Annually recurring erythema annulare centrifugum: A distinct entity?

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Four patients presenting a peculiar clinical variant of erythema annulare centrifugum are reported. The lesions were clinically and histopathologically indistinguishable from classic superficial erythema annulare centrifugum but constant annual and seasonal recurrences for many years or decades were observed. No clear precipitating factor could be identified. No associated symptoms were present and the eruption regressed spontaneously after a variable period of days to months. Annually recurring erythema annulare centrifugum seems to represent a rare distinct clinical entity that has received little attention in literature. Clinicopathologic features of this peculiar clinical disorder and the differential diagnosis with other recurrent seasonal eruptions are reviewed. (J Am Acad Dermatol 2006;54:1091-5.)

A peculiar form of superficial erythema annulare centrifugum (EAC) presenting constant yearly recurrences for many years was first reported by Christine in 1930.1 This peculiar variant of annually recurring (AR) EAC received little attention in the literature, and only isolated reports in the European literature1 were published afterward. In 1986, Yoshikuni et al,2 pointed out the possible association between AR EAC and hereditary lactate dehydrogenase (LDH) M-subunit deficiency.

We review the clinical, histopathologic, and biochemical features of 4 patients presenting with this peculiar and recurrent form of EAC.

CASE REPORTS

Case 1

A 76-year-old woman was referred for evaluation of a relapsing self-healing annular eruption involving her trunk and extremities that had recurred yearly for the last 8 years. Medical history included diabetes mellitus, hyperthyroidism, valvular heart disease, cholecystectomy, and breast carcinoma (October 2000) treated with operation and chemotherapy. She was following treatment with acenocoumarol, glibenclamide, hydrochlorothiazide, and diltiazem chlorhydrate.

The patient presented annually relapsing nonpruritic annular lesions located on her chest, back, arms, and legs that constantly appeared in the summer and resolved spontaneously in autumn. The eruption began as small erythematous papules that coalesced into annular plaques with central clearing and centrifugal spread. No precipitating factors were identified. No fever, general symptoms, or mucosal lesions were present.

Physical examination revealed an apparently healthy woman with multiple 2- to 8-cm erythematous urticariform and annular lesions on her chest, back, arms, and thighs (Fig 1). A peripheral scaling border was occasionally noted. The lesions regressed spontaneously 4 months after onset. Neither inguinal nor axillary lymph nodes were present.

Case 2

An 83-year-old man was referred to our department for evaluation of a 23-year history of an AR pruritic annular eruption that appeared constantly during the summer months (May-June) and regressed spontaneously in autumn (September-October).
Medical history disclosed arterial hypertension and squamous cell carcinoma of the tongue diagnosed in 1988 treated with operation, radiotherapy, and chemotherapy in 1990.

During the last 5 years, physical examination had revealed multiple erythematous, purpuric infiltrated papules and plaques with centrifugal extension and central clearing that led to urticarial, non-scaly plaques with arcuate or annular elevated borders and central patchy hyperpigmentation. The lesions involved symmetrically the internal aspects of both arms and legs (Fig 2).

Case 3

A 55-year-old man came to our department for evaluation of a peculiar recurrent summer eruption. Medical history was unremarkable.

For the last 13 years he referred to the development of a peculiar and constant skin eruption in summer. No other precipitating factors were identified. The lesions were pruritic, erythematous, and violaceous annular plaques involving both legs and arms. They progressed centrifugally with fine peripheral scaling, persisted for 15 days and tended to disappear spontaneously. During the last 4 years the disorder was partially controlled with systemic steroid therapy. No mucosal lesions were present and the rest of the physical examination disclosed no abnormalities.

Case 4

A 55-year-old woman presented a 15-year history of recurrent symmetric violaceous purpuric annular erythematous plaques showing a central clearing and peripheral spread on her arms and legs. Medical history disclosed a goiter treated with surgical excision. The patient was treated with thyroidal substitution treatment.

The eruption appeared in the spring and/or summer months and regressed spontaneously after 4 months. Physical examination revealed an apparently healthy patient with multiple annular papules and plaques on both arms and legs. The lesions were occasionally purpuric and painful, presented an active border, and progressed centrifugally with a discrete scaly peripheral rim and leaving occasional residual hyperpigmentation. The rest of the physical examination was unremarkable.

Laboratory studies

In all 4 patients a complete routine laboratory investigation including hematologic, biochemical (glucose, hepatic and renal parameters, serum electrophoresis), and immunologic (antinuclear factor, rheumatoid factor, A [Ro]/[La], organ-specific antibodies, immunoglobulins, radioallergosorbent) tests disclosed no abnormalities. *Borrelia burgdorferi* antibodies were constantly negative. Direct potassium hydroxide examination and cultures for fungi and bacteria from skin lesions failed to identify micro-organisms. No phototests were performed. Chest radiographs were consistently normal. Electrophoretic analysis of erythrocyte LDH isozymes was not performed (not available in our laboratory).

