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REVIEW

Annular Erythema of Infancy

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Abstract

Many skin diseases appear as annular lesions. Some are more typical of adults or older children, whereas others usually appear in young children. Annular or figurate erythema of infancy comprises a group of dermatoses in which the primary lesion adopts an annular, oval circinate, or polycyclic pattern. Similarities in clinical presentation, age at onset, and duration of lesions mean that these conditions are difficult to diagnose; sometimes, they can only be identified by subtle differences in their clinicopathologic features. Clinical pictures enable us to distinguish one member of this group of diseases from another and also to differentiate them from other annular eruptions. For ease of description, we classify annular erythema of infancy into 2 types: conditions with a known etiology and conditions with characteristic reaction patterns but uncertain etiology.

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Eritemas anulares en la infancia

Resumen

Un gran número de entidades dermatológicas adoptan formas anulares. Algunas de ellas son más propias de la edad adulta o de niños mayores, mientras que otras característicamente aparecen en niños pequeños.

Los eritemas anulares o figurados de la infancia son un grupo de dermatosis en los que la lesión primaria adopta una configuración de tipo anular, circinada oval o policíclica.

Sus similitudes en la forma de presentación clínica, edad de aparición y duración de las lesiones hacen que se trate de entidades de difícil diagnóstico, en ocasiones únicamente distinguibles por sutiles diferencias en sus manifestaciones clínico-patológicas.

Dentro de este grupo de enfermedades distinguimos una serie de cuadros clínicos con unas características peculiares, que permiten diferenciarlos entre sí y respecto a otras erupciones de carácter anular.

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A modo práctico, hemos clasificado los eritemas anulares de aparición en la infancia en entidades cuya etiología está claramente establecida y en entidades cuyos patrones de reacción son característicos, pero de etiología incierta.

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Introduction: Annular or Figurate Lesions

Figurate lesions are those that adopt an annular, arciform, polycyclic, concentric, or rosette pattern. The annular pattern is ring-shaped, and the border of the lesion is distinguished from the center by its height and coloration and the presence of scales.¹ The curved or arciform lesion occurs when the peripheral ring is partially resolved, leaving fragments in the shape of an arch.

The pattern results from the confluence of several circular lesions, leaving a larger lesion with festooned borders (Figure 1).¹

Many skin conditions appear as annular lesions. Some are more typically found in adults or older children, whereas others usually appear in infancy. Although ringworm is the most common annular skin condition in very young children, other skin diseases should be included in the differential diagnosis (Table 1). The following review covers the conditions known as annular or figurate erythemas

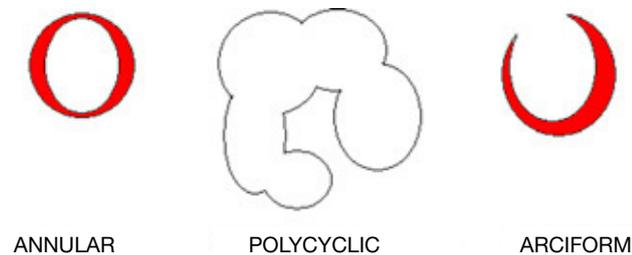


Figure 1 Patterns of figurate erythema.

Formation of Annular Lesions

Several mechanisms have been postulated to explain the annular pattern of the lesions; however, these explanations are not always satisfactory.

One proposed mechanism is based on irrigation, by which each round macule is an area irrigated by a single arteriole. Another hypothesis is that the lesion is the centrifugal extension of a pathologic-infectious, neoplastic, or allergic-process.

Table 1 Classification of the Main Annular Skin Conditions According to the Predominant Component

Annular Erythema with or without Desquamation	Annular Erythema with Raised Borders and Desquamation	Annular Erythema with Raised Borders	Annular Urticaria with Raised Lesions	Macular or Urticarial Annular Erythema
Neonatal lupus	Neonatal lupus	Erythema marginatum rheumatica	Erythema annulare centrifugum	Urticaria
Psoriasis	Necrolytic migratory erythema	Erythema chronicum migrans	Familial annular erythema	Acute annular urticaria/Urticaria multiforme
Pityriasis alba		Erythema gyratum repens	Annular erythema of infancy	Erythema multiforme
Pityriasis versicolor		Erythema gyratum atrophicans transiens neonatale	Eosinophilic annular erythema	
Bullous impetigo		Sarcoidosis	Neutrophilic figurate erythema of infancy	
Lupus vulgaris		Granuloma annulare		
Ringworm (<i>Tinea corporis</i>) Seborrheic dermatitis Actinic porokeratosis		Mycosis fungoides		

