Paraneoplastic erythema annulare centrifugum associated with mycosis fungoides

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Key words: cutaneous T-cell lymphoma (CTCL); erythema annulare centrifugum (EAC); mycosis fungoides (MF); paraneoplastic erythema aunnulare centrifugum eruption (PEACE).

INTRODUCTION

Erythema annulare centrifugum (EAC) is a reactive erythema that is typically a waxing and waning, often chronic condition. The presentation is highly variable but characteristically manifests as annular or arcuate, erythematous patches or plaques with trailing scale along the inner portion of the advancing edge of the lesion.[1] Although its pathomechanism remains unclear, EAC is most commonly associated with infection, drug exposure, autoimmune disease, and malignancy.[2] The term "paraneoplastic erythema annulare centrifugum eruption" (PEACE) has been proposed to designate EAC associated with underlying malignancy.[1]

Among hematolymphoid neoplasms linked to PEACE-associated malignancies, primary cutaneous T-cell lymphoma (CTCL) has not been well recognized, although mycosis fungoides (MF) resembling EAC has been infrequently described.[3-8] To better characterize the clinical and pathologic features of PEACE in CTCL, an institutional review board–approved, targeted, systematic inquiry of the University of Iowa Cutaneous Lymphoma registry was conducted to extract information on all CTCL patients with concurrent EAC. Of 162 eligible CTCL registry patients, 2 had concurrent clinicopathologically confirmed CTCL and EAC, and both of their electronic medical records were audited in detail. Two additional patients detected in the query diagnosed with EAC and MF did not have available histopathologic confirmation of EAC and were not included in this study. A review of the literature via PubMed was also conducted, employing all combinations of "EAC," "erythema annulare centrifugum," "paraneoplastic," "mycosis fungoides," "CTCL," and "cutaneous T-cell lymphoma," with additional survey of manuscript references.

Abbreviations used:

CTCL:	cutaneous T-cell lymphoma
EAC:	erythema annulare centrifugum
MF:	mycosis fungoides
PEACE:	paraneoplastic erythema annulare centrifugum eruption

CASE REPORT

Clinicopathologic analysis of the 2 patients with concurrent CTCL and EAC is summarized in Table I. Both patients were older men (age, 71 to 75 years) and also shared in common an MF stage of IIB (manifesting nodular morphology). Both patients had been similarly treated with a variety of skin-directed and systemic therapies over several years for their MF before the onset of EAC. The 2 patients differed from each other in their MF histopathology, with one showing features of granulomatous MF and the other showing folliculotropism (Figs 1 and 2). No other potentially more likely EAC association, such as temporally associated active infection (eg, tinea

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Funding sources: None.
IRB approval status: Not applicable.

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JAAD Case Reports 2021;17:65-8.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.09.027

Table I. Clinicopathologic analysis of two patients with concurrent CTCL and EAC

		CTCL features				EAC features			
Patient no.	Sex	Age at diagnosis (years)	Type and stage when EAC appeared	History pre-EAC diagnosis	History post-EAC diagnosis	Age at diagnosis (years)	Clinical presentation	Pathology	Course
1	M	68	FMF, stage IIB	Patches and plaques disseminating over extremities and trunk, then remitting with treatment with topical steroids, acitretin, bexarotene, phototherapy (PUVA, N-UVB, TSEBT, interferon, vorinostat)	Variably responsive to succession of therapies: vorinostat (second course), methotrexate, gemcitabine, brentuximab, mogamulizumab; currently (age, 83 years) limited skin disease off therapy	71	During one active phase of worsening MF, several new distinct 3- to 8-cm annular to arcuate erythematous plaques with central clearing and trailing scale appeared on trunk and extremities (Fig 1)	Subacute spongiotic dermatitis with superficial perivascular lymphocytic infiltrate, compatible with superficial EAC. No epidermotropism, folliculotropism, or lymphocyte atypia	Cleared after 3 months treatment with topical steroids
2	M	68	Granulomatous MF, stage IIB	Scattered scaly plaques with progressive dissemination and development of nodules, variably responsive to PUVA, methotrexate, bexarotene, local radiation therapy, N-UVB, vorinostat	Progression of disease despite successive treatment with local radiation, extracorporeal photopheresis, and then TSEBT (age, 80 years)	75	During a period of acutely worsening MF, new clinically distinct, annular, erythematous to violaceous plaques with trailing scale appeared on upper extremities and chest (Fig 2)	Spongiotic epidermis with patchy parakeratosis, exocytosis, and an underlying perivascular lymphoid infiltrate compatible with superficial EAC	Cleared with treatment with topical steroids

