Recurrent episodes of palpable migratory arciform erythema associated with intravenous immunoglobulin infusions

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Abstract

Palpable migratory arciform erythema (PMAE) is an uncommon T cell pseudolymphoma characterized by erythematous, annular-to-arciform papules and plaques. Although the eruption is self-limited in most cases, recurrences are routine. Diagnosis requires attention to clinical history as well as histopathologic analysis, which allow for differentiation from other T cell pseudolymphomas and gyrate erythemas. A common triggering factor has not been identified. We report a 60-year-old man who developed PMAE after intravenous immunoglobulin infusion. Interestingly, although the individual eruptions were self-limited and resolved after several weeks, subsequent infusions predictably resulted in recurrence of PMAE, confirming the association. To our knowledge, this is the first reported case of recurrent PMAE in association with intravenous immunoglobulin infusions.

Keywords: intravenous immunoglobulin, palpable migratory arciform erythema, pseudolymphoma,

Introduction

Palpable migratory arciform erythema (PMAE) is a rarely-reported T cell pseudolymphoma characterized by erythematous, indurated, annular-to-arciform papules and plaques with predilection for the upper trunk. Diagnosis requires attention to clinical history as well as histopathologic analysis, which allow for differentiation from other T cell pseudolymphomas and gyrate erythemas. One differentiating factor is the impermanence of PMAE. Unlike other cutaneous lymphocytic infiltrations, PMAE tends to be transient. However, recurrences are common and treatment is often unsuccessful. A common etiologic factor in the development of PMAE has not been identified, though various etiologies have been singularly recognized in case reports. We add intravenous immunoglobulin (IVIg) to the list of potential etiologic factors as the following case supports.

Case Synopsis

A 60-year-old man presented to our dermatology clinic for evaluation of a recurrent asymptomatic rash consisting of variably-sized, arcuate-to-annular, erythematous papules and small plaques of the upper back (**Figure 1**). At the time of evaluation, he reported that he had developed the eruption at least five times previously, which predictably resolved several weeks after initial appearance. The patient's only major medical issue was myasthenia gravis with significant oculomotor involvement, which had necessitated recent initiation of IVIg infusions in addition to the pyridostigmine and mycophenolate mofetil that he took regularly to manage his condition. His only other relevant dermatologic history was vitiligo affecting his dorsal hands and forearms.

On further questioning, the patient noted that the first episode of this eruption occurred after starting

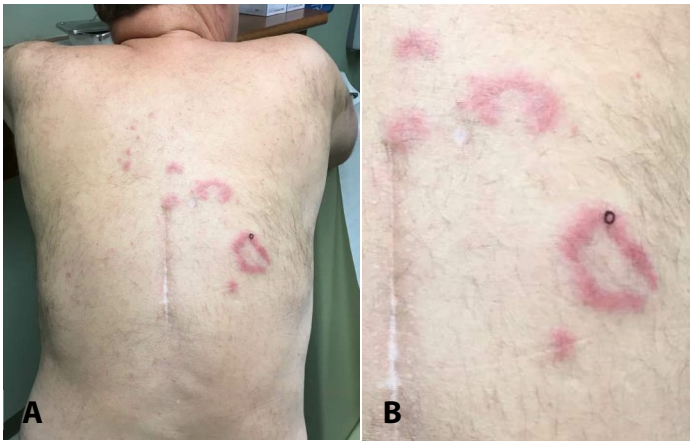

Figure 1. ***A)*** *Well-demarcated, erythematous and indurated arciform papules and plaques of the mid back one week following intravenous immunoglobulin infusion.* ***B)*** *Closer view of well-demarcated, erythematous and indurated arciform papules and plaques.*

IVIg treatments. He then noted that rash had occurred predictably after every IVIg treatment, always within one week. Although his skin was clear at his initial visit, he subsequently followed up intentionally two weeks after an IVIg infusion with significant rash on his back. At this visit a biopsy was performed and histopathologic examination was notable for a dense infiltrate consisting of monomorphic lymphocytes oriented around superficial and deep vascular and adnexal structures (**Figure 2**). Epidermal change, plasma cells, and dermal mucin were notably absent. Immunohistochemistry confirmed the presence of a predominately T cell population. The histopathology, in conjunction with the patient's history and clinical appearance, supported the diagnosis of palpable migratory arciform erythema (PMAE). The patient's rash resolved within ten days of biopsy but continued to recur after subsequent IVIg infusions.