Table 2 Annular Erythema With Onset During Infancy

Known Etiology	Uncertain Etiology
Erythema marginatum rheumatica	Erythema gyratum atrophicans transiens neonatale
Erythema chronicum migrans	Annular centrifugal erythema
Neonatal lupus	Familial annular erythema Annular erythema of infancy Eosinophilic annular erythema Figurate neutrophilic erythema of infancy

Annular lesions with macular or slightly raised borders appear in different types of figurate erythema, such as erythema marginatum rheumatica, drug-induced eruption, or neonatal lupus. Annular lesions with scales point to pityriasis rosea, syphilis, ringworm, or psoriasis, whereas lesions such as mycosis fungoides, syphilis, or granuloma annulare, are composed of papules or nodules that can adopt an annular distribution.

Annular or Figurate Erythema of Childhood

Annular or figurate erythema of early childhood comprises a group of reactive vascular dermatoses in which the primary lesion adopts an annular, oval, or polycyclic pattern. Diagnosis is difficult and the lesions are occasionally identified only by subtle differences in clinicopathologic manifestations.

Within this group, we can distinguish a series of clinical pictures (Table 2) with specific, well-defined characteristics that make it possible to distinguish one entity from another within the group and also to differentiate them from other annular eruptions.

In the literature, the classification of annular or figurate erythema is vigorously debated and plagued by disconcerting doubts, contradictions, and synonyms. The clinical presentation, age of onset, duration of individual lesions, and total duration of the eruption have generated a plethora of descriptive terms to classify these disorders.²

For ease of description, we classify annular erythema of infancy into 2 types: conditions with a known etiology (Table 3) and conditions with characteristic reaction patterns but uncertain etiology (Table 4).

Annular Erythemas of Known Etiology

Erythema Marginatum Rheumatica

Erythema marginatum rheumatica is an evanescent erythema that appears during rheumatic fever in 10% to

20% of cases. It is more common in children than in adults, a reflection of the higher prevalence of rheumatic fever in children,^{3,4} and is highly characteristic of this fever, to the extent that it is one of the diagnostic criteria of the disease (Table 5).⁵ Rheumatic fever is a multisystemic inflammatory disease that appears in up to 3% of patients who have had an untreated nasopharyngeal infection caused by group A α -hemolytic streptococci.⁴

The eruption is transient (lasting from a few hours to a couple of days) and asymptomatic. It is more pronounced in the evenings and manifests as erythematous papular plaques that extend peripherally to form annular or polycyclic plaques with central clearing but no desquamation or epidermal abnormalities. The lesions are found mainly on the trunk and proximal portions of the extremities, although they can progress rapidly and affect the face and hands.

Histopathology reveals a superficial perivascular lymphocytic infiltrate and neutrophils without vasculitis.⁵ Treatment should target the underlying streptococcal infection, against which β -lactam antibiotics are effective.⁵ The course of cutaneous disease is not affected by treatment of the underlying infection, although symptoms have been observed to be milder and the lesions have sometimes disappeared.

Erythema Chronicum Migrans

Erythema chronicum migrans is considered the most common annular erythema in pediatric patients. This disorder is caused by a bite from a tick of the genus *Ixodes* and infection by the *Borrelia burgdorferi* spirochete. It is a specific cutaneous manifestation of Lyme disease and can appear as an initial manifestation in up to 90% of children who suffer from the disease.^{6,7}

A blue-red macule or papule appears at the inoculation site approximately 7 to 15 days after the tick bite and expands rapidly to form an erythematous annular plaque with central clearing. The diameter of the plaque is directly related to the duration of the lesion and presumably indicates the extension of the organism from the entry point. The lesions usually appear on the trunk and at proximal portions of the extremities (Figure 2).⁸

Associated urticaria and involvement of the hands and neck are more common in pediatric patients. The eruption resolves spontaneously over a period of 3 days to 8 weeks. Associated general symptoms may include fever, arthralgia, headache, regional lymphadenopathy, and cranial or peripheral neuropathy.

