ABSTRACT

In the absence of universally accepted staging systems, the assessment of both basal and squamous cell carcinomas presents a formidable challenge. The NCCN Guidelines, which reflect the most up-to-date, evidence-based data relating to the evaluation and management of these nonmelanoma neoplasms, provide criteria for their risk stratification. Moreover, the current treatment algorithms discussed to aid in risk category–based clinical decision-making. Case reports demonstrate the practical application of the NCCN Guidelines and highlight the importance of a multidisciplinary approach.

“For patients with basal cell carcinomas [BCCs] or squamous cell carcinomas [SCCs], staging is challenging,” commented Jeremy Bordeaux, MD, MPH, Professor, Department of Dermatology, School of Medicine at Case Western Reserve University; Director, Mohs Micrographic and Dermatologic Surgery, University Hospitals Cleveland Medical Center; Director, Melanoma Program, University Hospitals Cleveland Medical Center; and Chair of the NCCN Guidelines Panels for BCC and SCC. At the NCCN 2024 Annual Conference, he identified characteristics of each risk status classification, reviewed the corresponding treatment options, and presented relevant case reports.

Basal Cell Carcinoma

Staging and Risk Stratification

“Not all BCCs are the same,” commented Dr. Bordeaux. Drawing on examples of a <1-cm superficial BCC compared with a deeply infiltrative BCC, he stated, “What these 2 cancers need is very different.”

“It is hard to get information on BCCs, [because] we don't have any large databases,” Dr. Bordeaux remarked. “We don't even know how many [cases] there are each year in the United States.”

There has been an attempt to implement T staging systems. AJCC provides guidelines for head and neck cancers, albeit not specifically designed for BCC. In 2021, Brigham and Women’s Hospital introduced a novel T staging system for BCC. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) stratify BCCs into 4 categories: low risk, high risk, locally advanced disease, and initial presentation of regional or distant metastatic disease. Dr. Bordeaux acknowledged that approximately 99% of cases fall into the first two categories. “The main thing we are doing with BCCs is differentiating between low-risk and high-risk disease,” he stated.

Within the framework of the NCCN Guidelines are criteria for the stratification of low-risk versus high-risk BCC (Figure 1). In particular, tumor location and size, tumor borders, history of recurrence, immunosuppression, history of radiation therapy (RT), histologic subtype, and whether there is perineural invasion should be considered.

Treatment Options

“[Patients with low-risk BCC] can be treated in multiple ways,” Dr. Bordeaux explained. Among the recommended options in the NCCN Guidelines are “scrape and burn” (curettage and electrodesiccation), shave removal, and standard excision with 4-mm clinical margins without tissue rearrangement. Nonsurgical candidates may be treated with RT, topicals, photodynamic therapy, or cryotherapy.

“For patients with high-risk disease, we are going to do Mohs micrographic surgery or some form of margin control. [Or], if we don't have that, we can do excision with wider margins ... [without] tissue rearrangement,” Dr. Bordeaux remarked. “For patients who are nonsurgical candidates, we can do a multidisciplinary consult and consider definitive RT.”

Advanced Disease

Per the NCCN Guidelines, advanced BCCs may be classified as locally advanced, nodal, or metastatic. “If you have
a patient who has [metastatic or nodal] BCC, you need to recheck your pathology 2 or 3 times and have someone else look at it,” Dr. Bordeaux commented. These types of disease are rare and often misdiagnosed, he noted. “If you do find yourself in the true situation where you have metastatic or nodal disease, you are going to want to do a multidisciplinary consultation … and you are going to talk about RT, systemic therapy, or a clinical trial.”

In locally advanced disease, surgery and/or RT may not result in a cure or could possibly produce significant functional limitation; thus, multidisciplinary consultation is recommended. Systemic therapy is indicated when the aforementioned treatment options aren’t deemed feasible.

**Locally Advanced BCC: Case Reports**

The case of an 80-year-old woman with locally advanced BCC of the left upper eyelid and forehead was presented. Both CT and MRI did not reveal any evidence of bony or orbital invasion. Dr. Bordeaux performed Mohs micrographic surgery, which resulted in a defect with exposed bone of the forehead; he used a galeal/periosteal flap to cover the bone before placing a full-thickness skin graft. The patient declined postoperative RT and has since been under the regular monitoring of a general dermatologist for approximately 5 years.

