Mechloretamine Gel Usage in Patients with Mycosis Fungoides in a Lymphoma Clinic

Robert Duffy, Tara Jennings, Joya Sahu

From the Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, PA, USA.
E-mail: Joyasahum@gmail.com

Sir,

Mechloretamine gel functions as an antineoplastic therapy via three unique mechanisms: attachment of alkyl groups to DNA bases, resulting in fragmentation and cell death, DNA damage via the formation of cross-links, and induction of mispairing of nucleotides leading to mutation.\(^1\) Mechloretamine, or nitrogen mustard, was traditionally used as a wartime gas, but in 1940s, it was compounded into a petrolatum-based topical ointment and was used as one of the earliest forms of topical antineoplastic therapies.\(^2\) Mechloretamine gel was approved by the Food and Drug Administration (FDA) in 2013.

At the Jefferson Multi-Disciplinary Cutaneous Lymphoma Clinic (MCLC), mechloretamine gel (0.016%) is used as a primary treatment modality, for maintenance therapy after patients receive systemic or radiation therapy, and as an adjuvant therapy. The method in which we choose to utilize mechloretamine gel is based on disease burden and staging.

Mechloretamine gel is often used as an adjuvant therapy with both topical and systemic therapies. Mechloretamine gel is used in combination with topical treatment for a skin-directed synergistic effect and used in combination with systemic treatment for patients with lymph node, blood, or visceral organ involvement. For the additive skin-directed effects, adjuvant mechloretamine gel has been used in combination with class one topical steroids, narrowband ultraviolet B (NB-UVB), psoralen and ultraviolet A (PUVA), imiquimod, or pimecrolimus.

Mechloretamine gel can be used for any type of MF provided the lesions are not open and weeping and not in mucosal or intertriginous areas.

Providers at the Jefferson MCLC utilize a specific approach for the timeline in which mechloretamine gel should be applied. This is a two-tiered approach based on whether the treatment is initiated to treat active lesions or maintain disease clearance. Patients are
Mechlorethamine gel is selected due to the dose burden and patient tolerance. For those patients using mechlorethamine gel to treat active disease, providers advise applying mechlorethamine gel to the active lesions every other day, daily, or twice daily. When using mechlorethamine gel to maintain disease clearance, patients are advised to apply medication on a range from once to four times weekly, slowly uptitrating.

Patients are commonly prescribed topical steroids as a primary treatment before initiation of mechlorethamine gel. Though topical steroids are an appropriate initial treatment due to their efficacy and low rate of adverse events, mechlorethamine gel is selected as an additional treatment modality when patients demonstrate progressive disease. The topical steroid is not discontinued as it takes care of the dermatitis induced by mechlorethamine.

There are certain areas of the body that have demonstrated greater susceptibility to the side effects of both mechlorethamine gel and topical steroids. The most sensitive areas are the intertriginous areas, face, genitalia, and anus. The risk for dermatitis from mechlorethamine gel and skin thinning increases in intertriginous areas due to thin skin, occlusion, and skin maceration. Therefore, providers in the MCLC do not typically use mechlorethamine gel or topical steroids in these areas, and alternatively administer pimecrolimus, a calcineurin inhibitor, at varying dosages. It is important to note that pimecrolimus and tacrolimus should not be used in areas actively affected by irritant dermatitis as this will cause severe burning and discomfort. Systemic absorption secondary to the use of mechlorethamine gel has not been demonstrated to be significant.

It is important to note that systemic absorption secondary to the use of mechlorethamine gel has not been demonstrated to be significant in previous studies. The randomized controlled trial resulting in FDA approval of the drug demonstrated no systematic pattern of change in any laboratory value measured, consistent with lack of systemic absorption. Furthermore, high-performance liquid chromatography serum assays performed revealed no detectable blood levels or evidence of systemic absorption of mechlorethamine. Due to the low likelihood of systemic absorption, no investigations are recommended in order to monitor the systemic side effects.

The risk of nonmelanoma skin cancer (NMSC) secondary to the use of mechlorethamine gel in the Lessin et al. study was found not to be significant, as the few cases that were diagnosed commonly occurred on sun-exposed areas and in patients with a history of skin cancer or prior skin-directed therapies, including phototherapy. We advise patients using mechlorethamine that they have the same risk of NMSC as those not applying the medicine. Sun avoidance and the use of sunscreen are paramount.

At the MCLC, we dedicate time ensuring that patients prescribed mechlorethamine gel understand how to store the medication and how and when to apply the medication.

