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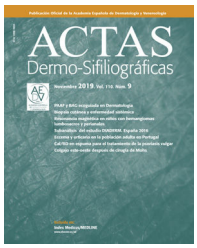

BRIEF COMMUNICATION

[Translated article] Erythema Papulatum Centrifugum: A Clinically Distinct Dermatosis. CLINI-AEDV Case Series

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KEYWORDS
Erythema papulatum centrifugum;
Erythema papulosa semicircularis recidivans;
Annular;
Papular;
Paraneoplastic syndrome

Abstract Erythema papulatum centrifugum is a rare condition marked by a centrifugally growing border dotted with small papules and a relapsing course, often worse in spring and summer. There are not any specific diagnostic tests to confirm it. This study analyzes the clinical characteristics of seven cases, representing the largest series of non-oriental patients to date. Our findings confirm the pruritic and seasonally relapsing nature of this condition. Lesions are typically few, primarily located on the trunk, and generally exceed 5 cm in diameter. Interestingly, in one patient, two outbreaks correlated temporally with the COVID-19 vaccine. In two other cases, the condition was linked to hematological malignancies: multiple myeloma and Hodgkin lymphoma. These observations, along with other neoplasm-associated cases reported in the literature, suggest that this entity might function as a paraneoplastic syndrome.
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PALABRAS CLAVE
Eritema papuloso centrífugo;
Eritema papuloso semicircular recidivante;
Anular;

Eritema papuloso centrífugo: una dermatosis clínicamente reconocible. Serie de casos CLINI-AEDV

Resumen El eritema papuloso centrífugo es un cuadro poco frecuente caracterizado por un borde de crecimiento centrífugo salpicado de pequeñas pápulas y un curso recidivante, con predominio en primavera y verano. No existen pruebas complementarias que certifiquen el diagnóstico. Se analizan las características clínicas de 7 casos que conforman, hasta la fecha, la serie más extensa de pacientes no orientales, confirmando su carácter pruriginoso y recidivante

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Papuloso;
Síndrome
paraneoplásico

estacional. Las lesiones suelen ser escasas en número, de predominio en tronco, y su diámetro es generalmente superior a 5 cm. Como posible papel desencadenante, en uno de nuestros pacientes, 2 de los brotes tuvieron una relación temporal con la vacuna para COVID-19, y en otros 2 casos se relacionó con sendas neoplasias hematológicas: un mieloma múltiple y un linfoma de Hodgkin. Estos y otros casos asociados a neoplasias referidos en la literatura plantean que esta entidad pueda comportarse como un síndrome paraneoplásico.
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Introduction

Papular centrifugal erythema (PCE) is an uncommon condition that presents as a pruritic figurate erythema that enlarges in an annular or semiannular pattern with central clearing and a rim peppered with small erythematous papules. In 2013, Ohmori et al. published the first 5 cases in the Western literature and reviewed 152 cases from the Japanese literature, defining its clinico-epidemiologic features.[1] PCE is more frequent in men and predominates in middle age. It usually presents as a single lesion or $\leq$5 lesions, most often on the abdomen and extremities. In more than half of cases, it is recurrent with a summer predominance. Occasional tumor associations have been reported. Our objective was to describe the characteristics of this entity in our setting.

Methods

We conducted a cross-sectional observational study with ambispective data collection within the AEDV CLINI-AEDV platform, approved by *Hospital Universitario Puerta de Hierro–Majadahonda* (Madrid, Spain) Research Ethics Committee for Medicinal Products (Minutes no. 18/2022).

The study population comprised all patients of any age and sex seen by each recruiting dermatologist with a clinical diagnosis of PCE.

Dermatologists were invited to participate through AEDV dissemination channels and national dermatology social networks (February 2024). Participants included all cases with this diagnosis from their centers.

Data were collected in an online case-report form via the REDCap platform.

Demographic, clinical, and epidemiologic variables were recorded, and descriptive statistics were performed.

Results

Seven PCE cases from 6 dermatologists were included. Demographic, clinical, and epidemiologic data for the patients in the present series (numbered 31–37) and for those reported in the English- and Spanish-language literature are detailed in Table 1. Cases cited by Ohmori from the Japanese literature were not included.