Although diagnosis is based on symptoms, serology testing can help to distinguish this condition from other types of annular erythema.⁸ Skin biopsy reveals a perivascular lymphocytic infiltrate with abundant plasma cells, mast cells, and eosinophils. Silver staining reveals spirochetes in 50% of cases.⁸

Erythema chronicum migrans resolves spontaneously, but antibiotic therapy can accelerate the process. The age of the patient must be taken into consideration when deciding on the antibiotic regimen. Children over 9 years of age should receive oral doxycycline at 2-4 mg/kg/d for

Table 3 Annular Erythema of Infancy of Known Etiology

Name of the Entity	Age at Onset	Morphology	Distribution	Histology	Etiology	Other Characteristics
Erythema marginatum rheumatica	Common in children	Symptomatic erythematous papules and plaques with peripheral extension and central clearing	Trunk and proximal portions of the extremities	Perivascular lymphocytic infiltrate with abundant neutrophils in the dermis	Active rheumatic fever Infection by group A α hemolytic streptococci	The lesions resolve in hours or a few days, although they may reappear for weeks
Erythema chronicum migrans	Adults and young people	Blue-red papules that progress rapidly with an annular erythematous border and central clearing	Trunk and proximal portions of the extremities	Deep and superficial perivascular lymphohistiocytic infiltrate of plasma cells and eosinophils	Infection by <i>Borrelia burgdorferi</i>	May be associated with arthralgia, myalgia, and cardiac or neurologic involvement
Erythema gyratum repens	Almost exclusive to adults Extremely rare in infancy	Multiple annular pruriginous erythematous lesions, with a wood-grain pattern and scaling at the borders	Any part of the body, sparing face, hands, and feet	Hyperkeratosis, focal parakeratosis, areas of spongiosis, and perivascular lymphohistiocytic infiltrate	Paraneoplastic eruption	Considered a hypersensitivity reaction to tumor antigens
Neonatal lupus	From 0 to 6 months (more common at 3 months)	Persistent annular erythematous plaques Resolution at 6-12 months. May leave telangiectasia, atrophy, or scarring on resolution	Face and scalp	Epidermal atrophy, hyperkeratosis, follicular plugs, vacuolar degeneration and necrotic keratinocytes	Placental transmission of maternal anti-Ro/SS-A, anti-La/SS-B, and anti-U1-RNP antibodies	Congenital heart block in 20% to 50% of affected children

Abbreviation: U1-RNP, U1 ribonuclear protein.

Table 4 Annular Erythema of Infancy of Uncertain Etiology

Name	Age at Onset	Morphology	Distribution	Histology	Other Characteristics
Erythema gyratum atrophicans transiens neonatale	First days of life	Annular erythematous plaques that progress with a raised border and atrophic center	Trunk, neck, and lips	Epidermal atrophy and mononuclear infiltrate. Direct immunofluorescence reveals granular deposition of IgG, C3, and C4 at the dermoepidermal junction	Resolves in months with no residual lesions. Considered a variant of neonatal lupus
Erythema annulare centrifugum	More frequent in adults, although there have been reports in children and neonates Two variants: superficial and deep	Erythematous papule that migrates slowly, with central clearing and formation of a ring • Superficial: desquamation at the border, pruriginous • Deep: raised border	Anywhere on the body, but mainly on the trunk and proximal portion of the extremities	<ul style="list-style-type: none"> • Superficial: focal parakeratosis, spongiosis, and superficial perivascular lymphohistiocytic infiltrate • Deep: deep and superficial mononuclear infiltrate, vacuolization, and necrotic keratinocytes 	Associated with infection (more common in children), drugs, neoplasm, and other causes (eg, sarcoidosis, subacute lupus erythematosus), although in most cases it is idiopathic
Familial annular erythema	Within a few days of birth	Intensely pruriginous urticarial papules with peripheral growth and central clearing that leave hyperpigmentation	Anywhere on the body	Similar to findings in EAC	Autosomal dominant variant of EAC. Individual lesions last a few days, although disease course is prolonged
Annular erythema of infancy	First months of life	Similar to EAC and FAE, annular erythematous papules. Lesions last a few days	Face, trunk, and extremities	Superficial and deep perivascular lymphohistiocytic infiltrate, with abundant eosinophils	Usually resolves in <1 y. Persistent annular erythema of infancy associated with EAC is an unremitting variety
Eosinophilic annular erythema	Mainly in adults	Similar to EAC, with lesions that persist for weeks or even months. New lesions appear over a period of years	Trunk and extremities	Superficial and deep perivascular lymphohistiocytic infiltrate, with abundant eosinophils, vacuolar degeneration, and dermal mucin	Considered a variant of AEI Differential diagnosis with Wells syndrome Treatment with antimalarial drugs
Neutrophilic figurate erythema of infancy	Early infancy	Lesions similar to those of EAC. Disappear in 2-4 weeks with no sequelae. Tend to become chronic	The lesions appear first on the face and may subsequently appear on the upper and lower extremities.	Perivascular lymphohistiocytic infiltrate, with abundant eosinophils and leukocytoclasia in the interstitial space	Considered a variant of AEI. The response to topical and systemic corticosteroids is poor.

