

ORIGINAL ARTICLES

Eruptive Pseudoangiomatosis: Study of 7 Cases

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Abstract. *Introduction.* Eruptive pseudoangiomatosis consists in the acute development of small vascular lesions in the face and extremities that resolve in several weeks without scarring. Lesions are described as 3-4 mm asymptomatic macules and papules with peripheral whitish halo that blanch upon pressure. Initially it was considered a disease limited to children but it has also been described in adults. It overlaps with the entity known in Japan as «erythema punctatum Higuchi», possibly caused by an insect named *Culex pipiens pallens*. *Methods.* We report a serie of 7 patients that consulted for lesions compatible with eruptive pseudoangiomatosis. We performed a detailed clinical history and histological, microbiological and serological studies. Follow-up time was up to 4 years.

Results. Eighty-five percent of patients were women and the mean age was 62 years. All cases appeared in spring/summer and 71 % relapsed. Lesions predominated in the face and extremities and the outbreak lasted 2-4 weeks. The anamnesis did not disclose any specific etiologic agent in any of the cases. Complete laboratory tests including serologies and cultures were negative or within normal limits. Histological study revealed vascular dilatation in all cases with endothelial cell protrusion and a peripheral lymphohistiocytic infiltrate.

Conclusions. Currently, the etiology of this entity is not well established although it probably represents a reactive disorder to different etiologic processes.

Key words: eruptive pseudoangiomatosis, erythema punctatum Higuchi, *Culex pipiens pallens*.

PSEUDOANGIOMATOSIS ERUPTIVA: 7 CASOS CLÍNICOS

Resumen. *Introducción.* La pseudoangiomatosis eruptiva consiste en la aparición aguda de lesiones de aspecto angiomatoso de pequeño tamaño en cara y extremidades y su desaparición en el curso de varias semanas sin dejar cicatriz residual. Las lesiones se describen como máculo-pápulas de 3-4 mm, con un halo blanquecino periférico, asintomáticas y que blanquean a la vitropresión. En un principio se pensaba que era un cuadro limitado a niños, pero posteriormente se ha descrito también en adultos. Se considera superponible a un cuadro conocido en Japón como *erythema punctatum Higuchi* y posiblemente causado por un insecto denominado *Culex pipiens pallens*.

Métodos. Presentamos una serie de 7 pacientes que consultaron en nuestro Servicio por un cuadro compatible con la pseudoangiomatosis eruptiva. Se les realizó una historia clínica detallada, estudio histológico, microbiológico y serológico. El seguimiento fue de hasta 4 años.

Resultados. El 85 % de los pacientes fueron mujeres, y la edad media fue de 62 años. Todos los casos se iniciaron en los meses de primavera/verano y el 71 % sufrieron recidivas. Las localizaciones predominantes fueron la cara y las extremidades y la duración del brote fue de 2 a 4 semanas. La historia clínica no permitió establecer un agente desencadenante en ninguno de los casos. Las analíticas, estudios histológicos, serologías y cultivos estuvieron dentro de los rangos de normalidad. En las imágenes histológicas apreciamos en todos los casos dilatación vascular, con cierta protrusión de las células endoteliales hacia la luz del vaso y un infiltrado de predominio linfocitario periférico.

Conclusiones. Hoy en día la etiología de este cuadro clínico sigue sin estar bien establecida, aunque probablemente suponga una manifestación clínico-patológica reactiva a distintos procesos etiológicos.

Palabras clave: pseudoangiomatosis eruptiva, erythema punctatum Higuchi, *Culex pipiens pallens*.

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Introduction

Eruptive pseudoangiomatosis is characterized by outbreaks of erythematous, maculopapular lesions measuring 2 to 4 mm in diameter. They look like normal

angiomas and are generally located on the face and limbs. They blanch when pressed and many of them, particularly those on the arms or legs, are surrounded by a light-colored halo measuring 1 to 4 mm in diameter. They are asymptomatic or slightly pruritic, and resolve without residual scarring in a period of 2 to 18 days in children and 1 to 3 months in adults. The eruptions may recur.