Dr. Bordeaux subsequently presented the case of a woman with locally advanced BCC over the scapula who was undergoing treatment with the Hedgehog pathway inhibitor vismodegib. She had a history of positive margins following excision but had not undergone definitive surgery; thus, Dr. Bordeaux performed Mohs micrographic surgery, revealing no bony invasion. The patient declined postoperative RT in favor of a “natural” approach. After approximately 3.5 years, she presented with recurrent disease and again declined radiation and systemic therapies. During surgery, Dr. Bordeaux noted infiltration into the scapula. “After a tumor board meeting[,] we treated her with PD-1 inhibition …. Then she underwent RT,” he commented. “She has been healed [for approximately 2 years].”

### Squamous Cell Carcinoma

Dr. Bordeaux noted that, akin to BCC, staging of SCC presents challenges; he briefly referred to the relevant AJCC, Brigham and Women’s Hospital, and Salamanca T staging systems. Given these protocols, the NCCN Guidelines stratify SCCs into 3 risk categories: low, high, and very high. The risk factors for classification appear similar to those of BCC, with the additional considerations of growth rate, neurologic symptoms, and risk based on pathology.

“Scrape and burn,” shave removal, and standard excision may be considered for the treatment of low-risk patients, per the guidelines. Mohs micrographic surgery is also an option, but Dr. Bordeaux noted it is “usually not needed.” Patients who decline surgery are recommended to undergo RT. “For low-risk SCC, [the primary treatment options are] all the same as for low-risk BCC, except we are not using topical [or] light therapies,” he said.

For the treatment of patients with high-risk or very high-risk disease who have a high likelihood of cure, “we can consider doing a sentinel lymph node biopsy [followed by] Mohs micrographic surgery or peripheral margin control, [or] standard excision with larger margins,” according to Dr. Bordeaux. “We can also consider definitive RT for our nonsurgical candidates.”

Regarding treatment planning for patients with very high-risk disease and a significant risk of extensive local recurrence or nodal metastasis, the NCCN Guidelines recommend radiologic staging. Furthermore, akin to the approach for those with a high likelihood of cure, sentinel lymph node biopsy may be considered. “With newer data, we can [also] consider neoadjuvant therapy with cemiplimab-rwlc after tumor board discussion,” Dr. Bordeaux added.
Case Reports
Dr. Bordeaux discussed the case of a man with chronic lymphocytic leukemia (CLL), which was undiagnosed at the time, who presented with a lesion on the dorsal forearm. It met the following NCCN criteria for very high-risk SCC: >4 cm clinically, poorly differentiated, >6 mm in depth, invasion beyond the fat, significant perineural invasion, and lymphatic or vascular invasion. Based on imaging, the tumor had not infiltrated the bone.

“This was before the data for neoadjuvant PD-1 inhibition had come out, so that was not an option at the time,” Dr. Bordeaux explained. “If he presented at this point, it is something we definitely would think about.”

The patient underwent Mohs micrographic surgery, during which Dr. Bordeaux noted muscular invasion, followed by a skin graft procedure. RT was subsequently delivered.

“His arm is doing okay, but then he developed Merkel cell carcinoma,” Dr. Bordeaux commented. “He is still living with metastatic disease.”

The final case focused on a 71-year-old man with a history of rheumatoid arthritis and remitted lymphoma who presented with recurrent SCC on the forehead. He previously underwent Mohs micrographic surgery, after which the defect was repaired with a paramedian forehead flap. A few months later, the patient noted a scaly plaque extending from the flap, which ultimately expanded to encompass the entire nasal dorsum, nasal root, glabella, and bilateral nasofacial sulci. He opted to undergo Mohs micrographic surgery, one of several options proposed during a multidisciplinary conference; clear margins were achieved. Dr. Bordeaux and his colleague published the techniques used to repair the final defect.

Given the history of recurrence after surgery, he stated, “We wanted to act as soon as possible.” The patient had 2 pedicles feeding his nose, which reportedly needed to remain in place for 4 to 6 weeks. He received PD-1 inhibition as a bridge until RT could be safely delivered and reconstruction could be completed.

“This was a truly multidisciplinary team effort,” Dr. Bordeaux concluded. “There is no way we could’ve done this without all of us and all of our specialties.”

Disclosures: Dr. Bordeaux has reported no relevant financial relationships.
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References