

Oral smoothed inhibitor for advanced basal cell carcinoma of the hand: a case report

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Introduction

Smoothed inhibitors have recently emerged as a nonsurgical, targeted therapy for treating advanced basal cell carcinomas (BCC) [8]. This novel small-molecule drug class suppresses Hedgehog pathway signaling by binding the membrane protein, Smoothed [7, 9]. Dysregulation of Hedgehog signaling is a hallmark of BCCs and is thought to play an integral role in maintaining cancer growth [1]. Treatment of locally advanced and metastatic basal cell carcinomas with the Smoothed inhibitor vismodegib demonstrated a 40–50 % response rate in Phase I and II trials, paving the way for FDA approval in early 2012 [10]. This therapy is most useful in patients for whom surgical resection is difficult or contraindicated due to tumor size, location, recurrence after surgery, or co-morbid medical conditions. Here, we report a case of a 43-year-old man with numerous and large BCCs of the hand that led to significant disability. The extent of disease suggested that surgical treatment might result in unacceptable functional results. There was involvement of a significant portion of the surface of the hand, and surgical excision would have created a large soft tissue defect requiring skin grafting, with the potential for scar formation, contractures with limitation of motion, and poor aesthetic outcome. Management with oral vismodegib resulted

in dramatic tumor regression, with good functional and aesthetic results.

Case Report

A 43-year-old Caucasian man with a known history of genetic predisposition to BCC presented with multiple large ulcerated, biopsy proven BCCs on his head, trunk, arms, and legs [2]. In particular, he noted the inability to type on a keyboard, drive a car, or carry out activities of daily living due to the large BCCs studding his dorsal hands, including some that traversed the joints. He had a 2.5-cm multilobular BCC on the distal tip of the left small finger (Fig. 1a).

After a discussion of his treatment options, the patient elected to begin therapy with oral vismodegib 150 mg daily, due to the size and extent of his tumors. After 1 month, shrinkage of all of the BCCs was apparent (Fig. 1b). After 6 months of treatment, the BCCs had regressed further, with the lesion on the distal fifth digit receding the slowest (Fig. 1c). Continued treatment led to further BCC shrinkage (Fig. 1d). Due to his vismodegib treatment, he regained the ability to carry out activities of daily living, with good functional and aesthetic results. While there are visible scars in areas of previous BCC, the patient reported no limitation in hand movement. In addition, several areas of erosion and erythema were persistent at 3 years and 4 months of follow-up, including the web space between the third and fourth digits, suggesting that a small amount of residual BCCs remained. However, the patient declined biopsy in the absence of lesion growth. He continues to be monitored with full body skin examinations every month for BCC chemoresistance.

Over the course of treatment, the patient experienced commonly reported side effects, including hair loss and mild muscle cramping in the legs. He did not require treatment for his muscle cramping. Otherwise, the drug was well tolerated.

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Fig. 1 **a** Bulky BCC tumors on dorsal hands and fingers prior to treatment with vismodegib. **b** After 4 weeks of vismodegib therapy, shrinkage of the BCCs was clinically evident. **c** After 6 months of

vismodegib therapy, the BCCs continued to regress. **d** After 3 years of vismodegib therapy, the BCCs were nearly eradicated without surgery. **a** has previously been published in Gomez-Ospina et al [2]

Discussion/conclusion

In conclusion, we present this case to illustrate the utility of a new targeted therapy, oral Smoothened inhibitor treatment, for BCCs of the hand that are not amenable to surgical resection. While surgical excision of the majority of small BCCs is highly effective, with 2- to 5-year recurrence rates of under 5 % for margins of 2–5 mm [3], patients with multifocal, extensive and/or large tumors may not be good candidates for surgical treatment. Although other treatment modalities such as radiotherapy may be considered for these complex cases, there are still long-term risks for secondary cancers and scarring [4–6].

Currently, the response rate of advanced BCCs of the hand compared to those of other anatomic locations is not known. In the largest study of vismodegib for BCCs published to date, a phase II clinical trial, the independently reviewed objective response rate for locally advanced BCCs were 43 % [8], and included BCCs of various anatomic locations.

We highlight three noteworthy aspects of the clinical management in this case. First, definitive diagnosis of the tumor by histopathology is essential prior to initiation of Smoothened inhibitor therapy, since other cutaneous malignancies such as squamous carcinomas have not been reported to be dependent on the Hedgehog signaling pathway [11]. Second, tumor shrinkage can be apparent early in the treatment course. Our patient's BCCs visibly decreased in size within 1 month of starting vismodegib but did not achieve maximal regression until 3 years of drug usage. Third, Smoothened inhibitor treatment can produce durable results without significant scarring or functional sequelae that might occur after surgical treatment.

Further studies are under way to assess the use of Smoothened inhibitors to shrink BCCs preoperatively and/or in combination with other treatment modalities. In cases where Smoothened inhibitors alone fail to cure the disease or to arrest tumor growth, improved outcomes may be achieved with concomitant surgery or radiation therapy.

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Statement of human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of informed consent Informed consent was obtained from all patients for being included in the study.

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