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Lindsay C. Strowd

Update on Current Treatment Recommendations for Primary Cutaneous Melanoma **397**

Jessica Dowling, Sean P. McGregor, and Philip Williford

Primary cutaneous melanoma describes any primary melanoma lesion of the skin that does not have evidence of metastatic disease. This article reviews the current workup, treatment, and follow-up recommendations for primary cutaneous melanoma (stages 0, I, and II). Specific attention is focused on recent updates with regard to staging, sentinel lymph node biopsy, and surgical modalities.

Systemic Therapies for Advanced Melanoma **409**

Leonora Bomar, Aditi Senithilnathan, and Christine Ahn

The incidence of metastatic melanoma continues to increase each decade. Although surgical treatment is often curative for localized stage I and stage II disease, the median survival for patients with distant metastases is less than 1 year. The last 2 decades have witnessed a breakthrough in therapeutic options with the development of immune checkpoint inhibitors, small molecule targeted therapy, and oncolytic viral therapy. This article provides an overview of the treatment options available for advanced melanoma, including chemotherapy, targeted therapy, immunotherapy, interleukin-2, and oncolytic viral agents.

Review and Update on Evidence-Based Surgical Treatment Recommendations for Nonmelanoma Skin Cancer **425**

Megan E. Shelton and Adewole S. Adamson

Nonmelanoma skin cancer (NMSC) is the most commonly diagnosed malignancy in the United States. Surgery is considered the gold standard treatment. Techniques include curettage and electrodesiccation, surgical excision, and Mohs micrographic surgery. While each is effective, there are relative advantages and disadvantages with respect to cost, time, quality of life, and role in patients with limited life expectancy. Preventing local tumor recurrence is the primary objective; however, recurrence rates are based on retrospective data, and high-quality comparator studies assessing effectiveness are scarce. Prospective and randomized controlled trials are imperative to create comprehensive, evidence-based recommendations for the surgical management of NMSC.

Nonsurgical Treatments for Nonmelanoma Skin Cancer **435**

Alexandra Collins, Jessica Savas, and Laura Doerfler

Although surgical intervention remains the standard of care for nonmelanoma skin cancer, other treatment modalities have been studied and used. Nonsurgical treatment methods include cryotherapy, topical medications, photodynamic therapy,

radiation therapy, Hedgehog pathway inhibitors, programmed cell death protein 1 inhibitors, and active nonintervention. Despite the favorable efficacy of surgical treatment methods, many factors, including but not limited to patient age, preference, and severity of disease, must be taken into consideration when choosing the most appropriate, patient-centered treatment approach.

Diagnosis and Management of Cutaneous B-Cell Lymphomas

443

Stephen J. Malachowski, James Sun, Pei-Ling Chen, and Lucia Seminario-Vidal

Primary cutaneous B-cell lymphomas are a group of diseases with indolent and aggressive behavior. The goal of the initial workup is to evaluate for systemic involvement, provide adequate staging, and guide therapy. Histopathological studies are a critical part of the workup for classification of these lymphomas because they are similar to their nodal counterparts. There are limited data for treatment guidelines, and thus, therapy differs among institutions. Overall, localized therapies are preferred for indolent types and chemotherapy or immunotherapy for the aggressive forms.

Cutaneous T Cell Lymphoma: A Difficult Diagnosis Demystified

455

Erik Peterson, Jason Weed, Kristen Lo Sicco, and Jo-Ann Latkowski

Cutaneous T cell lymphoma (CTCL) represents a heterogeneous group of extranodal non-Hodgkin lymphomas in which monoclonal T lymphocytes infiltrate the skin. The mechanism of CTCL development is not fully understood, but likely involves dysregulation of various genes and signaling pathways. A variety of treatment modalities are available, and although they can induce remission in most patients, the disease may recur after treatment cessation. Owing to relatively low incidence and significant chronicity of disease, and the high morbidity of some therapeutic regimens, further clinical trials are warranted to better define the ideal treatment option for each subtype of CTCL.