Case Discussion

Palpable migratory arciform erythema is a rare T cell pseudolymphoma characterized by well-defined, erythematous, indurated, annular-to-arciform papules and plaques with predilection for the upper trunk. Plaques tend to follow a waxing and waning course over days to weeks with gradual peripheral, arciform expansion before resolution without scarring. Recurrence is common with or without treatment [1]. Histopathologically, PMAE is characterized by a dense, superficial and deep perivascular and periadnexal T cell infiltrate. Epidermal changes are notably absent [2]. Palpable migratory arciform erythema likely exists on a spectrum with other T cell pseudolymphomas characterized by perivascular and/or periadnexal lymphocytic infiltration. Thus, the differential diagnosis includes related entities, namely Jessner lymphocytic infiltrate, erythema annulare centrifugum (particularly the deep variant), lupus tumidus, and reticular erythematous mucinosis (REM). Less likely entities to consider given histologic findings include polymorphous light eruption and gyrate erythemas. Alternative diagnoses can largely be excluded on the basis of clinical history or histopathologic examination. The clinical history, characterized by annular-to-arcuate plaques without predilection for sun-exposed areas as well as the more acute, self-limited course (although frequently with recurrences) suggests against Jessner lymphocytic infiltrate and tumid lupus. The differentiation is strengthened by the lack of plasma cells and muci n on histopathologic analysis, which would also be a prominent feature of REM. Deep erythema annulare centrifugum is a closely related, controversial entity in which the lymphocytic infiltration is primarily perivascular and spares adnexal structures.

Like other T cell pseudolymphomas, the pathogenesis of PMAE is incompletely understood but likely involves a benign, reactive proliferation of polyclonal T-lymphocytes in response to an external

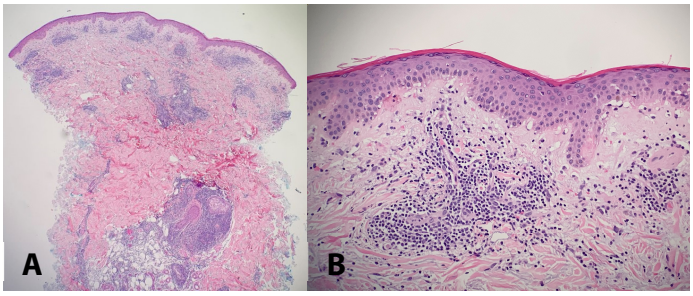

Figure 2. *H&E histopathology showing* ***A)*** *dense, superficial and deep perivascular and periadnexal lymphocytic infiltrate with notable absence of significant epidermal changes, 4×.* ***B)*** *Dense, superficial perivascular lymphocytic infiltrate with notable absence of significant epidermal changes, 20×.*

stimulus [3]. Reports of PMAE in the literature are few and a common triggering factor has not been identified. Although some clinicians have reported success in using systemic antibiotics to induce remission of PMAE, no causative infectious etiology has been identified. Other proposed associations based on case reports have included the administration of several different medications, HIV infection, and the presence of a preceding B-cell pseudolymphoma [3-5]. Presumably, the large majority of cases present idiopathically. In the only other report that documents two cases of potential drug-induced PMAE, the specific medication is not clear owing to multiple medication administration [4]. To date, this is the first report of recurrent PMAE in association with IVIg infusions. Features of all three cases of proposed drug-induced PMAE are documented in **Table 1**; however, the limited number of cases makes drawing definitive conclusions about drug-induced PMAE difficult.

Treatment is aimed at decreasing the length of the eruption and/or the frequency of recurrences. Temporary successes have been reported with use of systemic antibiotics, topical corticosteroids with or without occlusion, and UVA phototherapy. A recent case report highlighted hydroxychloroquine as a possible therapeutic option as well [6]. However, most reports disclose a recurrence after treatment is discontinued [7].

Conclusion

Primary migratory arciform erythema is a rare form of T cell pseudolymphoma that is likely underdiagnosed owing to overlap and/or similarity with other T cell pseudolymphomas and gyrate erythemas. Although no common etiology has been identified for reported cases of PMAE, this case suggests that IVIg may precipitate a recurrent form of PMAE.

Potential conflicts of interest

The authors declare no conflicts of interest.

Table 1. *Proposed cases of drug-induced palpable migratory arciform erythema.*

	Patient	Dantes et al. 2015 [1]	Dantes et al. 2015 [2]
Age (years)	60	60	47
Sex	M	F	F
Ethnicity	Caucasian	Unknown	Unknown
Drug	IVIg infusions	Daily clomipramine, nimesulide, paracetamol	Statin (daily); dipyrone and diclofenac (sporadically)
Condition Treated	Myasthenia gravis	Fibromyalgia, osteoarthritis	Not reported
Time to rash onset	7-14 days following drug administration	20-30-day intervals	Not reported
Location	Upper trunk	Upper trunk and arms	Neck, upper trunk, and arms
Average duration of individual lesions	14 days	7-10 days	21 days
Treatment	None	Drug discontinuation	Drug discontinuation
Resolution	N/A	Brief remission followed by reappearance on acral sites	Complete remission 12 weeks after drug discontinuation
Recurrence	Lesions continued to recur with subsequent IVIg administrations	Yes	No

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