Abbreviations: AEI, annular erythema of infancy; EAC, erythema annulare centrifugum; FAE, familial annular erythema; Ig, immunoglobulin.

Table 5 Jones Criteria for the Diagnosis of Rheumatic Fever**Major Criteria**

Carditis
 Polyarthritits
 Chorea
 Subcutaneous nodules
 Erythema marginatum rheumatica

Minor Criteria*Clinical manifestations*

Fever
 Arthralgia

Laboratory findings

Elevated ESR
 Elevated CRP
 Lengthening of the PR interval

Evidence of previous streptococcal infection

Elevated ASLO titer
 Positive pharyngeal culture or rapid detection of streptococcal antigen

Abbreviations: ASLO, antistreptolysin O; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.



Figure 2 Erythema chronicum migrans on the leg days after a tick bite.

3 weeks, whereas children under 9 years of age should receive oral amoxicillin at 25-50 mg/kg/d for 3 weeks.⁹

Erythema Gyrratum Repens

Erythema gyrratum repens is considered a paraneoplastic eruption that, in most cases, is associated with cancer of

the lung, breast, esophagus, stomach, and genitourinary tract. There are no reports in pediatric patients⁵; however, some disorders mimic the condition and manifest with lesions resembling erythema gyrratum repens.⁹ Pathogenesis is considered to involve a cross-hypersensitivity mechanism between similar tumor antigens and epidermal antigens.^{10,11}

Patients present multiple polycyclic or annular erythematous lesions that rapidly cover the body but spare the face, hands, and feet. These lesions, which are generally intensely pruriginous, grow by as much as 1 cm daily and form concentric figures in a wood-grain pattern, with scales on the advancing border.^{8,11}

Histologic findings are nonspecific, consisting of hyperkeratosis, focal parakeratosis, areas of spongiosis, and a perivascular lymphohistiocytic infiltrate.⁸

Erythema gyrratum repens usually progresses along with neoplastic disease and resolves when the underlying cause disappears. The lesions reappear if the tumor recurs.¹²

Neonatal Lupus

Neonatal lupus is an autoimmune disease that affects newborns and is associated with placental transmission of maternal antibodies. The main manifestations of this disease are transient skin lesions and heart lesions, which are responsible for the morbidity and mortality of this condition.

The maternal antibodies involved in the development of this disease are immunoglobulin (Ig) G1 anti-Ro/SS-A antibodies in 82% to 100% of affected newborns, while anti-La/SS-B antibodies (47%) and anti-U1 ribonucleoprotein antibodies are present in a minority of patients.⁵

Cutaneous manifestations appear in 40% to 50% of cases of neonatal lupus and may be present at birth or, more commonly, appear during the first weeks of life.⁸ They can be classified clinically as papulosquamous and annular. Annular lesions first manifest as erythematous macules and extend peripherally to form annular plaques that usually have a slight scale (Figure 3).

Any part of the skin may be affected, although neonatal lupus lesions appear most frequently on the face and scalp, especially around the orbit and on the cheeks, where they are exacerbated by exposure to sunlight.

The disease is transient and the lesions resolve towards 6 months of age, when maternal antibodies disappear completely from the infant's bloodstream. There is usually no scarring, although depigmentation may persist for several months and, in some children, there may be residual telangiectasia, hypopigmentation, and/or mild atrophy.^{2,8}

Histopathology findings, which are similar to those of subacute cutaneous lupus, include epidermal atrophy, hyperkeratosis, follicular plugs, vacuolar degeneration, and necrotic keratinocytes at the dermoepidermal junction accompanied by an intense periadnexal and superficial perivascular lymphocytic infiltrate. Direct immunofluorescence is positive in 50% of cases, with IgG, IgM, and C3 deposits found at the dermoepidermal junction and around vessels.