We studied a total of 7 patients (2 men, 5 women) aged 39–75 years. At inclusion, lesion count ranged from 1 to 3. In 4 patients, lesions were annular (at least one complete ring) and in 3 semiannular (Fig. 1). Six patients reported pruritus. Maximum lesion diameter exceeded 5 cm in all but one case, with the largest reaching 40 cm. The papules peppering the rims were numerous (20–60) and small (2–6 mm). The most frequent sites were the abdomen, followed by the back and upper limbs. Five patients had a recurrent course, with spring–summer onset in 4; timing could not be specified in 2. The number of recurrences per patient ranged from 2 to 9, although 2 patients had only a single episode. Each flare lasted 1–6 months and resolved with residual pigmentation in 5 cases.

Regarding ancillary testing, no fungal studies were performed; patch testing was run in only 2 cases – negative in case 33 and weakly positive on day 4 to dodecyl gallate and gallate mix with unknown relevance in case 37. Two patients had ANA >1:160; one of them also had low C4, anticentromere antibodies, and antimitochondrial antibodies (M2), and a third had mildly elevated C-reactive protein and low LDH. Six patients underwent biopsy; all showed a perivascular lymphohistiocytic infiltrate (superficial and deep in 3), with occasional eosinophils (4 cases) and neutrophils (3 cases). Three patients exhibited epidermal changes – acanthosis, spongiosis, and exocytosis – but none showed abnormalities of the eccrine sweat glands.

No triggers such as alcohol, spicy foods, sweating, or infections were identified. In case 37, two flares occurred after the administration of 2 Pfizer COVID-19 vaccines. One patient had concomitant diarrhea, one had Hodgkin lymphoma, and another had IgG-kappa myeloma. Treatments used included topical corticosteroids (6 cases), oral corticosteroids (2), and – one case each – hydroxychloroquine, oral terbinafine, famciclovir, and antihistamines. All responses were partial and flares were considered to remit spontaneously, except in one patient (case 7) who was successfully treated with betamethasone dipropionate plus fusidic acid. The patient in whom myeloma was diagnosed from the PCE evaluation had no further recurrences after induction with six VRD cycles (bortezomib, lenalidomide, dexamethasone) and autologous hematopoietic stem-cell transplantation, despite >8 years of recurrent flares beforehand. The patient in case 35 had a single episode that resolved when Hodgkin lymphoma was diagnosed and treated. These two patients have been recurrence-free for nearly 2 years.

Discussion

PCE is a rare dermatosis with distinctive clinical features. ''Recurrent papular semicircular erythema,'' described by

Table 1 PCE cases: literature review.

Case	Author (country/year)	Sex	Age	Seasonality	Flares/yr	Pruritus	No. lesions	Recurrent	Perieccrine inflammation	Associated disease
1	Ohmori et al.[1]	Male	54	Yes (summer)	Unknown	Yes	>1	No	NP	–
2	(Japan/2013)	Male	55	Yes (summer)	Unknown	Yes	1	No	NP	Polymyositis, interstitial pneumonitis
3		Male	23	Unknown	Unknown	Yes	>1	Yes	Yes	–
4		Male	89	Unknown	Unknown	Yes	>1	Unknown	NP	–
5		Male	63	Unknown	Unknown	Yes	>1	Unknown	NP	Gastric cancer
6	Song et al.[2]	Male	39	Yes (summer)	3	Yes	>1	Yes	NP	–
7	(China/2012)	Male	37	Yes (summer)	2	Yes	>1	Yes	No	–
8		Male	30	Yes (summer)	3	Yes	1	Yes	NP	–
9		Male	28	Yes (summer)	3	Yes	1	Yes	NP	–
10		Male	36	Yes (summer)	2	Yes	1	Yes	NP	–
11		Male	34	Yes (summer)	5	Yes	>1	Yes	No	–
12		Male	24	Yes (summer)	2	Yes	>1	Yes	No	–
13		Male	35	Yes (summer)	3	Yes	1	Yes	No	–
14		Male	29	Yes (summer)	4	Yes	>1	Yes	No	–
15	Rodríguez-Lomba et al.[4] (Spain/2018)	Female	50	Yes (summer)	20	Yes	1	Yes	No	–
16	Bernia et al.[5] (Spain/2020)	Female	70	Yes (spring/summer)	6	Yes	1	Yes	No	–
17	Oba et al.[6]	Male	30	Unknown	2	Yes	1	Yes	No	–
18	(Turkey/2022)	Male	54	Unknown	5	Yes	>1	Yes	No	–
19	Franco et al.[7] (USA/2018)	Male	21	Yes (summer)	1	Yes	1	No	Yes	–
20	Ueda et al.[8]	Male	38	Unknown	5	Yes	1	Yes	Yes	–
21	(Japan/2013)	Male	38	Unknown	1	Yes	>1	No	Yes	–
22	Wang et al.[9] (Taiwan/2015)	Male	35	No[a]	>1	Yes	1	Yes	Yes	Melanoma
23	Zhang et al.[10]	Female	32	Yes (autumn)	6	Yes	1	Yes	No	–
24	(China/2020)	Male	63	Yes (autumn/winter)	20	Yes	3	Yes	No	–
25		Female	32	Yes (winter)	2	Yes	1	Yes	No	–
26		Female	33	Yes (spring)	2	Yes	2	Yes	No	–
27		Female	48	Yes (spring)	5	Yes	1	Yes	No	–
28		Male	31	Yes (summer)	3	Yes	3	Yes	No	–
29		Female	27	Yes (summer/winter)	7	Yes	1	Yes	No	–
30	Inoue et al.[13] (Japan/2016)	Female	39	Yes (summer)	3	Unknown	1	Yes	No	B-cell lymphoma
31	Allegue et al.	Female	51	Yes (spring/summer)	9	Yes	3	Yes	No	–
32	(Spain/2024)	Female	64	Yes (spring/summer)	9	Yes	3	Yes	No	Myeloma
33		Female	54	Not clarified[b]	4	Yes	1	Yes	No	–
34		Male	75	No	1	Yes	2	No	No	–
35		Female	39	Yes (summer)	1	Yes	3	No	No	Hodgkin lymphoma
36		Female	58	No	2	No	1	Yes	No	–
37		Male	42	Yes (spring/summer)	3	Yes	1	Yes	No	–
	Totals	Male 65% (24/37)	Mean 43 (SD, 16)	Yes 93% (35/37)	–	Yes 85% (29/37)	–	Yes 83% (29/35); No 17% (6/35)	No 83% (24/29); Yes 17% (5/29)	–