CTCL, Cutaneous T-cell lymphoma; *EAC*, erythema annulare centrifugum; *FMF*, folliculotropic mycosis fungoides; *MF*, mycosis fungoides; *N-UVB*, narrow-band ultraviolet B therapy; *PUVA*, psoralen and ultraviolet A therapy; *TSEBT*, total skin electron beam therapy.

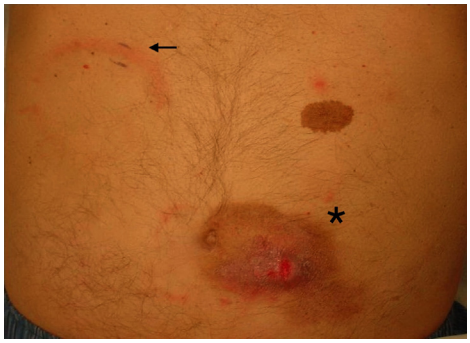

Fig 1. Erythematous arcuate plaque of erythema annulare centrifugum on the right side of the abdomen (*arrow*) with adjacent large nodular plaque of mycosis fungoides (*star*) and a congenital nevus in patient 1.

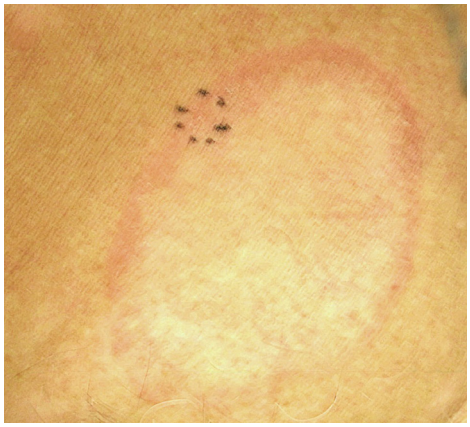

Fig 2. Annular erythematous plaque of erythema annulare centrifugum several centimeters in diameter on the right side of the chest in patient 2. The circle of black dots is where we took the punch biopsy from this patient.

pedis), suspect medication, endrocrinologic abnormality, rheumatologic disorder, or other malignancy, was identified in either patient. Although differentiation between MF and EAC can be challenging, the histopathologic findings for both patients demonstrated the typical pattern seen in EAC, with superficial perivascular lymphocytic infiltrates with variable overlying spongiosis (Fig 3).

The literature review revealed multiple PEACE cases associated with non-Hodgkin lymphoma, but in none of these was the non-Hodgkin lymphoma clearly classified as CTCL.[2,9] Significantly, several cases of MF manifesting with EAC morphology were recognized. However, in all cases, with 1 exception, the condition presented was explicitly regarded as MF, with a clinical appearance resembling EAC but with histopathology consistent with MF. In 1 case, the initial presentation of the patient described was interpreted as EAC-like with nondiagnostic histopathology but with subsequent clear evolution to MF.[8]

DISCUSSION

Distinction between CTCL-associated PEACE and MF with EAC-like morphology is uniquely challenging, given their overlapping clinical presentations combined with the nuanced histopathologic features of early MF.[10] Restricting the focus to established CTCL patients with additional classic clinical and pathologic EAC lesions, our inquiry of 162 CTCL registry patients identified 2 older male patients, yielding a prevalence of 1.2%. Notably, in