Figure 3 Neonatal lupus. Characteristic annular lesions on the forehead and scalp.

As for treatment of the cutaneous manifestations, although this disease is self-limiting, we stress the importance of sun protection measures in children with this complaint. Low-to-medium potency corticosteroids may be beneficial.

Martin et al¹³ reported on the long-term follow-up of 49 children with neonatal lupus and their 45 unaffected siblings. Six of the children had rheumatic or autoimmune disease. The results of the 55 serology tests performed were positive for antinuclear antibodies in 4 children (2 in 33 affected children and 2 in 22 healthy siblings) and negative for anti-Ro/SS-A antibodies and anti-La/SS-B antibodies in all the children. These data suggest that a small percentage of these patients could develop systemic lupus erythematosus or other autoimmune diseases during adulthood; therefore, they should undergo periodic evaluation to establish diagnosis and early treatment where necessary.¹³



Figure 4 Erythema gyratum atrophicans transiens neonatale in an infant. Note the atrophy in the center of the lesion and the raised border.

Annular Erythema of Uncertain Etiology

Erythema Gyratum Atrophicans Transiens Neonatale

Some authors consider erythema gyratum atrophicans transiens neonatale to be a variant of neonatal lupus.^{14,15}

Onset is during the first days of life, as annular erythematous plaques appear mainly on the trunk, neck, and lips. During the following weeks, the lesions progress, developing a raised border and atrophic center, and resolve spontaneously over subsequent months (before the end of first year of life) with no residual lesions (Figure 4).¹⁶

Histopathology reveals epidermal atrophy in the center of the lesion, sparing of the stratum basale, dermal edema, mucinosis, and a perivascular mononuclear infiltrate. Direct immunofluorescence reveals granular IgG, C3, and C4 deposition at the dermoepidermal junction and pericapillary space.¹⁴ These histopathologic characteristics are not typical of neonatal lupus, even though spongiosis and mucinosis can be observed in other types of cutaneous lupus erythematosus, with no involvement of the dermoepidermal junction.¹⁴

Although there are no specific laboratory findings for this condition, anti-Ro/SS-A, anti-La/SS-B, and

antinuclear antibodies should be investigated in the mother and the newborn in order to screen for neonatal lupus.⁸ Gianotti and Ermacora¹⁶ reported a case in which the results of both patient and maternal antinuclear antibody tests were negative; there was no possibility of testing for anti-Ro/SS-A antibodies. Puig et al¹⁴ reported a case of erythema gyratum atrophicans transiens neonatale in which the results of testing for anti-Ro/SS-A, anti-La/SS-B, and antinuclear antibodies were positive; they concluded that the case involved a subtype of neonatal lupus.

As the eruption is asymptomatic and resolves spontaneously, treatment is not necessary.

Erythema Annulare Centrifugum

Erythema annulare centrifugum is a migratory annular erythema that is considered to be a hypersensitivity reaction to a variety of antigens.¹⁷ Although it occurs mainly in adults, cases in newborns and children have been reported.⁸

Of unknown etiology, this condition has been associated with infections (eg, Epstein-Barr virus, molluscum contagiosum, candidiasis, dermatophytosis, ascaris, and tuberculosis), drugs (mainly amitriptyline, piroxicam, hydroxychloroquine, hydrochlorothiazide, and cimetidine), cancer (Hodgkin lymphoma, multiple myeloma, leukemia, prostate cancer, nasopharyngeal carcinoma, and spinocellular carcinoma), and other disorders such as sarcoidosis, subacute lupus erythematosus, Sjögren syndrome, liver disease, and thyroid abnormalities. In pediatric patients, erythema annulare centrifugum is most frequently associated with infection by *Candida albicans*, dermatophytes, Epstein-Barr virus, and poxvirus. Although this condition is not often associated with neoplasms, it can occur along with those that are most common in children, such as leukemia and Hodgkin lymphoma.⁸



Figure 5 Erythema annulare centrifugum in an infant after insect bites.

Erythema annulare centrifugum is usually asymptomatic or barely pruriginous and remits spontaneously in 2 to 3 weeks, although it can reappear at the same or other sites at different intervals. Lesions may be single or multiple and appear on any part of the body, although they are mainly seen on the trunk and the proximal areas of the extremities. They take the form of erythematous papules that migrate slowly (2-3 mm/d), flattening as they grow. The center then clears, after which the lesions become annular or arciform. There are 2 variants: an intensely pruriginous superficial lesion with a peripheral desquamative border and a deep lesion with a pronounced border with infiltrates but no desquamation or symptoms (Figure 5).