Lymphomatoid Papulosis and Other Lymphoma-Like Diseases

471

Adrian Moy, James Sun, Sophia Ma, and Lucia Seminario-Vidal

Pityriasis lichenoides et varioliformis acuta and pityriasis lichenoides chronica are the 2 main subtypes of pityriasis lichenoides. They represent the acute and chronic forms of the disease; both may have clonal T cells. Several treatment modalities are used, but it has been difficult to determine efficacy because of the possibility of spontaneous remission. Cutaneous CD30+ lymphoproliferative disorders constitute many cutaneous T-cell lymphomas and comprise lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma (ALCL). Both have an excellent prognosis. Lymphomatoid papulosis often only requires observation or treatment of symptoms. First-line therapies for primary cutaneous ALCL are surgical excision or radiotherapy.

Dermatofibrosarcoma Protuberans

483

Aubrey Allen, Christine Ahn, and Omar P. Sangüeza

Dermatofibrosarcoma protuberans (DFSP) is an uncommon dermal neoplasm that exhibits a high rate of local recurrence and infiltrative behavior, but has a low risk of metastasis. It arises as a slowly progressive, painless pink or violet plaque. Histologically, DFSP is characterized by a monomorphous spindle cell proliferation in a storiform pattern. The gold standard of treatment is surgical resection with negative margins. In cases where obtaining clear margins is not possible, radiation and

systemic therapy with tyrosine kinase inhibitors, such as imatinib mesylate, has been shown to be effective.

Updates on Merkel Cell Carcinoma

489

Drew A. Emge and Adela R. Cardones

Merkel cell carcinoma (MCC) is a rare but aggressive skin cancer associated with the Merkel cell polyoma virus. Its incidence and mortality are increasing. There have been many advances in the last several decades in the etiology, detection, and management of MCC, but much about its natural history and most effective treatment remains unknown. Surgical excision with margins of 1 to 2 cm remains first-line therapy for early-stage MCC, but robust evidence supporting immunotherapy for patients with advanced disease has led to recent approval of immune checkpoint inhibitors in the treatment of advanced MCC.

Kaposi Sarcoma Updates

505

Shervin A. Etemad and Anna K. Dewan

Kaposi sarcoma (KS) is an angioproliferative mesenchymal neoplasm caused by Kaposi sarcoma-related herpesvirus. This review outlines our current understanding of the epidemiology, pathogenesis, clinical presentation, and staging for this disease. Recent research has informed a more comprehensive understanding of the epidemiology of KS in the post-antiretroviral therapy era, and highlights the continued need to better characterize the African endemic subtype. Advances in clinical oncology, including checkpoint inhibitors and new skin-directed therapies, have translated into exciting new developments for the future of KS treatment options.

Basal Cell Carcinoma, Squamous Cell Carcinoma, and Cutaneous Melanoma in Skin of Color Patients

519

Latrice Hogue and Valerie M. Harvey

Skin cancers are relatively rare in patients with skin of color; however, they are an important public health concern because of disparities in patient outcomes. Gaps in skin cancer knowledge exist because of lack of large-scale studies involving people of color, and limitations in data collection methods and skin classification paradigms. Additional research is needed to address questions regarding risk and reasons for disparate skin cancer outcomes in these patients. We summarize the clinical and epidemiologic features for basal cell carcinoma, squamous cell carcinoma, and melanoma and touch on some of their unique features in patients with skin of color.

Skin Cancer Detection Technology

527

Deborah N. Dorrell and Lindsay C. Strowd

Skin cancer is the most common malignancy in the United States. Health care providers and patients alike are tasked with identifying suspicious skin lesions in order to diagnose skin cancers early and treat them quickly. The normal pathway to skin cancer diagnosis is visual, with dermoscopic assessment of the lesion followed by biopsy and histopathologic evaluation. Recently, many innovative skin cancer detection technologies have been developed to increase diagnostic accuracy for skin cancers. These noninvasive technologies offer benefits over biopsy but are limited by expense, training, and poor specificity. The skin cancer detection techniques are reviewed in this article.

