A new case of segmental neurofibromatosis in a young female

Katy Lynn Modlin DO, Danielle Neal DO, FAAD

A 38-year-old Caucasian woman presented to our clinic with a few new skin-colored papules on her left shoulder. The patient noted that the first new growth appeared 10 years prior, but she was not concerned at the time and did not see a dermatologist. Over the next several years, a few new lesions formed annually, and the patient subsequently had multiple biopsies that were all consistent with neurofibromas. The patient denies any family history of neurofibromatosis and any personal history of neurological deficits or seizures. On examination she did not exhibit axillary freckling, café-au-lait macules, or lisch nodules. However, the patient had several skin-colored soft papules concentrated on her left posterior shoulder. A diagnosis of segmental neurofibromatosis was made. Segmental neurofibromatosis is a rare somatic mosaicism as a result of the postzygotic mutation in the NF1 gene. Patients with segmental neurofibromatosis are less likely to pass on neurofibromatosis to their children and less likely to have anyone in their family with the condition. Segmental neurofibromatosis is more common in women. In this case, the clinical features, pathology, and potential treatments are discussed.

http://dx.doi.org/10.1016/j.ijwd.2019.04.014

Palisaded neutrophilic granulomatous dermatitis as manifestation of Hodgkin lymphoma: Report of a rare case with literature review of paraneoplastic granulomatous dermatitis

Susan Pei MD, Molly Hinshaw MD
Department of Dermatology, University of Wisconsin Hospitals and Clinics, Madison, Wisconsin

Background and aims

Palisaded neutrophilic granulomatous dermatitis (PNGD) is classically characterized by skin-colored to erythematous papules that are symmetrically distributed on the extremities. Since its recognition as an entity in 1994, the clinical morphology of PNGD has broadened to include plaques, nodules, linear bands, and annular, gyrate, and/or urticarial lesions. Histologic findings include neutrophilic inflammation of varying density with karyorrhectic debris, collagen degeneration, and palisades of histiocytes including small granulomas and variable leukocytoclastic vasculitis. PNGD typically occurs in the setting of an underlying systemic disease, such as connective tissue disease, infection, or rarely malignancy.

Methods

We report the second case of a patient with paraneoplastic PNGD leading to a diagnosis of Hodgkin lymphoma. In addition, we include a comprehensive literature review of the spectrum of paraneoplastic granulomatous dermatitides.

Results

A 47-year-old woman presented with a several month history of a new, progressively worsening, asymptomatic eruption of erythematous, variably annular papules, and thin plaques on the bilateral lower legs and left hand. Biopsies of the skin lesions revealed in the dermis in palisaded and interstitial array an infiltrate of lymphocytes; histiocytes, some multinucleated; neutrophils; and karyorrhexis. Special stains for acid fast bacilli and fungal organisms were negative. Alcian blue and colloidal iron stains did not reveal increased mucin.

The patient also presented with concomitant symptoms of fevers, chills, night sweats, weight loss, arthralgia, poor sleep, and malaise. Extensive laboratory work-up for autoimmune and infectious conditions was unremarkable except for elevated inflammatory markers (ESR 70 mm/hr, CRP 6.4 mg/dL), mild normocytic anemia, and mild thrombocytosis. A pan-computed tomography scan demonstrated retroperitoneal adenopathy. Excisional retroperitoneal lymph node biopsy was diagnostic for nodular lymphocyte predominant Hodgkin lymphoma. The patient is currently undergoing chemotherapy treatment for her Hodgkin lymphoma.

Conclusions

Of the noninfectious granulomatous dermatitides, PNGD, and interstitial granulomatous dermatitis, which share overlapping clinicopathologic features, are typically considered secondary to an underlying systemic condition. Granulomatous dermatitis as a paraneoplastic manifestation is rare. Literature review shows only 36 reported cases, with the majority being hematologic neoplasms (lymphoma, leukemia, myelodysplastic syndromes, other lymphoproliferative disorders). Only 7 cases are associated with solid organ tumors (breast, endometrial, lung, prostate, esophageal, and hypopharyngeal cancers). We summarize these cases in table format, detailing the clinical presentation and histologic features of the paraneoplastic granulomatous dermatitis, the underlying neoplasm, and any reported response of the dermatitis to treatment.