Histological findings are unremarkable although there may be noticeable capillary dilation with plump endothelial cells protruding into the lumen. The affected vessel is normally surrounded by a predominantly lymphohistiocytic infiltrate of varying intensity. There is no vasculitis or vascular proliferation and the epidermis is generally unaffected.

Differential diagnosis should be based on the appearance of the lesions, clinical signs, and histological findings. It should include, among others, cherry hemangiomas, telangiectasias, and bacillary angiomatosis, and eruptive angiomatosis.

We describe our experience with eruptive angiomatosis and present a brief review of the few articles that discuss this disorder.

Materials and Methods

We present a series of 7 patients who visited our department in the last 10 years with a clinical picture compatible with eruptive pseudoangiomatosis. We obtained a detailed clinical history and performed a histological study in all cases. Complementary tests (routine laboratory and serological tests and cultures) and clinical follow-up were performed in most patients.

Results

The series included 6 women (86%) and 1 man (14 %), with a mean age of 62 years (Table 1). All the patients had

Table. Clinical Characteristics and Complementary Studies in 7 Patients

	Time	Age, y	Sex	Lesion Site	Duration	Triggering Agent	Recurrence	Laboratory Tests	Biopsy
1	1996-1999	52	F	Face, upper limbs, lower limbs	2-3 weeks	Not related	Yes (several) spring/summer	Normal (biochemistry, profiles, CBC and differential WBC count, ANA, anti-dsDNA, protein profile, C3, C4) Serology Rickettsia, Borrelia, EBV, CMV(-) Skin, bacterial, viral, and fungal cultures (-)	Compatible
2	2000-2002	48	F	Face, sternal region, upper limbs	2 weeks	Not related Improved with change in normal place of residence	Yes (several) spring/summer	Normal (biochemistry, profiles, CBC and differential WBC count)	Compatible
3	2001-2005	38	M	Face, upper limbs	15-20 days	Not related	Yes, in spring	Normal (biochemistry, profiles, CBC and differential WBC count) ANA (-) ASO (-) CMV (-), EPV (-)	Compatible
4	2002	77	F	Face, upper limbs	2 weeks	Mosquito bites Affected neighborhood	None	Not done	Compatible
5	2005	73	F	Mostly lower limbs	2-4 weeks	Not related	Yes (3 episodes)	Normal (biochemistry, profiles, CBC and differential WBC count) Nonspecific parvovirus Other serology tests: CMV, EBV, enterovirus, entamoeba histolytica, fasciola hepatica, Echinococcus granulosus (-)	Compatible
6	2005	68	F	Face, upper limbs	2 weeks	Not related	Yes, in summer (2 episodes)	None	Compatible
7	2005	78	F	Face, upper limbs	15-20 days	Not related	None	None	Compatible

Abbreviations: ANA, antinuclear antibodies; ASO, antistreptolysin O titer; CBC, complete blood count; CMV, cytomegalovirus; ds, double-stranded; EBV, Epstein-Barr virus; WBC, white blood cell



Figure 1 (A, B y C). Angiomatous lesions with a whitish peripheral halo on the face and limbs of 2 different patients.

