Case Report

Eruptive pseudoangiomatosis - cherry angiomas with perilesional halo

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Abstract

Eruptive pseudoangiomatosis is a rare viral exanthem characterized by acute onset of hemangiomata-like lesions, however, histological findings are distinct from that of true angiomas. This entity has been reported from Europe, North America, Japan, and Korea till date. Here, we report 12 cases of eruptive pseudoangiomatosis from a tertiary care hospital in Punjab.

Key words: Angiomas, eruptive pseudoangiomatosis, hemangiomata-like lesions

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Introduction

In 1969, Cherry *et al*. described the acute onset of hemangiomata-like lesions and high fever in 4 children, resolving after just a few days.[1] The papules appeared similar to hemangiomata.[2] Later, first adult cases of the disease were reported in 2000.[3,4] Clinically, the lesions resemble angiomata. Histologically, because there is no vasculitis or vascular proliferation of blood vessels, in 1993, Prose *et al*. named the disease as eruptive pseudoangiomatosis (EP).[5] It overlaps with the entity known in Japan as erythema punctatum Higuchi, which is possibly caused by an insect named Culex pipiens pallens.[6] All the cases reported so far, regardless of the age of the patient, are from North America and Europe, with Korea and Japan being the only Asian countries having reported such cases so far.[7,8] We are reporting a case series of 12 patients with this condition from a tertiary care hospital in Punjab.

Case Reports

Twelve patients presented to the dermatology outpatient department (OPD) of the Government Medical College and Rajindra Hospital, Patiala over a period of 40 days during March–April 2016 with eruption of 2–5 mm discrete, purpuric-looking but blanchable lesions [Figure 1]. The lesions were moderately pruritic papules with a characteristic perilesional halo, distributed mainly on extremities [Figure 2], face, neck and trunk.

Details of patients presenting to our OPD are tabulated in Table 1. Six of our 12 patients, including two children, had reduced total leucocyte count and 9 had lymphocytosis. Other routine laboratory tests like liver function tests, renal function tests, blood sugar levels, and urine complete examination were normal. Histopathology of the lesions revealed normal epidermis with mild perivascular lymphohistiocytic infiltrate in papillary dermis [Figure 3a and b] and dilated capillaries with prominent, plump endothelial cell lining [Figure 3c].

Discussion

EP is a rare disease characterized by initial prodrome of mild fever, sore throat, or gastrointestinal symptoms, followed by the appearance of hemangiomata-like cutaneous lesions, resolving in a few days. This entity was first described by Cherry *et al*. in 1969 in four children with enteroviruses-enteric cytopathic human orphan (ECHO) virus infection.[1] They isolated ECHO virus 25 in 2 children and ECHO virus 32 in other 2. Biopsy was not done by them, however, they believed the disease to be a viral exanthem. In 1993, Prose *et al*. described a similar eruption of acute onset in 3 children but could not confirm its viral origin.[5] They biopsied a lesion from 1 patient, and reported dilation of the dermal vessels, endothelial projections, and a discrete perivascular infiltrate without vascular proliferation. In 2000, Navarro *et al*. reported the first adult case in a 37-year-old woman with clinical evidence of EBV infection.[3] The same year, Guillot *et al*. described 9 cases in adults and observed that adult females were more commonly affected than males and that eruption lasted longer in adults than that in children.[4]

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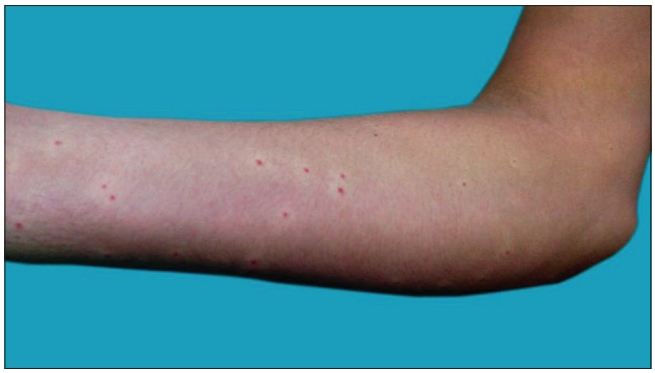