The immunopathogenesis of paraneoplastic granulomatous dermatitis is unknown but has been postulated to result from abnormal neutrophil activation, circulating immune complex deposition, a delayed-type hypersensitivity reaction, or low-grade small vessel vasculitis. We present the second reported case of PNGD leading to a diagnosis of Hodgkin lymphoma. Our case and literature review highlight the emerging nature of granulomatous dermatitides as a paraneoplastic phenomenon, which may be the initial presenting symptom for which the patient seeks medical attention. Awareness of the potentially paraneoplastic nature of granulomatous dermatitis may expedite early diagnosis of an underlying malignancy.

http://dx.doi.org/10.1016/j.ijwd.2019.04.015

PMMA-collagen gel dermal filler post-marketing safety experience

Wendy E. Roberts MD[a], Alayne Lehman RN, BSN, MS[b]
[a]*Rancho Mirage, California*
[b]*Suneva Medical, San Diego, California*

Background and aims

Polymethylmethacrylate (PMMA) collagen gel dermal filler (Bellafill, Suneva Medical, San Diego, CA) is approved by the Food and Drug Administration (FDA) for the correction of moderate-to-severe nasolabial folds and moderate-to-severe atrophic, distensible facial acne scars on the cheek in patients aged >21 years. PMMA collagen gel dermal filler is the only FDA-approved long-lasting filler currently on the market. Previous reports, including a 5-year post-approval study, have detailed PMMA collagen gel safety, as well as clinical approaches for optimizing patient results and satisfaction. This report synthesizes >10 years of post-marketing surveillance (PMS) experience. The objective of this report is to disclose the post-marketing experience of PMMA collagen gel and share with clinicians the safety profile of PMMA collagen gel in the real-world setting.

Methods

PMS data were collected as required by the FDA between February 2007 and December 31, 2017. Events reported to the manufacturer or

FDA and those ascertained via public disclosure (journal articles, abstracts, or presentations) were included. Data were evaluated to determine the overall adverse event (AE) rate, severity, and on- or off-label nature of the reported events. The overall AE rate was calculated by dividing the total number of AEs by the number of syringes sold during that time frame. Data were analyzed to exclude reports in which AEs were determined not to be related to PMMA collagen gel dermal filler. AEs were stratified into one of four categories: on label, off label, both, or unknown. All off-label–related AE reports were examined to determine the area represented in each report.

Results

In the 10-year period between February 2007 and December 31, 2017 a total of 775 AEs were reported. The number of syringes distributed worldwide during this same time period was 650,387, resulting in an overall AE rate of 0.12%. Of these AEs, 724 were confirmed to be PMMA collagen gel related or classified as product relationship unknown. The three most commonly reported AEs were lump or bump (278 of 775 AEs; 36%), swelling (127 of 775 AEs; 16%), and nodule (124 of 775 AEs; 16%). Of note, confirmed granulomas accounted for 15 of 775 AEs (2%; .002% overall rate) and unconfirmed granuloma accounted for 58 of 775 AEs (7%; .009% overall rate). Off-label areas with reported AEs at a rate >1% included periocular (30.2%), malar/midface (19.6%), temples (8.5%), marionette lines (9.1%), perioral (6.5%), chin (6.2%), lips (5.5%), jawline (5.0%), brow/forehead (4.8%), glabella (2.3%), and nose (1.5%). Complete 2018 data are forthcoming and will be included in the final presentation.

Conclusions

PMMA collagen gel has been proven safe and efficacious in four U.S. clinical trials with >1500 patients treated and 5500 patient years of exposure. The PMS data presented herein show an overall AE rate of 0.12% (775 AEs) between February 2007 and the end of 2017. The safety profile of PMMA collagen gel is comparable with that of other dermal fillers reported in the literature. The post-marketing experience of PMMA collagen gel is consistent with safety data reported previously from pivotal clinical studies and further confirms the safety of PMMA collagen gel.

http://dx.doi.org/10.1016/j.ijwd.2019.04.016

Immunotherapy and chemotherapy for cutaneous angiosarcoma: A systematic review

Gaurav Singh MD, MPH[a], Bryan Haimes MD, MPH[b], Drew Klug MD[c]