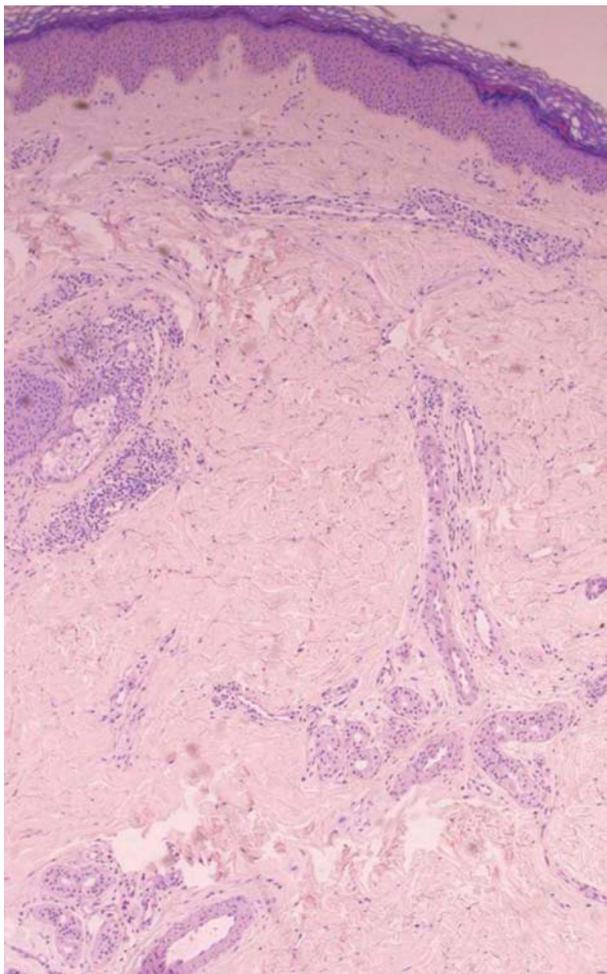


Figure 2. The dermis shows dilated thin-walled vessels with a protruding endothelium surrounded by a lymphocytic infiltrate (hematoxylin–eosin, $\times 100$)

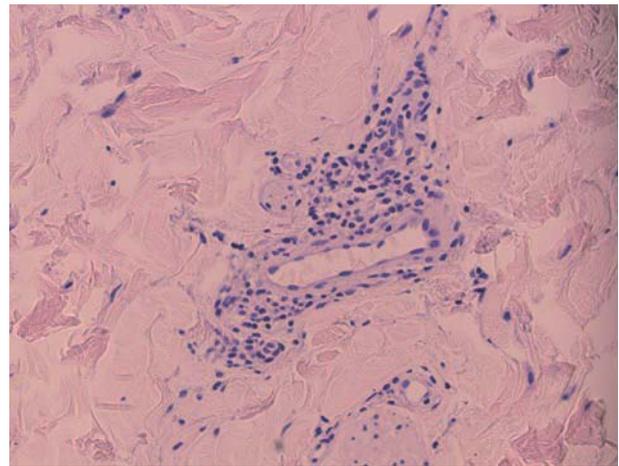


Figura 3. Image of characteristic vessel at greater magnification (hematoxylin–eosin, $\times 200$)

their first visit between the months of May and August. Five patients (71%) reported recurrences, particularly in the spring and summer. Follow-up lasted for up to 4 years. Several patients did not return for check-up visits or undergo

the complementary tests indicated, probably because their lesions resolved spontaneously. Patients 5, 6, and 7 only came once but we were able to contact 2 of them (patients 6 and 7) by telephone after several months to assess progress.

The main areas of the body affected were the face and limbs (Figure 1) and the outbreaks lasted between 2 and 4 weeks (average of 18 days). None of the clinical histories provided any clues to a possible cause; only 1 patient suggested an association with mosquito bites and mentioned that other people in her neighborhood also had these lesions, although we were unable to confirm this. None of the patients had associated infections or systemic diseases. The results of the routine laboratory tests (laboratory workup, general profiles, liver function, lipid profile, antinuclear antibodies, antidouble-stranded DNA, protein profile, complement levels, and antistreptolysin-O titers), serological tests (cytomegalovirus, Epstein–Barr virus, enterovirus, parvovirus B19, entamoeba histolytica, fasciola hepatica, *Echinococcus granulosus*, *Rickettsia*, and *Borrelia*), and cultures (skin biopsy and viral, bacterial, and fungal cultures) were within normal ranges for all the

patients that underwent the tests. Histological examination revealed vascular dilation in all cases, and the endothelial cells protruded slightly towards the lumen of the vessel, which was surrounded by a predominantly lymphohistiocytic infiltrate (Figures 2 and 3).