Figure 1: 2–5 mm discrete papules with a halo around the lesions

In 2007, Barrio *et al*. described a series of 7 patients from Spain, 6 females and 1 male, over a period of 10 years from 1996 to 2005 having lesions compatible with EP. All their cases appeared in spring/summer and 6 cases relapsed.[6]

Three cases in middle-aged Korean women (50, 52 and 55 year old) were described by Jung and Kim in 2003. None of their patients complained of any acute illness. Only 1 had mild pruritus with seasonal recurrences in 3 consecutive autumns and 2 were asymptomatic. Biopsy findings common to all the three were a normal epidermis, upper dermal edema and lymphocytic infiltration around the telangiectatic capillaries, and extravasated erythrocytes in the patient with seasonal recurrences.[7]

Table 2 summarizes the previous case series/reports. This rare viral exanthem erupts as asymptomatic or slightly pruritic discrete cherry angioma-like tiny blanchable papules (1–4 mm) surrounded by a perilesional halo on the face, neck, extremities, and trunk.[6] The rash resolves without residual scarring in 2-18 days in children and 1–3 months in adults.[6] The halo may not be seen around spots on the face.[9] The eruptions may recur.[6]

The patients presented to us in the months of March/April 2016 (spring/summer in India).

Out of the 12 patients, 8 were females and 4 were males. Two of our patients were children (4 year-old male and 14 year-old female), and the remaining 10 were adults. Three of the 10 adult patients returned to us with recurrence of eruption within 1–2 weeks following complete resolution of the rash.

The etiology of this eruption is still unknown. Association with insect bites,[9] infection with ECHO virus E25 and E32, coxsackie B, Epstein-Barr virus, and cytomegalovirus[10] have been described in patients in whom eruption occurred after prodromal symptoms.[8] In 1965, Ohara *et al*. speculated that EP might be associated with mosquito bites, including bites by Culex pipiens pallens, which is similar to erythema punctatum Higuchi in Japan. In 2004, Ban *et al*. described 26 cases of EP-like lesions in hospitalized patients and attributed the lesions to mosquito bites.[8]

Recently, in 2016, Alcántara-Reifs *et al*. reported a case of a 73-year-old female with EP from Spain.[11] In 2013, Kim *et al*. conducted a clinicopathological study on 32 Korean patients with EP. Two of their patients developed lesions after outdoor activities. Two presented with simultaneous occurrence in family members.

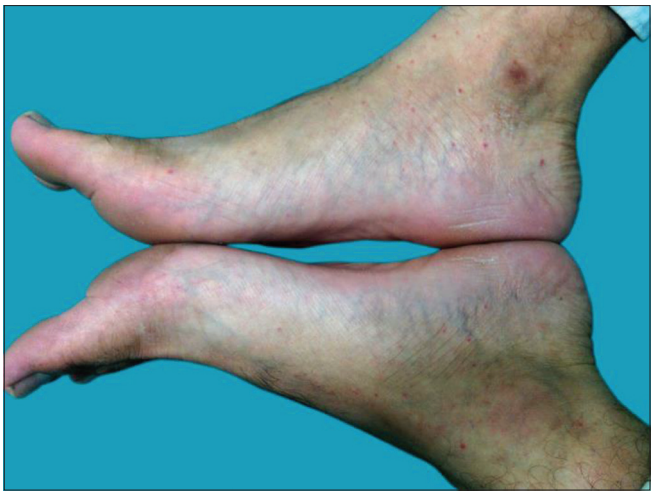

Figure 2: Lesions on extremities

One patient reported having taken herbal medicine. No prodromal or systemic symptoms were observed by them.[12]

Seven of our patients gave a history of malaise, 4 had sore throat, and 1 gave a history of diarrhea preceding the onset of rash by 2–7 days. One male gave history of both diarrhea and sore throat along with fever, malaise and myalgia 7 days prior to onset of lesions. Two of our adult female patients, 19 years old and 40 years old, gave history of the development of eruption 3–4 weeks following mosquito bite and insect bite, respectively. In almost all, i.e., 11 patients, the rash started from the extremities and spread to involve the face, neck, and trunk over 2–3 days. Only 1 patient (26 years/male) reported having initial lesions on the neck and trunk. Three had cervical lymphadenopathy (2 adult females and 1 female child), and our 50-year-old male patient had cervical and axillary lymphadenopathy. Lymphadenopathy was appreciated in those who presented 3–4 days after the onset of lesions.