[a]*The Ronald O. Perelman Department of Dermatology, New York University, New York, New York*
[b]*Department of Medicine, Department of Pediatrics, Christiana Care Health System, New Castle, Delaware*
[c]*Department of Dermatology, University of Missouri School of Medicine, Physician, Columbia, Missouri*

Background and aims

Cutaneous angiosarcomas are malignant neoplasms of vascular endothelium differentiation. They most commonly arise in individuals aged >70 years on the head and neck or breast. Risk factors for angiosarcoma include radiotherapy (termed radiation-associated angiosarcoma) and chronic lymphedema (termed Stewart-Treves syndrome). The treatment of choice for cutaneous disease is surgical excision with postoperative radiotherapy. In patients with extensive disease and/or poor surgical candidacy, systemic agents can be used. However, guidelines do not exist on the preferred systemic agent of choice. We aim to describe the current body of evidence for systemic therapies used in cutaneous angiosarcoma.

Methods

We performed a systematic literature search of PubMed Medline, Scopus, and Google Scholar from their inception up to September 2018 using relevant keywords and MeSH terms (cutaneous, angiosarcoma, chemotherapy, immunotherapy). The database search identified 248 records. Inclusion criteria were studies that were published in English through August 31, 2018, reported cutaneous angiosarcoma, used systemic treatment, described the treatment used, and outlined treatment response. The abstract and title review excluded 193 articles due to the article type (language, not germane to cutaneous angiosarcoma, systemic therapy not discussed). Full-text review of 55 articles resulted in exclusion of 14 articles due to a lack of systemic therapy use or discussion of treatment response. The manuscripts were appraised and classified per the Joanna Briggs Institute levels of evidence. The exclusion process and data extraction were performed by two independent authors. Methodological quality was evaluated with the Cochrane Collaboration's risk-of-bias assessment guideline by two independent authors.

Results

A total of 41 studies encompassing 945 subjects met the inclusion criteria. All were case reports/series, retrospective reviews, or phase 2 trials. Chemotherapies showing response ratios ranging from 25% to 89% include anthracyclines alone or with ifosfamide (11 articles with 108 cases), paclitaxel (4 articles with 165 cases), docetaxel (4 articles with 39 cases), and gemcitabine (2 articles with 25 cases). Chemoradiotherapy with docetaxel, anthracyclines, razoxane, or vindesine also showed response (4 articles with 54 cases) but showed no benefit to adjuvant or neoadjuvant chemotherapy with doxorubicin, ifosfamide, paclitaxel, and/or methotrexate in four retrospective reviews encompassing 261 patients. Other successful treatments reported in small series of <20 patients included vascular endothelial growth factor receptor inhibitors such as bevacizumab, multiple kinase inhibitors such as sorafenib or pazopanib, alkylating agents such as trabectedin, antibodies against platelet-derived growth factor receptor alpha such as olaratumab, microtubule targeting agents such as eribulin, and nonselective beta-adrenergic receptor blocking agents such as propranolol.

Conclusions

Guidelines on the management of advanced cutaneous angiosarcoma with systemic therapy do not exist. Surgery and radiation are first-line treatments, but the role of neoadjuvant and adjuvant therapy is unclear. Based on this review, the greatest level of evidence exists for taxanes such as paclitaxel and anthracyclines such as doxorubicin as first-line chemotherapy agents. A variety of second-line therapies can be considered, including bevacizumab, sorafenib, olaratumab, and eribulin mesylate. Much is unknown about this grim disease, and immunotherapy's role in treatment presents a promising horizon for managing these cases.

http://dx.doi.org/10.1016/j.ijwd.2019.04.017

Immunosuppression-associated primary cutaneous diffuse large B-cell lymphoma mimicking cellulitis in a woman with dermatomyositis

Leah A. Swanson MD[a], Elika Hoss MD[a], Mansi Sarihan MD[b], Hannah E. Hill MD[a], Steven A. Nelson MD[a], David J. DiCaudo MD[a], Aaron R. Mangold MD[a], Aleksandar Sekulic MD, PhD[a]
[a]*Department of Dermatology, Mayo Clinic, Scottsdale, Arizona*
[b]*Department of Dermatology, Maricopa Integrated Health System, Phoenix, Arizona*