Dermatology in the Diagnosis of Noncutaneous Malignancy: Paraneoplastic Diseases 537

Jesse J. Keller, Nicole M. Fett, and Lynne H. Morrison

It is important to recognize paraneoplastic dermatoses because they allow the practitioner to begin an early, directed workup to detect an underlying malignant neoplasm. In this review, several paraneoplastic dermatoses are outlined using existing data to detail each one's association with underlying malignancy, demographics, prognosis, and treatment considerations.

Cutaneous Metastasis of Internal Tumors 545

Evan Alexander Choate, Alexander Nobori, and Scott Worswick

Cutaneous metastasis portends a poor prognosis. Therefore, a high clinical index of suspicion is necessary so that a clinician knows how to recognize the presentation of a cutaneous metastasis, while the pathologist must know the appropriate stains to order. In this review, the authors summarize the common and uncommon ways that these tumors will present. Frequently a metastatic cancer will present as a firm red nodule or as a plaque, ulcer, or papule. Less commonly they will present with a clinical clue that can alert a clinician to a likely diagnosis; these manifestations include alopecic, vesicular, blue color, sclerodermoid, acrochordon-, or pellagra-like.

Cutaneous Adverse Reactions of Anticancer Agents 555

Subuhi Kaul, Benjamin H. Kaffenberger, Jennifer N. Choi, and Shawn G. Kwatra

Cutaneous adverse effects are one of the most frequently observed adverse reactions with anticancer agents. This has only intensified with newer targeted and immunologic agents that present with a wide array of drug toxicities and skin reactions. The spectrum ranges from benign, localized dermatoses to generalized, life-threatening cutaneous toxicities. Herein, the authors review the cutaneous adverse effects observed with conventional chemotherapy as well as targeted agents, including the emerging immune checkpoint inhibitors, which have been revolutionary in the treatment of many malignancies.

Review of Graft-Versus-Host Disease 569

Vignesh Ramachandran, Sree S. Kolli, and Lindsay C. Strowd

Graft-versus-host disease (GVHD) is an adverse immunologic phenomenon following allogeneic hematopoietic stem cell transplant. Cutaneous manifestations are the earliest and most common presentation of the disease. This article describes the pathophysiology, clinical presentation, diagnosis, and treatment options available for acute and chronic GVHD. Acute and chronic GVHD result from an initial insult triggering an exaggerated inflammatory cascade. Clinical presentation for cutaneous acute GVHD is limited to maculopapular rash and oral mucosal lesions, whereas chronic GVHD can also include nail, scalp, and genitalia changes. Diagnosis is often made clinically and supported by biopsy, laboratory and radiology findings.

Phakomatoses 583

Benjamin Becker and Roy E. Strowd III

Phakomatoses present with characteristic findings on the skin, central or peripheral nervous system, and tumors. Neurofibromatosis type 1 is the most common syndrome and is characterized by Café-au-lait macules, intertriginous freckling, Lisch

nodules, and tumors including neurofibromas, malignant peripheral nerve sheath tumors, and gliomas. Tuberous Sclerosis Complex is characterized by benign hamartomas presenting with hypomelanotic macules, shagreen patches, angiofibromas, confetti lesions and tumors including cortical tubers, subependymal nodules, subependymal giant cell astrocytomas and tumors of the kidney, lung, and heart. Managing these disorders requires disease specific supportive care, tumor monitoring, surveillance for selected cancers, and treatment of comorbid conditions.

Hereditary Tumor Syndromes with Skin Involvement

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Ramiz N. Hamid and Zeynep M. Akkurt

Cutaneous findings that appear in childhood may be the first sign of a hereditary tumor syndrome. Early detection of genodermatoses allows the patient and at-risk family members to be screened for associated malignancies. This article provides a brief description of the pathogenesis and clinical manifestations of various inherited disorders with skin involvement, along with treatment updates. Advances in molecular-based therapy have spurred development of novel treatment methods for various genodermatoses such as xeroderma pigmentosum (XP) and Gorlin-Goltz syndrome. Further studies are needed to better assess the efficacy of many of these new treatment options.