Mechlorethamine gel is not stable in water; completely dry skin is essential in order for the medication to be absorbed and function correctly. Furthermore, patients are instructed to moisturize 2 hours before or 2 hours after application of the medication. Patients are instructed to wash their hands with soap immediately after application (unless they have disease on their hands in which case they can wash their hands 30 minutes post application, if so desired) and if any caregivers are applying the medication, they must wear disposable nitrile gloves.

In order for mechlorethamine gel to work appropriately, it must be stored in the refrigerator. Patients must apply the medication within 30 min of removal from the refrigerator and return it to the refrigerator immediately after use. If patients are traveling or do not have direct access to a refrigerator for an extended period of time, the manufacturer provides a cold pack for the patients in order to keep the medication at the appropriate temperature.

MF patients are assessed at each follow up visit for response to therapy. The first 3–4 weeks on mechlorethamine gel, the lesions will become more pronounced, erythematous, and weepy. After this point, the lesions responding to therapy will show vast improvement, leaving behind postinflammatory hyperpigmentation (PIH). The PIH must not be mistaken for patch stage MF. Non-response to therapy is the development of increased number of plaques or tumors, the evolution to erythroderma or the progression to significant blood involvement while on therapy. If patients are not responding to therapy or progressing, one can treat with the next line of appropriate therapy.

Mechlorethamine gel is a common medication for the treatment of mycosis fungoides. The Jefferson MCLC uses it as both a primary therapy for patch and plaque disease, adjunctive therapy, and as a prevention modality for patients in order to prolong clinical remission. We have found great success with this drug, which we attribute to careful attention to correct patient application and minimization of side effects, enhancing patient compliance.

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Conflicts of interest
There are no conflicts of interest.

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A Rare Case of Persistent Xanthoma Disseminatum without Any Systemic Involvement
Akhilesh Behra, Dilip Kumar Sa, Reena Naik1, Rakesh Kumar Patel
From the Departments of Dermatology and Pathology, LSLAM Government Medical College, Raigarh, Chhattisgarh, India.

Sir,
Xanthoma disseminatum (XD) is a rare nonfamilial, histiocytic proliferative disorder involving skin and mucous membrane and frequently associated with diabetes insipidus. It is clinically characterized by asymptomatic, discrete, erythematous to yellow-brown papules, and nodules distributed symmetrically over the face, trunk, eyelids, flexural areas such as axillae, inguinal folds, antecubital, and popliteal fossae. Mucous membrane is involved in about 30% of cases. Systemic involvements such as the upper respiratory tract, skeletal, and the central nervous system are not uncommon. Based on the evolution and prognosis there are three clinical variants of XD, namely, (a) a self-healing form, (b) a persistent form (most common), and (c) a progressive form.

A 38-year-old male patient from nonconsanguineous parentage presented with multiple, asymptomatic, discrete, yellowish-brown, smooth-surfaced papules, and nodules distributed mostly around the mouth [Figure 1]. Similar lesions were also present over the nose, eyelids, axillae, inguinal areas, antecubital and popliteal fossae, and palms [Figure 2]. The lesions started around the mouth 7 months back and then gradually appeared over the other parts. Mucosal examination revealed multiple yellowish papules over the soft palate. There was no history of polydipsia, polyuria, visual impairment, bone pain, dyspnea, or dysphagia. Family history was noncontributory. Ophthalmologic and otorhinolaryngological workup were normal. Differential diagnoses, such as XD, eruptive xanthoma, histoid leprosy, post kala-zar dermal leishmaniasis, generalized eruptive histiocytoma, and multicentric reticulohistiocytosis were kept in mind before investigation.

Laboratory investigations - hemogram, erythrocyte sedimentation rate, blood sugar, liver function test, renal function test, lipid profile, urine analysis, and thyroid function test were normal. Ultrasonography, electrocardiography, and chest X-ray were also normal. Skin biopsy showed diffuse dermal infiltration of histiocytes, many foamy cells, Touton giant cells, and chronic inflammatory cells [Figure 3]. Immunohistochemistry (IHC) was positive for CD68 [Figure 4]. On the basis of clinical, histopathological, and IHC, the diagnosis of XD was reached.

The patient was treated with oral prednisolone 20 mg once daily and azathioprine 50 mg twice daily. There was no improvement in lesions after 3 months of treatment. He was lost to follow-up after 3 months of treatment.

XD is a rare normolipidemic, non-Langerhans cell histiocytosis occurring mostly in children and young adults. Involvement of the upper respiratory tract may manifest as dyspnea and stridor. Involvement of conjunctiva and cornea may lead to blindness. Meningeal involvement is common, and infiltration to hypothalamus and pituitary may lead to diabetes insipidus in up to 40% of cases.