NP: not performed.

[a] Humid, warm climate year-round without seasonal variation.

[b] Not clarified (the patient lived between Spain and Argentina and had flares in both countries with different seasons).

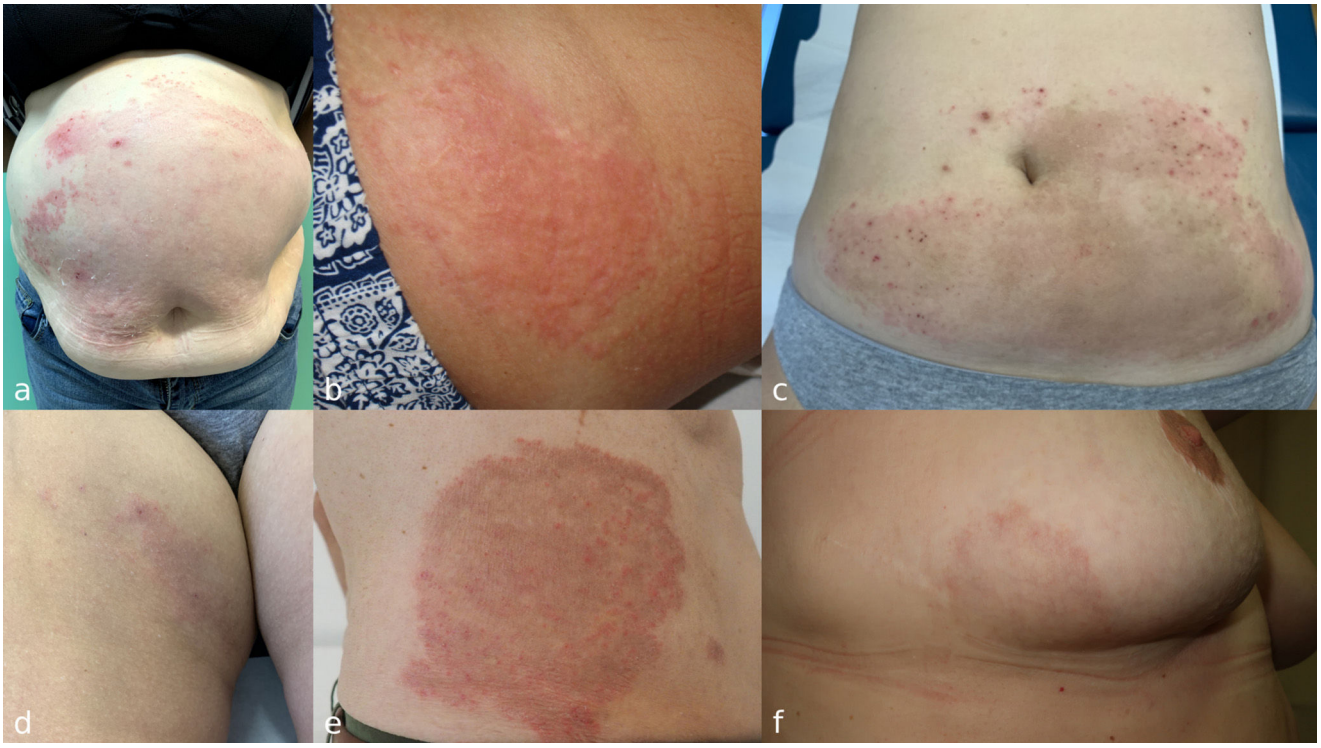

Figure 1 Large annular plaque occupying the entire abdomen with a rim peppered with papules in patient 32 (a); semiannular plaque with a papular rim on the abdomen in patient 33 (b); extensive annular erythema with papule-studded borders and central pigmentation in patient 34 (c); another plaque on the thigh in patient 34 (d); large plaque with a tendency to central clearing and numerous predominantly peripheral papules in patient 35 (e); semiannular plaque on the breast with an erythematous papular rim in patient 36 (f).

Song et al.[2] in Chinese patients, is indistinguishable from PCE,[3] and we include it in this review, understanding that both terms denote the same entity.

It predominates in East Asian patients, with only 5 cases described in non-Asian patients to date.[4–7] The 7 cases we present constitute the largest series in Western patients. Although male predominance reaches nearly 90% in Japan,[1] our review (Table 1) shows 71%; however, among Spanish cases,[4,5] including our series, 78% were women. Lesions are typically >10 cm and may reach 50 cm, appearing mainly on the trunk and proximal limbs. More than half of cases recur, usually in summer, and resolve spontaneously over weeks to months without sequelae or with central post-inflammatory hyperpigmentation,[3,4,6] as in 5 of our cases. Initially, inflammation of eccrine ducts in the dermis and epidermis was considered a defining feature,[1,8,9] but later work showed it is neither constant nor even frequent.[2–6] In our series, no eccrine changes were found. Histopathology is nonspecific, showing mild epidermal changes (parakeratosis, spongiosis) and a perivascular lymphocytic infiltrate with or without perieccrine inflammation. Eosinophils and neutrophils may be more common than reported: we found them in 4 and 3 cases, respectively, whereas the literature mentions neutrophils in only 2 cases.[4,7]