Histopathologic examination

Histologic examination of 5 skin biopsy specimens revealed an inflammatory perivascular lymphohistiocytic infiltrate of variable intensity in the papillary and middermis with occasional eosinophils.
(3 biopsy specimens) (Fig 3). Neither fibrinoid necrosis nor vascular damage was detected. Papillary dermal erythrocyte extravasation was observed in 3 biopsy specimens. Edema of the papillary dermis was an inconstant feature (two skin biopsy specimens). Discrete acanthosis (one biopsy specimen) and mild spongiosis (two biopsy specimens) were also occasionally noted.

Direct immunofluorescence study from involved skin in 4 specimens failed to demonstrated IgM-, IgG-, IgA-, or C3-specific deposits.

**DISCUSSION**

“Erythema annulare centrifugum” is the term most often used for all gyrate erythemas except erythema marginatum, erythema chronicum migrans, and erythema gyratum repens. The term was originally used by Darier in 1916 and defines a clinical disorder manifested by solitary or multiple annular, erythematous lesions, which may spread outward or remain stationary. A fine scale may be present inside the advancing edge. The lesions often involve the trunk and proximal parts of the extremities.

The pathogenesis of EAC is unknown. A hypersensitivity reaction to many external or internal stimuli has been postulated. EAC has been associated with many entities: infectious diseases (bacterial, viral, fungal, mycobacterial, and parasitic), hormonal disturbances (menstrual cycle, hyperthyroidism), some food and drugs (salicylate, antimalarial, cimetidine, amitriptyline, gold sodium thiomalate, and etizolam), and even occult malignant solid or hematologic neoplasms have been incriminated as causative factors. However, in a large proportion of cases no causative agent can be detected (idiopathic EAC).

Two distinct forms of EAC (superficial and deep) have been distinguished. In the superficial variant the lesions tend to be clinically nonindurated and manifest scaling along the ring-shaped or gyrate border. Histologically, a well-demarcated “coat-sleeve” superficial perivascular dermal lymphohistiocytic infiltrate with eosinophils is observed. Slight papillary edema, spongiosis, and parakeratosis can also be present. In the deep type, a similar perivascular infiltrate is seen, but in addition, the inflammatory infiltrate involves in addition the reticular dermis.

The reported cases fulfill the classic clinical and histopathologic features of superficial EAC, but a characteristic pattern of constant AR for many years or decades was noted. This peculiar variant of idiopathic EAC (AR EAC) has exceptionally been reported in the literature (Table 1).

AR EAC is usually observed in women (2:1) with ages ranging from 16 to 83 years (mean age: 49 years). The lesions tend to involve the upper and

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**Table 1. Annually recurring erythema annulare centrifugum: Review of the literature**

<table>
<thead>
<tr>
<th>Author</th>
<th>Sex/age, y</th>
<th>Affected area</th>
<th>Histologic features</th>
<th>Associations</th>
<th>Treatment</th>
<th>Evolution/onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piñol Aguadé et al 1966</td>
<td>F/60</td>
<td>Legs, elbows</td>
<td>Not done</td>
<td>None</td>
<td>Spontaneous resolution in 15 d</td>
<td>7 y/spring-summer</td>
</tr>
<tr>
<td></td>
<td>F/43</td>
<td>Legs, arms</td>
<td>Hyperkeratosis + edema dermis, perivascular infiltrate</td>
<td>None</td>
<td>Spontaneous resolution in 20 d</td>
<td>17 y/summer</td>
</tr>
<tr>
<td>Janss et al 1992</td>
<td>F/36</td>
<td>Arms, back</td>
<td>Normal epidermis, dense perivascular and periadnexal lymphocytic infiltrate</td>
<td>None</td>
<td>Spontaneous resolution in 6 wk</td>
<td>1 y previously/ not reported</td>
</tr>
<tr>
<td>Reported cases</td>
<td>F/76</td>
<td>Chest, back, arms, legs</td>
<td>All cases: perivascular lymphohistiocytic infiltrate dermis + eosinophils</td>
<td>None</td>
<td>Spontaneous resolution in autumn</td>
<td>8 y/summer</td>
</tr>
<tr>
<td></td>
<td>M/83</td>
<td>Internal aspect extremities</td>
<td>Normal epidermis</td>
<td>None</td>
<td>Spontaneous resolution in autumn</td>
<td>23 y/summer</td>
</tr>
<tr>
<td></td>
<td>M/55</td>
<td>Legs, arms</td>
<td>No vasculitis</td>
<td>None</td>
<td>Spontaneous resolution in 15 d</td>
<td>13 y/summer</td>
</tr>
<tr>
<td></td>
<td>F/55</td>
<td>Legs, arms</td>
<td>None</td>
<td>Spontaneous resolution in 4-5 mo</td>
<td>15 y/spring</td>
<td></td>
</tr>
</tbody>
</table>

F, Female; M, male.
lower extremities and occasionally the trunk. The face, palms, and soles are constantly spared. No associated symptoms can be detected. The lesions appear invariably during the spring or summer months, tend to persist from 15 days to 5 months, and regress spontaneously in the summer or autumn. No effective treatment has been described.

