Dengue fever in a psoriasis patient treated with anti-tumor necrosis factor agent

(Poster reference number 5443)

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Background: Dengue fever (DF) is a mosquito-borne viral disease that affects humans in tropical and subtropical regions. Hemorrhagic manifestations, including skin or mucosal hemorrhage, associated with low platelet counts (below 100,000/mm^3) and plasma leakage are characteristics of dengue hemorrhagic fever, a severe form of disease, with higher mortality. Incidence of DF has been rising in the Americas. In Brazil, the average incidence rate during 2000-7 was more than 200 cases per 100,000 inhabitants and, in 2010, 261 deaths were reported. The disease has no specific treatment as yet.

Case report: A 61-year-old man presented with severe plaque-type psoriasis since puberty, with recurrent episodes of erythroderma. Previous systemic treatments included acitretin as well as methotrexate, which were discontinued after the disease became unresponsive. In 2008, he was started on etanercept 50 mg a week with good control of psoriasis, reaching PASI 75 after 4 months of therapy. The only complaints were occasional mild flu-like symptoms. In 2009, he was admitted to the emergency room with high fever, headache, and myalgia. The skin examination evidenced a diffuse exanthema along with purpuric lesions on lower extremities. Blood work revealed thrombocytopenia, lymphocytopenia, and elevated liver enzymes. Dengue fever was confirmed by positive serology. Support measurements, vigorous hydration and symptomatic drugs were administered and, after 3 days, the fever subsided and laboratory examinations became normal. Etanercept was discontinued for a week. Skin changes took slightly over a week to resolve.

Discussion: Hemorrhage is an important clinical manifestation of DF, and tumor necrosis factor (TNF)-alfa may play a role in its pathogenesis. High serum levels of TNF and its receptors are associated with severity of DF. Our patient had a severe form of dengue and potentially fatal outcome. Inhibition of an essential inflammatory pathway may have contributed to a favorable progression. A study using a mouse model demonstrated that treatment with anti-TNF reduced mortality. A literature review showed no other reports of DF in patients on anti-TNF therapy. Although this case illustrates a positive outcome possibly resultant from an anti-TNF agent, we encourage caution when managing similar cases, given the immunosuppressive state and risk of other infections common in these tropical areas.

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Impact of oral bexarotene therapy on the outcome of patients with tumor stage mycosis fungoides: The Vanderbilt experience

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Mycosis fungoides (MF) and other variants of cutaneous T-cell lymphoma (CTCL) are rarely curable. The goal of treatment for CTCL includes controlling the disease and minimizing harmful side effects from topical and systemic treatments. Therefore, it is important to gather long-term clinical data to analyze the impact of different therapies on patient outcome. The specific aim of this study is to determine if those patients who received oral bexarotene therapy for treatment of tumor stage mycosis fungoides had improved outcome compared to patients who did not receive bexarotene. The participants in this retrospective study are patients who were followed at the Vanderbilt University Cutaneous Lymphoma Clinic with tumor stage MF between July 1995 to July 2010. Forty patients (27 male [67.5%] and 13 female [32.5%]) met study criteria for the retrospective cohort analysis. Twenty-six patients (65%) received oral bexarotene therapy and 14 patients (35%) did not receive bexarotene therapy. Demographic data for the bexarotene and nonbexarotene groups included: median age at diagnosis (61 vs 56 years), early clinical stage (IA, IB, or IIA) at diagnosis (7 bex vs 2 non-bex), and late clinical stage (IIB and higher) at diagnosis (19 bex vs 10 non-bex). All of these patients had tumor stage MF at some point in their disease course and received other therapies. Median time of follow-up for the bexarotene and nonbexarotene groups was 25 months versus 18 months. Durable responses to bexarotene were achieved in 13 of 26 patients (50%). The median overall survival for patients receiving oral bexarotene therapy compared to patients not receiving bexarotene therapy was 36.5 months and 33 months, respectively. Based on this retrospective cohort analysis, patients with tumor stage MF who received bexarotene therapy did not have improved outcome in terms of overall survival compared to patients who did not receive bexarotene therapy.