Etiopathogenesis is unknown. Ohmori et al.[1] place PCE among annular erythemas of uncertain cause, alongside erythema annulare centrifugum (EAC), with which the main differential diagnosis arises – particularly a rare EAC variant that also tends to recur annually in summer.[10–12] In PCE, however, the erythema border is papular, lesions are fewer and larger, and they predominantly involve the trunk, unlike EAC. Although laboratory abnormalities or associated diseases are generally not described,[1,3] PCE is thought to be a reactive process in which infectious, drug-related, or neoplastic triggers may be involved; heat, humidity, sweating, alcohol, and spicy foods have been proposed as precipitants.[1,3,8,9] We could not confirm these triggers in our patients, although in case 37 two flares appeared 2 weeks after COVID vaccination. There is no established therapy; topical corticosteroids are most used, with inconsistent responses.

A relevant issue is the potential paraneoplastic nature of this eruption. In our series, 2 of 7 cases were associated with tumors. In cases 32 and 35, PCE preceded the diagnoses of myeloma and Hodgkin lymphoma, respectively, which were discovered during the dermatosis workup. Three tumor-associated cases appear in the literature: metastatic gastric adenocarcinoma,[1] melanoma,[9] and primary pancreatic B-cell lymphoma.[13] Although details are lacking for the gastric adenocarcinoma case, in the melanoma and pancreatic lymphoma cases the PCE began with the tumor and disappeared after remission or treatment,[9,11] as in our 2 patients – supporting the hypothesis that this dermatosis may sometimes be paraneoplastic, analogous to EAC.[14]

PCE is a rare dermatosis with an annular erythema that expands centrifugally and a characteristic rim peppered with erythematous papules. Together with its recurrent, summer-predominant course, these features allow clini-

cal distinction within the annular erythema group, given the absence of pathognomonic histopathology. Its potential paraneoplastic nature is also important to consider in affected patients.

Conflicts of interest

None declared.

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