The 2 variants are distinguished by the location of the perivascular infiltrate. Superficial lesions are characterized by focal parakeratosis at the border of the lesion, spongiosis, and a superficial perivascular lymphohistiocytic infiltrate. Deep lesions, on the other hand, do not have epidermal abnormalities and are characterized mainly by both superficial and deep infiltrates of perivascular mononuclear cells, melanophages, mild vacuolization, and necrotic keratinocytes at the dermoepidermal junction.

Antihistamines have proven effective against pruritus, especially in children. In the absence of proven disease, antibiotics, antifungals, and systemic corticosteroids have been very useful in isolated cases.^{18,19}

Familial Annular Erythema

Familial annular erythema is an uncommon autosomal dominant disease²⁰ that occurs during the first days of life and may be associated, in very few cases, with other developmental abnormalities, such as mental retardation, chronic blepharitis, and nystagmus.²¹ It is believed to be a hereditary abnormality in the immune response to different antigens.

Urticarial papular lesions are intensely pruriginous with peripheral growth and central clearing that appear on any



Figure 6 Annular erythema of infancy in a 2-month-old infant.

part of the body and usually disappear in about 5 days leaving residual hyperpigmentation. Marked dermatographism is observed and may be associated with vesiculous lesions and geographic tongue. Disease course is prolonged, and there have been reports of cases lasting more than 15 years.

Histopathology findings are similar to those for erythema annulare centrifugum, namely, a nonspecific perivascular infiltrate in the superficial or middle dermis.²¹

Treatment is aimed at minimizing symptoms.

Annular Erythema of Infancy

Annular erythema of infancy is a rare yet benign eruption that appears during the first years of life as a possible hypersensitivity reaction to as yet unidentified antigens.^{21,22}

Physical examination reveals urticarial papules or annular or circinate erythematous plaques that grow slowly with a raised border. The condition is asymptomatic and the lesions are found on the face, trunk, and extremities. Individual lesions resolve in a few days, but new ones appear until full resolution at around 1 year of age, when the skin acquires a completely normal appearance (Figure 6).

There have been reports of a persistent variant with longer-lasting lesions that do not resolve during the first year. Known as persistent annular erythema of infancy,^{15,22} this condition has been considered a variant of erythema annulare centrifugum.^{18,23}

Histopathology reveals a perivascular interstitial lymphohistiocytic infiltrate that characteristically contains eosinophils.

In some variants, histopathology reveals a predominance of neutrophils or eosinophils, thus leading to the description of 2 new conditions, as follows.

Eosinophilic Annular Erythema

Eosinophilic annular erythema has received little attention in the literature.^{24,25} The condition is considered a variant of annular erythema of infancy, and there is no association with peripheral eosinophilia, parasitic infestation, allergy, autoimmune disease, or neoplastic disease.

It manifests clinically as multiple erythematous papules extending centrifugally to form annular or polycyclic plaques with a raised border and central clearing. The lesions are asymptomatic or mildly pruriginous and appear mainly on the trunk and extremities, although they can also affect the face. The lesions typically persist for weeks or months, and resolve with no residual lesions. New lesions can appear at other sites for years.

Histopathology findings include a deep and superficial interstitial periadnexal and interstitial perivascular lymphohistiocytic infiltrate with abundant eosinophils that is associated with dermal mucin, vacuolar degeneration of the basement membrane, and nuclear dust. Eosinophil degranulation and flame figures are not present, distinguishing this condition from Wells syndrome.²⁵

Antimalarial drugs can inhibit eosinophilotoxicity,²⁶ with the result that they have been proposed as an effective means of treating these erythemas. Kahofer et al²⁷ reported a case

of eosinophilic annular erythema in which indomethacin completely resolved the eruption. However, symptoms reappeared when the drug was discontinued due to adverse effects.

Neutrophilic Figurate Erythema of Infancy

Neutrophilic figurate erythema of infancy can be considered a variant of annular erythema of infancy.