The origin of AR EAC remains unknown. In spite of a systematic search for possible causes no clear precipitating factors could be identified. A possible environmental factor (temperature, seasonal plants, or fungus) that could explain the periodic and constant course of the disease could be postulated. The absence of facial or trunk involvement and the presence of annular plaques on nonexposed skin seem to rule out the role of sun exposure.

The differential diagnosis of AR EAC should include some disorders manifested by periodic annular erythematous eruptions. Recurrent erythematous scaling lesions have been reported in association with hereditary LDH M-subunit deficiency. This disorder was originally described by Yoshikuni et al as an annular erythematous eruption with a characteristic exacerbation in summer and a constant spontaneous resolution in autumn, associated with muscular symptoms. Histologic features were hyperkeratosis, focal parakeratosis, and moderate acanthosis in the epidermis and a mild perivascular lymphocytic infiltrate in the papillary and middermis. Pale and swollen prickle cells in the upper epidermis, and abundant diastase-digestible granules that stained positive with periodic acid–Schiff were also observed. Our patients presented a similar cutaneous eruption but no extracutaneous symptoms were detected. LDH M-subunit deficiency was not investigated. A possible relationship between these cases and the clinical picture presented in our patients cannot be completely ruled out.

Recurrent annular erythema with purpura or leukocytoclastic vasculitis presenting as recurrent erythema annulare is a rare condition characterized by recurrent purpuric annular lesions, creating target or polycyclic patches. The lesions disappear spontaneously within 2 weeks, but recur monthly for years to decades. Histopathologic examination reveals changes consistent with leukocytoclastic vasculitis. No systemic involvement is detected. Although both disorders may share a similar clinical picture, in AR EAC the infiltrate is almost exclusively lymphocytic and no vascular damage (vasculitis) is present (Table II). Nevertheless, two of our 4 cases presented purpuric lesions and a possible relationship between both disorders (in the context of a common spectrum) cannot be completely ruled out.

Subacute cutaneous lupus erythematosus, polymorphous light eruption, solar urticaria, and Jessner lymphocyte infiltrate are some disorders that can manifest as recurrent seasonal crops of erythematous plaques with occasional arciform or annular distribution. However, the clinical and histopathologic features observed in our patients could permit these diagnoses to be discounted.

AR EAC represents a clinical subset of superficial EAC. Although neither associated symptoms nor

| Table II. Annually recurring erythema annulare centrifugum: Differential diagnosis |
|-------------------------------|-------------------------------|-------------------------------|
| Disease                      | AR EAC, current cases         | Erythematosquamous skin lesions in hereditary LDH M-subunit deficiency<sup>2,6,7</sup> | RAE-P<sup>5,8</sup> |
| Age and sex                  | 16-83 y                       | 16-51 y                       | 30-50 y |
|                             | M/F 1:2                       | M/F 1:2                       | M/F 1:1 |
| Localization                 | Trunk, extremities            | Extremities                   | Trunk, extremities |
| Clinical features            | Annular erythematous plaques; centrifugal spread | Small papules and annular erythematous; centrifugal spread | Annular erythematous plaques; centrifugal spread |
| Purpura                      | +/-                           | Negative                      | +++     |
| Recurrences                  | Annual (spring-summer)        | Annual (spring-summer)        | Monthly  |
| Duration                     | Weeks to 3-5 mo               | 3-6 mo                        | 2 wk     |
| Evolution                    | Years (2-30)                  | Years (6-40)                  | Years (2-30) |
| Histopathologic features     | Perivascular lymphocytic infiltrate; no vasculitis | Hyperkeratosis, parakeratosis, exocytosis, spongiosis, and perivascular infiltrate | Leukocytoclastic vasculitis |
| Associations                 | None                          | Deficiency LDH-subunit muscle disturbance | None |
| Treatment                    | Spontaneous resolution        | Spontaneous resolution        | Dapsone  |

AR, Annually recurring; EAC, erythema annulare centrifugum; F, female; LDH, lactate dehydrogenase; M, male; RAE-P, recurrent annular erythema with purpura.
precipitating factors could be identified, the participation of a possible environmental factor as a causative or precipitating factor cannot be ruled out. In conclusion, taking our observations into account and after reviewing the literature, it seems possible that a peculiar clinical variant of idiopathic EAC manifested by periodic and constant AR could be identified.

REFERENCES