

Tumor treating fields applied to the skin as a novel adjuvant oncology treatment: allergic contact dermatitis in a patient with glioblastoma multiforme

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To the Editor:

Glioblastoma multiforme (GBM) is a common, highly aggressive, grade IV astrocytoma found in the cerebral hemispheres. The standard therapeutic approach to this cancer involves resection, radiation, and temozolomide chemotherapy. Nevertheless, the median survival associated with a GBM diagnosis is approximately one year with <10% of patients surviving beyond 5 years [1]. The poor survival and low treatment response rates for GBM underscores the importance of investigating and incorporating novel adjuvant therapy options, such as Tumor Treating Fields (TTFields), into the treatment options offered to these cancer patients.

Optune® is an FDA-approved device for GBM that works via TTFields. This wearable, portable medical device consists of scalp transducer arrays placed on the scalp using flexible adhesive bandages (**Figure 1**) for 18 hours per day, creating an electric field that selectively interferes with cancer cell mitosis and inducing apoptosis of rapidly dividing cancer cells [1]. Combined with temozolomide for the treatment of GBM, TTFields increased progression-free and overall survival compared to temozolomide alone [1]. In three studies investigating the efficacy and toxicity of Optune® treatment, all reported Grade 1 or 2 dermatitis in a subset of patients compared to no reports of dermatitis in patients who received temozolomide alone [1-3]. Although TTFields like Optune® are well tolerated, the most common reported adverse events for this device are dermatologic (e.g., scalp irritation, itching, and

folliculitis) with nonspecific dermatitis reported in as high as 80% of patients [4]. The exact etiology of the dermatitis is often not elucidated in these reports. Also, the repeated application and removal of the discs and their adhesive material to multiple, overlapping skin areas makes it more difficult to tease out ceramic disc- or adhesive-induced allergic or irritation contact dermatitis.

We present a 60-year-old woman with stage 5 GBM who presented to the dermatology clinic with scalp irritation, dermatitis, and pruritus while receiving Optune®-temozolomide combination therapy. Prior



Figure 1. Patient wearing Optune electromagnetic transducer arrays secured by adhesive bandages on scalp.

to presentation, the patient was tolerating Optune®-temozolomide combination therapy until she complained of scalp pruritis and localized scalp dermatitis two weeks later. The oncologist noted a scalp rash and their differential diagnosis included dermatitis, folliculitis, infection, and skin toxicity secondary to temozolomide chemotherapy. Optune® treatment was halted and the patient was prescribed 1% hydrocortisone cream twice daily. There was slight improvement noted after three days of hydrocortisone use, so Optune® application was resumed. Five days later, the patient complained of scalp pruritis and the same rash. Optune® treatment was again stopped and the patient resumed the hydrocortisone cream along with topical clindamycin and clobetasol 0.05% foam as needed. After 5 days of treatment the rash improved and Optune® was restarted with a referral to dermatology for further evaluation.

On examination, the patient had erythematous patches with light scale arranged in a geometric distribution that correlated with the Optune® adhesive bandages with notable sparing where the ceramic discs had been (**Figure 2**). The patient and her caretaker, who applied and removed the Optune® treatments, also noted that the itching and redness was consistently beneath the adhesive bandages. Application of the discs to the skin using non-adhesive methods and several days without disc application both resulted in complete resolution of the itching and erythema. A diagnosis of allergic contact dermatitis secondary to the Optune® adhesive pads was made. Use of twice daily clobetasol 0.05% cream resulted in rapid improvement of the dermatitis following each treatment application. The patient was able to remain on Optune® with as-needed clobetasol use for more than 8 months of Optune®-temozolomide combination therapy before succumbing to her GBM.

The various adverse skin eruptions associated with TTFIELDS therapy like Optune®, including allergic



Figure 2. Scalp dermatitis in a geometric, linear distribution which corresponds with placement of Optune® adhesive bandages.

contact dermatitis from adhesive, are important for oncologists and dermatologists to recognize as these reactions can result in premature treatment discontinuation or the incorrect assumption of a drug-induced eruption. It is also important to be specific as to the potential etiology of the skin manifestations when reporting or documenting adverse reactions. By attempting to tease out the underlying mechanism of skin toxicities, clinicians may identify potential solutions to mitigate symptoms to allow GBM patients to optimize their chances of treatment success. Dermatologists and non-oncology specialties should be aware of this novel treatment modality for GBM as well as the potential skin reactions associated with TTFIELDS and Optune® therapy.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Stupp R, Taillibert S, Kanner A, et al. Effect of Tumor-Treating Fields Plus Maintenance Temozolomide versus Maintenance

Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial. *JAMA*. 2017;318:2306-16. [PMID:

- 29260225].
2. Stupp R, Wong ET, Kanner AA, et al. NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: a randomised phase III trial of a novel treatment modality. *Eur J Cancer*. 2012;48:2192-202. [PMID: 22608262].
 3. Song A, Bar-Ad V, Martinez N, et al. Initial experience with scalp sparing radiation with concurrent temozolomide and tumor treatment fields (SPARE) for patients with newly diagnosed glioblastoma. *J Neurooncol*. 2020;147:653-61. [PMID: 32206976].
 4. Lukas RV, Ratermann KL, Wong ET, Villano JL. Skin toxicities associated with tumor treating fields: case based review. *J Neurooncol*. 2017;135:593-9. [PMID: 28849343].