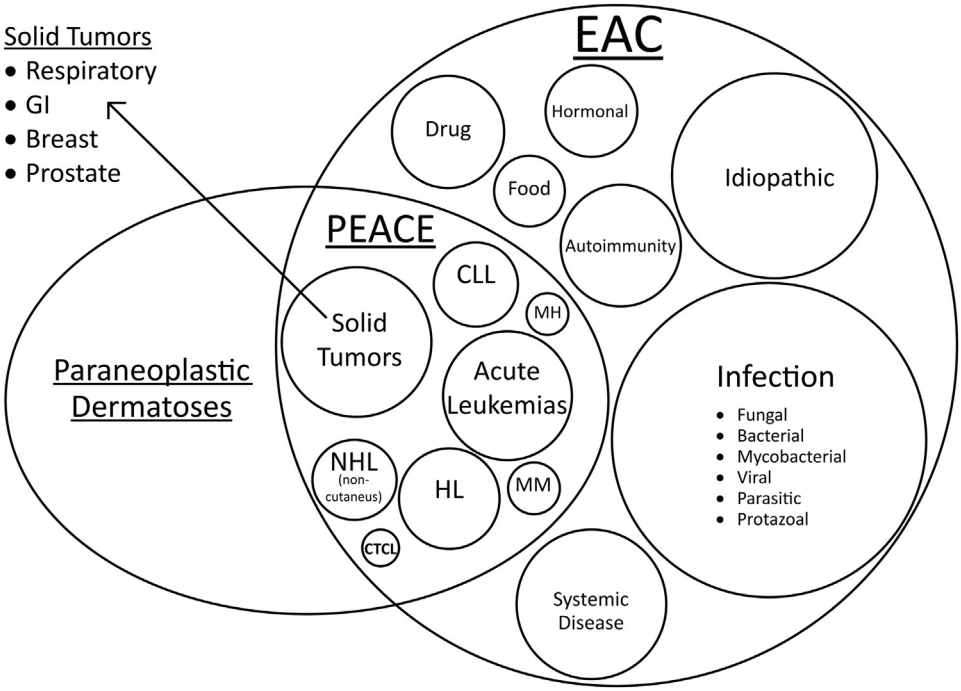

Fig 3. Tight perivascular lymphocytic inflammation, consistent with erythema annulare centrifugum.

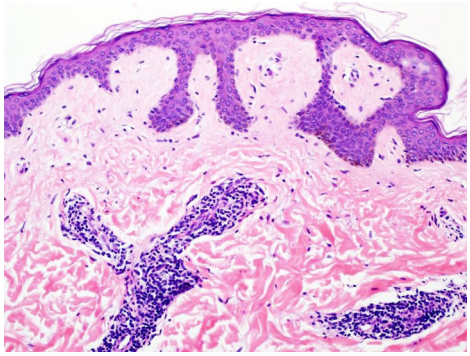

Fig 4. Venn diagram of conceptual scheme portraying PEACE as the intersection between EAC and paraneoplastic dermatoses. Associated underlying conditions are included. *CLL*, Chronic lymphocytic leukemia; *CTCL*, cutaneous T-cell lymphoma; *EAC*, erythema annulare centrifugum; *GI*, gastrointestinal; *HL*, Hodgkin lymphoma; *MH*, malignant histiocytosis; *MM*, multiple myeloma; *NHL*, non-Hodgkin lymphoma; *PEACE*, paraneoplastic erythema annulare centrifugum eruption.

both patients, the onset of EAC occurred in association with a flare or worsening of their CTCL, a key feature of paraneoplastic dermatoses.[11] Our series expands the associations of paraneoplastic EAC to include CTCL (Fig 4), emphasizing that its distinction from EAC-like CTCL by the clinician is critical for optimizing appropriate management.

Conflicts of interest

None disclosed.

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