This uncommon inflammatory condition—3 reports in the English-language literature—is characterized by the onset of polycyclic or annular erythematous lesions that grow centrifugally with a raised border and central clearing. The lesions usually disappear in 2 to 4 weeks without sequelae; however, the disease course is chronic, with new lesions appearing at the same sites. The lesions first manifest on the face, and secondary lesions can appear on the upper and lower extremities.^{28,29}

Histopathology reveals a perivascular lymphocytic infiltrate with the presence of abundant neutrophils in the interstitium and leukocytoclasia. There are no signs of vasculitis. The clinical characteristics, outcome, and



Figure 7 Acute annular urticaria in an infant. Note the annular purpuric maculopapules.

absence of systemic symptoms distinguish this condition from other neutrophilic dermatoses such as pyoderma gangrenosum and Sweet syndrome.

The response to topical and systemic corticosteroids is poor.

Other Conditions With an Annular Erythematous Component in Early Childhood

Acute Annular Urticaria/Urticaria Multiforme

Urticaria multiforme, which is also known as acute annular urticaria or acute urticarial hypersensitivity syndrome, is a histamine-mediated allergic hypersensitivity reaction that is drug-induced or occurs after viral and bacterial infections.³⁰

This subtype of urticaria is common in very young infants and children aged 4 months to 4 years.

Most authors consider that this is not an individual entity, but the form of presentation of urticaria in infancy³¹ (up to 49% of children aged 1 to 30 mo present acute hemorrhagic urticaria) (Figure 7). This condition is usually incorrectly diagnosed as erythema multiforme or serum sickness.

Clinically, onset is in the form of pruriginous maculopapules that grow rapidly to form evanescent annular, polycyclic, or arciform erythematous plaques that disappear in less than 24 hours. There may be central clearing or the lesions can take on an ecchymotic coloring, mimicking the target lesions of erythema multiforme although without the presence of epidermal necrosis, blisters, or mucosal involvement.³¹

The presence of dermographism, with erythema and edema at the site of the lesion, is characteristic of urticaria multiforme. Another typical sign is angioedema on the face, hands, and feet. This condition may be confused with serum sickness, in which the individual lesions are fixed and there is no associated dermographism.³¹

This eruption is self-limiting and resolves in approximately 8 to 10 days. Response to oral antihistamines was good. Systemic corticosteroids are used for more severe cases.³¹

Other Conditions of Early Childhood in Which Figurate or Annular Erythema Has Been Reported

Necrolytic Migratory Erythema

Necrolytic migratory erythema is an uncommon condition characterized by a fluctuating eruption associated in most cases with a glucagon-producing pancreatic tumor or glucagonoma. Nevertheless, there have been reports of cases unrelated to glucagonoma but rather associated with hepatic cirrhosis and cirrhosis caused by zinc deficiency. The condition can affect children and manifest in much the same way as enteropathic acrodermatitis, affecting mainly periorificial and acral locations.³

The skin lesion presents as an erythematous annular macule that subsequently blisters. It resolves in 1 to 2 weeks, with peripheral desquamation and residual hyperpigmentation. These lesions extend centrifugally

and coalesce into arciform patterns. They appear mainly on the lower abdomen, groin, buttocks, and thighs, and are accompanied by burning pain or itching. Necrolytic migratory erythema is usually associated with systemic manifestations such as weight loss, diarrhea, anemia, painful glossitis, and other, less frequent manifestations such as venous thrombosis and psychiatric manifestations.³

Treatment should be aimed at the underlying disease in case of zinc deficiency, with administration of dietary supplements until zinc deposits are restored.

Other Conditions

There have been reports of annular eruptions that, while not specific, can appear during the course of different conditions. Consequently, annular lesions may be seen in conditions as diverse as the following: Kawasaki disease,³² in which the cutaneous manifestations in the form of annular erythema predominate, thus allowing early diagnosis and treatment; primary Sjögren syndrome,³³ in which annular erythema with raised borders is recognized as a cutaneous manifestation of the syndrome; juvenile chronic myeloid leukemia,³⁴ in which cutaneous manifestations are frequent but nonspecific, including presentations in the form of recurrent annular erythema; and in women who are carriers of chronic granulomatous disease,³⁵ in whom the presence of fixed erythematous plaques on the face and back should lead us to suspect this condition.

Conclusions

Annular erythema in children is always a diagnostic challenge. Some presentations are difficult to classify, thus leading to the variety of descriptions in the literature. The clinical characteristics, together with data from complementary examinations, allow self-limiting conditions to be differentiated from more severe ones.

