Basal cell carcinoma: Additional subtypes and therapeutic advances

To the Editor: Cameron et al provided a superlative comprehensive review of basal cell carcinoma (BCC).[1,2] In addition to summarizing most of the clinical and histologic subtypes of BCC, they also introduced some of the systemic therapies for this tumor. For completeness, less common—but equally important—clinical and histologic subtypes of BCC, as well as recent advances in the management of advanced and metastatic tumors, are presented in this report.

Red dot BCC is a unique clinical variant of BCC that presents as a solitary small red macule or papule that morphologically mimics a telangiectasia or angioma. These carcinomas might blanch after diascopy, when a glass microscope slide is pressed against them. Noncontact dermoscopy can be helpful in differentiating this tumor from a benign vascular lesion; angiomas appear as well-demarcated red, maroon, blue, or black lacunae. In contrast, one would also expect to see the dermoscopic features observed in nodular and superficial BCC (ulceration, blue-gray globules, blue-gray ovoid nests, leaf-like areas, spoke wheel areas, white shiny structures, and vascular patterns [such as arborizing vessels and short fine telangiectasias and, less commonly, hairpin, glomerular, dotted, comma, and polymorphous vessels]) during dermoscopy of a red dot BCC. Mohs surgery is the treatment of choice because the cancer's lateral spread is often beyond the clinical margins of the neoplasm.[3]

Pleomorphic BCC is a distinctive pathologic variant of BCC. The tumor is partially composed of mononuclear or multinuclear giant cells containing nuclei that are not only irregularly shaped and hyperchromatic but also 2-10 times larger than the nuclei of the adjacent cancer cells. The clinical course of pleomorphic BCC is similar to BCC without pleomorphic giant tumor cells.[4]

Recent investigation into the genomic landscape of advanced and metastatic BCC has not only confirmed the benefit of precision treatment with targeted therapies, such as smoothened (SMO) inhibitors—vismodegib and sonidegib —and GLI inhibitors, but also demonstrated efficacy with novel therapeutics that block immune checkpoints, such as programmed cell death protein 1 (PD-1) and programmed death ligand 1 (PD-L1) inhibitors.[5] For example, an exceptional response to anti-PD1 therapy with nivolumab was observed in a man with BCC and hepatic metastases; next-generation sequencing of his tumor showed both a high mutation burden (103 mutations per megabase) and genomic amplification of PD-L1.[6] Subsequently, after achieving near-complete remission with nivolumab, new primary cutaneous BCCs (with a lower tumor mutational burden —45 mutations per megabase —than his metastatic disease) appeared while he continued to receive immune therapy, and the ongoing response of his metastatic tumor persisted. This clinical scenario demonstrated that although the treatment with targeted and cytotoxic therapies might be better for patients with genomically less complex tumors, immunotherapy might be more appropriate for individuals with advanced BCCs.[7]

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