the same time. Due to gastrointestinal problems, the patient refused to take vismodegib beyond 2 months. One year later, despite incomplete treatment, the vision of left eye was 20/200 and no recurrence was detected clinically or by imaging.

Keywords: Basal Cell Carcinoma; Intracranial Invasion; Radiotherapy; Vismodegib

Introduction

Basal-cell carcinoma (BCC), is the most common type of skin cancer [1]. Approximately 1 million new cases occur annually in the United States, with increasing incidence [1]. This cancer often appears as a raised area of skin, with small blood vessels running over it; or it may present as an ulceration nodules [1]. Basal-cell carcinoma is a slow growing tumor and can damage the tissue around. It is unlikely to spread to distant areas or to result in death [2] and for these advanced BCC cases; it is not easy to determine optimal treatment [2,3]. As vismodegib has been introduced recently for systemic therapy of BCC, it would be important to address how to best integrate this new treatment modality with other existing therapy [4-6]. Here in we report a patient with skin BCC of scalp that tumor extended to intracranial and orbital apex tissue and patient successfully managed with using novel combination of vismodegib and concurrent radiotherapy. The inform consent to publish these findings and images were taken from the patient.

Case Report

A 69 years-old white man referred to our ocular oncology clinic due to proptosis and gradual decreased visual acuity in his left eye. He had history of non-healing ulcerative lesion on the top of the head (about 20 cm far from eyebrow) for 7 years. He finally underwent a wide tumor excisional biopsy and due to periosteal involvement, local radiation therapy was performed for him about 3 years before. The patient was asymptomatic until suddenly he felt decrease visual acuity and mild proptosis in his left eye (OS). At this time, visual acuity was 20/25 in right eye (OD) and 20/100 in OS. Related afferent pupillary defect was significantly positive for his left eye. In slit lamp examination there was mild chemosis and fundus examination was unremarkable. There was also limitation of left eye ocular motility especially in abduction. In neurologic examination, patient had skin numbness in his left side of face and lips. Based on these findings we thought about orbital apex syndrome of left eye so, we prescribed brain and orbital MRI with contrast injec-

tion. In MRI pictures, there was noticeable 360 encircle thickening with soft tissue enhancement around orbital bony structure in her left eye (Figure 1). A lid crease orbitotomy approach was done for patient that revealed a subperiostal fragile mass with extension to frontal bone. Pathology report demonstrated incomplete resected BCC tumor. Two week later, the vision in OS decreased suddenly to light perception with remarkable positive Marcus gunn reflex and significant limitation in ocular motilities. After consult with radio-oncologist, patient underwent 50 rad stereotactic radiotherapy in 20 fractional doses for his left orbital tissue. At the same time, 150 mg daily oral Vismodegib was prescribed for him.

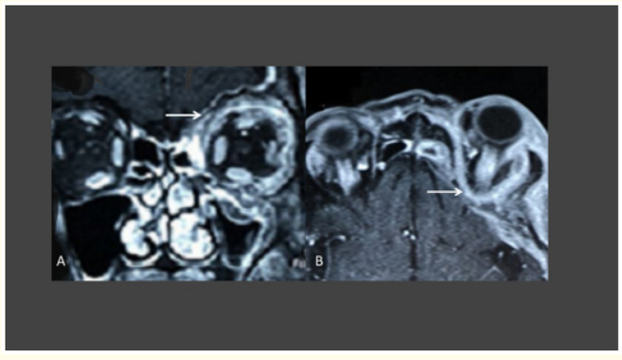

Figure 1: In T1 weighted fat suppression MRI after contrast injection, both coronal (A) and axial (B) views, demonstrating encircle significant thickening (arrow) around orbital cavity with soft tissue enhancement. There is not any invasion into the orbital cavity.

After 2 months, left eye vision was 20/400 and remarkable improvement in proptosis and ocular motility happened. Due to gastrointestinal problems, patient denied continuing oral vismodegib beyond 2 months. One year later, patient's visual acuity was 20/200 in his left eye and no recurrence was detectable clinically or in MRI pictures (Figure 2).

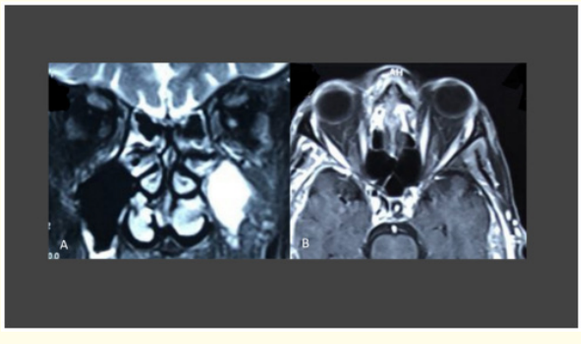

Figure 2: In MRI pictures of same patient 1 year after concurrent treatment with radiotherapy and vismodegib consumption, there is no remarkable thickening and enhancement after contrast injection (A and B).