What is most important is to distinguish between the most dangerous conditions, or those requiring specific treatment, and benign ones in which the self-limiting nature of the symptoms can be explained to parents.

In most cases, figurate erythema is not a specific entity, but a reaction pattern that can differ from individual to individual. Perhaps, with time, more information will become available on the etiology and pathogenesis of the different types of annular or figurate erythema, thus enabling us to define profiles more clearly and classify them more accurately. Until then, annular or figurate erythema of infancy should lead us to consider age at onset, characteristics of the lesion, duration and location, disease course, and histopathologic findings in order to establish a diagnosis and target therapy in those types with a known etiology (Figure 8).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

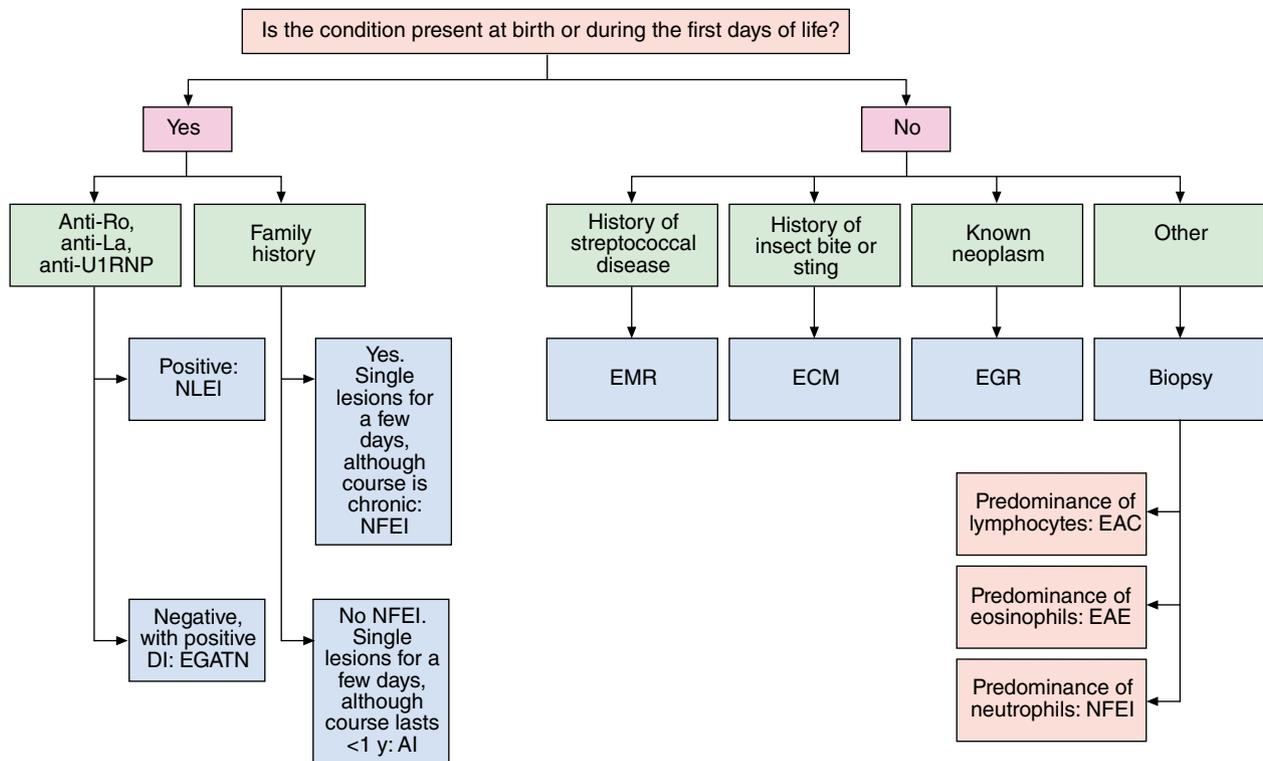


Figure 8 Diagnostic algorithm for annular erythema of infancy. AEI indicates annular erythema of infancy; DI, direct immunofluorescence; EAC, erythema annulare centrifugum; EAE, eosinophilic annular erythema; ECM, erythema chronicum migrans; EGATN, erythema gyratum atrophicans transiens neonatale; EGR, erythema gyratum repens; EMR, erythema marginatum rheumatica; NFEI, neutrophilic figurate erythema of infancy; NLE, neonatal lupus erythematosus; U1RNP, U1 ribonucleoprotein.

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