Discussion

In 1969, Cherry et al¹ described the acute onset of hemangioma-like lesions and high fever in 4 children, with symptoms resolving after just a few days. They performed cultures and serological tests, and isolated enteric cytopathic human orphan (ECHO) virus 25 in 2 of the patients and ECHO 32 virus in the other 2. Although they did not perform a skin biopsy, they suggested that given their appearance, the lesions might be due to capillary dilation caused either directly by a viral infection in the endothelium or indirectly via the binding of immunocomplexes to the endothelium. They believed that the disease was a variety of viral exanthem.

In 1993, Prose et al² saw a similar acute eruption in 3 children; they also suspected that it was of viral origin but could not confirm this. They performed a skin biopsy in 1 of the patients and found dilation of the dermal vessels, endothelial projections, and a discrete perivascular infiltrate without vascular proliferation. Electron microscopy did not reveal viral particles in the endothelium, as Cherry¹ had suggested. In view of their findings, they proposed the term eruptive pseudoangiomatosis to describe the disorder. In 1994, Calza and Suarat³ described the onset of the disorder in 2 brothers and also suggested that it might have been caused by a transmissible vector such as a virus. In Spain, the first case, involving a male child, was reported in 1997.⁴ In 2000, Navarro et al⁵ saw a similar clinical picture in a woman who had recovered from an infection of the upper airways and who had also tested positive for Epstein–Barr virus (immunoglobulin [Ig] M and IgG).

Guillot et al^{6,7} described 9 cases in adults and 4 in children. They noted that eruptions in adults were more common in women than in men, lasted longer than in children, and were not always preceded by fever. They added that they had not observed a specific age of onset and suggested a possible immunosuppressive role as several of the patients had a history of neoplastic disease, systemic corticosteroid treatment, or other situations that might compromise the immune system.

Five additional cases were described in 2000 by Neri et al,⁸ Larralde et al,⁹ and Angelo et al.¹⁰ In 2003, Joung and Kim¹¹ described the case of 2 middle-aged Asian women who had developed lesions that were seasonal in nature (appearing and recurring in summer-autumn).

On the other hand, the entity *erythema punctatum Higuchi* was first described in Japan about 50 years ago. In 1965,

Ohara et al suggested that eruptive pseudoangiomatosis might be associated with mosquito bites, including bites by *Culex pipiens pallens*. Almost 40 years later, in 2004, Ban et al¹² described 26 cases of eruptive pseudoangiomatosis-like lesions in patients hospitalized between autumn 2001 and spring 2002. They attributed the lesions to mosquito bites and suggested that these might have been linked to construction work on nearby sewer systems. They also suggested that the process might be the same as that seen in eruptive pseudoangiomatosis and that the viral origin and transmission by insect bites could both be true.

Venturi et al¹³ reported an outbreak of eruptive pseudoangiomatosis in 9 patients and 2 of the investigators in contact with them in an asylum in Parma, Italy. They believed that the origin was viral for several reasons, including the fact that they detected Epstein–Barr virus DNA by polymerase chain reaction in the leukocytes of 4 patients, suggesting a recent replication. One of the patients had a recurrent eruption, which until then had only been seen in children.

Like us, Neri et al¹⁴ did not see viral particles in an ultrastructural biopsy study performed in a patient aged 7 years. On analyzing the lymphocytic perivascular infiltrate, however, they saw apoptosis and clusters of particles that were suggestive of viral origin. In their opinion, eruptive pseudodystrophy might be a specific response of the body to different viruses, as is the case with Gianotti–Crosti syndrome or the papular–purpuric gloves and socks syndrome.

In a recent letter, Restano et al¹⁵ explained that several of the patients in their hospital had experienced similar eruptions in the summer months. Most of them were elderly women, immunodepressed patients, or bedridden patients. They attributed the disorder to mosquito bites and said that they had seen similar cases with flea bites.

Nonetheless, there are still doubts regarding the etiology of eruptive pseudoangiomatosis, and although the process seems to be relatively harmless, not being able to offer patients a logical explanation as to the cause of their lesions represents a problem. In our opinion, the disorder is a reactive clinical and pathological response to different etiological processes and is possibly underdiagnosed. Further studies and descriptions of cases are required to shed more light on this disease.

Conflicts of Interest

The authors declare no conflicts of interest.

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