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Resolution of malignant cutaneous lesions with brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large cell lymphoma

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Background: Brentuximab vedotin (SGN-35) is an anti-CD30 antibody conjugated to the potent antimicrotubule agent, monomethyl auristatin E (MMAE), by a plasma-stable linker. In a phase II study of brentuximab vedotin in 58 patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL), an objective response rate of 86% was observed by independent review.

Aims: To describe the experience with brentuximab vedotin in relapsed or refractory sALCL patients with malignant cutaneous lesions who participated in a phase II, single-arm, multicenter study.

Methods: Brentuximab vedotin 1.8 mg/kg was administered every 3 weeks as a 30-minute outpatient IV infusion for up to 16 cycles of treatment. Determination of antitumor efficacy was based on objective response assessments by independent review according to Cheson 2007; resolution of cutaneous lesions was assessed by the investigator.

Results: Fifteen patients with relapsed or refractory sALCL who participated in the phase II study had malignant cutaneous lesions at baseline. Among these patients, the median age was 57 years (range, 33-70), and ECOG performance status was 0 or 1. Median number of prior therapies was 2 (range, 1-5) and 4 patients (27%) had an autologous stem cell transplant prior to the study. The majority of patients (80%) had ALK-negative disease. Complete resolution of malignant cutaneous lesions was achieved in 93% of patients (14/15) with a median time to resolution of all lesions of 4.9 weeks (range, 2.6-36). Objective responses were achieved by all patients (12 CR, 3 PR); median duration of objective response was 12.6 months. The most common adverse events ($\geq$ 30%) of any grade among the 15 patients were diarrhea, pyrexia, constipation, nausea, peripheral sensory neuropathy, decreased appetite, fatigue, and rash; the majority of adverse events were grade 1/2 in severity.

Conclusion: In a phase II trial of brentuximab vedotin in relapsed or refractory sALCL, local and systemic responses were observed among 15 patients who had malignant cutaneous lesions at baseline: 93% of patients achieved complete resolution of cutaneous lesions and 100% had objective responses. Adverse events were manageable, and the safety profile was comparable to that observed among patients without cutaneous involvement. These results warrant further study of brentuximab vedotin in patients with CD30-positive cutaneous lymphomas.

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Dermatology specimen labeling quality improvement process: Application of a low-cost intervention developed by a physician-led safety committee

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Most dermatology practices generate a high volume of specimens destined for pathology review. Development of a standardized preanalytic (clinically oriented) specimen handling system has the potential to reduce the number of specimen labeling errors which may directly impact patient care. Measuring specimen labeling accuracy has been suggested as a possible measure for patient safety. The Department of Dermatology at Duke University Medical Center has seen significant growth over the past 3 years; our department currently encompasses three clinical sites, 16 providers, 10 resident physicians, and generated 6426 surgical specimens during fiscal year 2010 (FY 2008 = 5649 specimens). This clinical growth was associated with an upward trend in specimen labeling errors. To address these errors, a physician-led Safety Committee mapped 17 operational steps from provider initiation of specimen procurement to specimen submission for courier retrieval and delivery to surgical pathology. Five quick steps were considered essential to accurate specimen labeling: three steps were for providers, two for nursing staff. The five essential steps rely on "forced functions" or actions prompted by necessary steps in the baseline process: for example, placing the label on the specimen container prompts the provider to ask the patient to verbalize his/her name and birth date. The standardized process has empowered nursing staff to ask for provider clarification of discrepancies prior to submitting specimens. Other specific improvements included adding label printers to clinical exam rooms, facilitating bedside label generation and developing bright green "small specimen" stickers for applicable specimen containers to alert surgical pathology to carefully remove the lid so as not to inadvertently misplace a small specimen. Through improved communication with surgical pathology, operational areas for improvement with specimen handling were also identified. Following institution of this system, the number of specimen-labeling events declined despite increased specimen procurement: the error rate for FY 2009 was 6.3 events per 1000 opportunities; FY 2010 was 4.0/1000 (P = .09). The new policy was implemented midway during FY 2010. Based on the Kaizen philosophy, specimen labeling events are addressed via a safety debrief with the Safety Committee chair, the involved provider and nurse to identify opportunities for continuous improvement to the overall system.

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