Discussion

Basal cell carcinoma (BCC) usually develops on skin that gets sun exposure, such as on the head, face, neck, or back of the hands [1]. This type of skin cancer grows slowly but, treatment is important because BCC can grow wide and deep, destroying skin, tissue, and bone. About 90% of BCCs occur on head and neck area with low mortality rate (< 0.1%). So, complete resection of tumor is curative mostly. When tumor is large in size and invade deep structures, can be challenging for successful treatment [3].

Basal cell cancer is slow growing tumor and it is well-known fact that local invasion or metastasis by BCC is rare with approximate incidence about 0.03% [3]. The surgeries of skull bone defects with BCC are problematic by the fact, 53% of reported literature cases finally have recurrence [7]. Recurrence in scalp skin could be hazardous because this tumor have a tendency to proliferate surreptitiously along embryologic fusion lines destructing bones and eventually spreading to intracranial area [7].

There are a few reports of intracranial invasion from a scalp BCC that usually happens by intra-osseous and intra-dural spread. In all cases, there were locally advanced ulcerative lesions that mostly neglected by patients or patients has lost to follow-up [8-10]. As we mentioned before, our patients had his scalp lesion about 7 years before seeking dermatologist visit and intervention. For aggressive BCC with infiltration of deeper tissue, the standard therapy is the complete local excision of the lesion, histopathological evaluation and tight dermatological follow up of course, in some patients radiotherapy and chemotherapy are indicated and necessary [10].

Radiation-therapy (RT) has been used since long time before for treatment of cutaneous malignancies including BCC. Indication for treatment is primary curative, primary palliative for advanced or even metastasis BCC or postoperative curative for incomplete excised lesions [11]. The 5-year cure rate for typical BCC lesions treated with RT is about 84 - 96% but, this rate seems to decrease significantly with large and aggressive lesions to as low as 55% [12]. Radiotherapy is important modality treatment following diagnosis of orbital and intracranial involvement with BCC (advanced disease). Such patients apparently are not curable but adequate dose (50 Gy or more) should still be delivered to involved area.[11,12] Otherwise, radiotherapy more than CNS tolerable doses (50 - 60 Gy), may be associated with late CNS toxicity and necrosis [12]. So, it look like that, in severe advanced BCC cases, especially patients with recurrent disease, metastasis and intracranial involvement, treatment with combination of surgery and radiation may not be enough.

Until recently, there was no approved systemic therapy for BCC treatment but, response to systemic vismodegib for metastatic (30%) and locally advanced BCC (43%) was promising [4]. This

drug is a first-in-class FDA approved Hedgehog signaling pathway targeting agent that given once daily. Vismodegib has shown clinical efficacy for treatment of patients with advanced BCC who have failed prior treatment with surgery or/and radiation [4,5]. There are limited data that demonstrate acceptable result from combination of radiotherapy with Hedgehog signaling pathway inhibitors. For example, in esophageal cancer, vismodegib prescription was reported to increase radio-sensitivity [5]. Recently, the effectiveness of Concurrent prescription of vismodegib and radiotherapy for advanced BCC, has been shown in few separate case reports [4,5]. It seems that addition of systemic vismodegib can increase the effective of radiation.

In our patient, due to recurrence and aggressive nature of tumor (intracranial extension) and lower cure rate for such cases, we chose combination of modalities for treatment. The median duration of treatment with vismodegib has been recommended 7 to 11 months by different reports [5,6]. As we mentioned, our patient only took this medication for 2 months so, it seems that, even the short term usage of vismodegib along with standard radiotherapy could be helpful.

According to the authors of this report, our patient has several unique features that make the report valuable including: the distance between primary BCC tumor and the recurrence site, mysterious subperiostal expansion of tumor before vision loss and dramatic response to concurrent prescription of radiotherapy with oral vismodegib even with short time consumption.

Conclusion

In conclusion, advanced BCC on the scalp, could produce extensive skull and intracranial invasion if left unchecked so, follow up care with CT or MRI seems necessary to evaluate early sign of skull and intracranial invasion. In such cases, treatment should be considered multidisciplinary including combination of local (radiotherapy) and systemic (vismodegib) therapy. Of course, to determine the definite treatment plan, further prospective studies are needed in the future.

Disclosure

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