CASE REPORT

Rapid response to vismodegib in a patient with advanced basal cell carcinoma

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Key words: basal cell carcinoma; clinical benefit; Hedgehog signaling pathway; rapid response; vismodegib.

INTRODUCTION

Basal cell carcinoma (BCC) is the most common form of skin cancer, making up approximately 80% of all nonmelanoma skin cancers.[1] Traditional therapy includes various types of surgery (Mohs, cryosurgery, excision, electrodessication and curettage), topical therapies (5-fluorouracil, imiquimod), or radiation therapy. A new and effective treatment, vismodegib, became available recently. The mechanism of action of vismodegib is based on inhibition of the Hedgehog pathway, which is responsible for cell growth in more than 90% of BCC cases.[2] Response rates of 30% in metastatic disease and 43% in locally advanced disease, with complete response in half the patients with locally advanced disease, have been reported.[3]

Despite the large amount of data concerning response rate and response duration of this Hedgehog signaling pathway–targeting agent, there is no published information about time to response. This information is often requested by patients before treatment commences. The current case of locally advanced BCC, which responded quickly to treatment with vismodegib and showed signs of wound healing at the first assessment after 4 weeks, represents the type of information that patients request before treatment initiation.

CASE REPORT

A 45-year old man presented with a large, 7- × 13-cm, ulcerated lesion on his forehead, with extension to the left fronto-parietal region (Fig 1, *A*). The lesion had progressed over 8 years and had never been treated. Biopsy results showed BCC with keratotic differentiation. There was no history of family-related skin cancers, and no other suspicious lesions were detected on physical examination. Total body computed tomography scan found involvement of the underlying bones but no signs of distant spread.

Abbreviation used:

BCC: Basal cell carcinoma

The patient was started on treatment with vismodegib on 15 October 2013 at a standard dose of 150 mg once daily. On evaluation 4 weeks later, there was remarkable improvement, with a visible decrease in tumor size, signs of healing in the periphery (Fig 1, *B*), and minimal side effects, including grade 1 hair loss and fatigue.

Four months after treatment initiation, the patient experienced complete clinical response with a well-healed scar and small regions of residual crusts in the region where the giant tumor ulcer had previously persisted (Fig 1, *C*).

The patient continued the treatment with mild side effects, all grade 1, including alopecia, decreased appetite, muscle spasm, and fatigue, without any evidence of active disease in the previously involved area. Although the patient achieved complete clinical remission, it was not confirmed histologically (Fig 1, *D*). He is still in remission after 18 months of treatment.

DISCUSSION

According to previously published data from the ERIVANCE phase II trial, the most robust source for accurate information regarding drug efficacy and common adverse events, the first clinical evaluation of patients was conducted at 8 weeks of therapy, and most patients exhibited some degree of tumor

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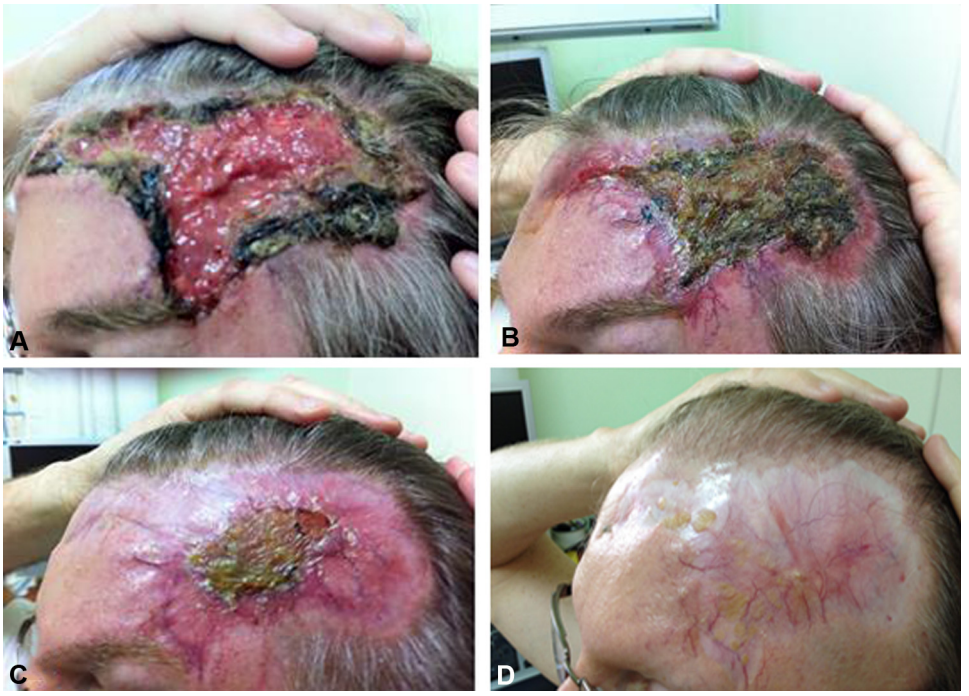

Fig 1. **A**, The lesion at treatment beginning. **B**, The lesion after 4 weeks of treatment. **C**, The lesion after 4 months of treatment. **D**, Complete clinical response after 8 months of treatment.

shrinkage at that time. From the range of response duration, 1.4 to 16.8 months, we learn that some of the responses accrued very quickly. Common adverse events observed in studies of vismodegib are hypothesized to be mechanism related. These events include muscle spasms (any grade, 68%; grade 3-4, 4%), dysgeusia (any grade, 58%; grade 3-4, 0%), alopecia (any grade, 63%), fatigue (any grade, 36%; grade 3-4, 4%), and weight loss (any grade, 46%; grade 3-4, 5%).[3] In a recent publication evaluating the clinical benefit to patients with locally advanced BCC in the ERIVANCE trial, 76% had clinical benefit, significant in 65%. The system of response assessment based on expert clinical judgment was found to have a high degree of interpanelist agreement and provided strong evidence that treatment with vismodegib results in clinically meaningful and durable responses in patients.[4] However, tumor recurrence after treatment cessation was reported in most of the cases.[5] In the most sensitive patient population, those with basal cell nevus syndrome, all carrying the *PTCH1* mutation that predisposes them to developing hundreds of BCCs, a reduction in the number of new surgically eligible BCC was seen after 1 month of treatment with vismodegib.[6]

The current case presents a good example of dramatic response with visible tumor shrinkage and wound healing in an unusually short period. Most of the patients with locally advanced BCC are old, and many fear starting new medications, preferring to delay treatment initiation. The information that healing is seen relatively rapidly can help patients in their decision making.

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