Histological findings show dilated dermal blood vessels with plump endothelial cells protruding into the lumen and mild-to-moderate perivascular lymphohistiocytic infiltrates.[13] The epidermis is generally unaffected and there is no evidence of vascular proliferation; these findings justify the disease being named as "eruptive pseudoangiomatosis," by Prose *et al*.[5]

The clinical features and histological findings in our patients were consistent with those described for EP.

Viral exanthema, papular urticaria, and leukocytoclastic vasculitis were considered in the differential diagnosis. Papular urticaria, a hypersensitivity reaction to insect bites commonly seen in children, shows mild acanthosis and spongiosis, exocytosis of lymphocytes, mild subepidermal edema, extravasation of erythrocytes, moderate superficial and deep mixed inflammatory infiltrate and interstitial eosinophils.[14] Papular urticaria mostly appears as crops of very itchy red papules whereas lesions of EP can be asymptomatic or mild-to-moderately itchy, rarely associated with severe pruritus. Leukocytoclastic vasculitis presents as palpable purpura, which is defined histologically as a predominantly neutrophilic perivascular infiltrate effecting cutaneous post

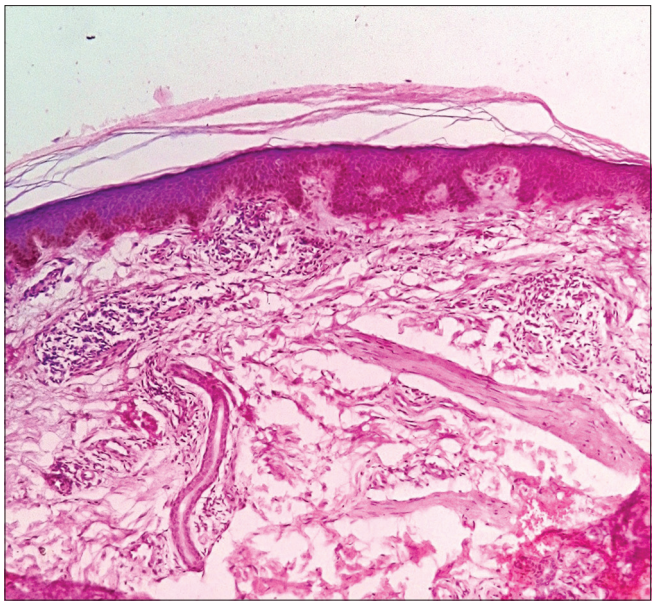

Figure 3a: Normal stratified squamous epithelium with mild to moderate perivascular lymphohistiocytic infiltrate around dilated dermal capillaries with prominent lining (H and E, ×100)

capillary venules with fibrinoid deposits in and around the vessel wall, endothelial swelling, leukocytoclasis (destruction of polymorphonuclear leukocytes with the formation of nuclear dust), and extravasations of red blood cells.[15] Common patterns of viral exanthemata include a superficial perivascular infiltrate of lymphocytes without associated epidermal changes, a superficial vacuolar interface dermatitis, which is sometimes associated with eosinophils and neutrophils, a lichenoid dermatitis, and a mild spongiotic dermatitis.[16] Some viral exanthemata can be recognized by distinctive changes, such as ballooning and multinucleated keratocytes in measles and keratocytes with steel-gray nuclei and margination of nucleoplasm in infections by herpesviruses.[17,18] The clinical finding of perilesional halos and plump endothelial cells with perivascular lymphohistiocytic infiltrate without vascular proliferation or vasculitis on histology is unique to EP.

EP is a rarely reported entity, and the precise cause of the vascular changes is still unclear. Previous studies have suggested it to be a "dermal hypersensitivity reaction" to viral infection or a direct viral effect on the vascular endothelium.[1]

No specific treatment is required for EP. Oral antihistamines and topical steroids may be indicated in symptomatic cases, although they do not affect the disease duration.[12] Out of 12 patients in our study, 6 reported mild-to-moderate itching which improved with second generation antihistamines, and 2 (an adult male with widespread eruption and a female with predominant upper-limb and upper back involvement) had severe pruritus, which responded to sedative antihistamines and topical calamine lotion. None of our patients required topical steroids. Average time for resolution of lesions was 6 days in children and 14 days in adults.

Limitation

No serological tests were performed to confirm viral etiology of the lesions.

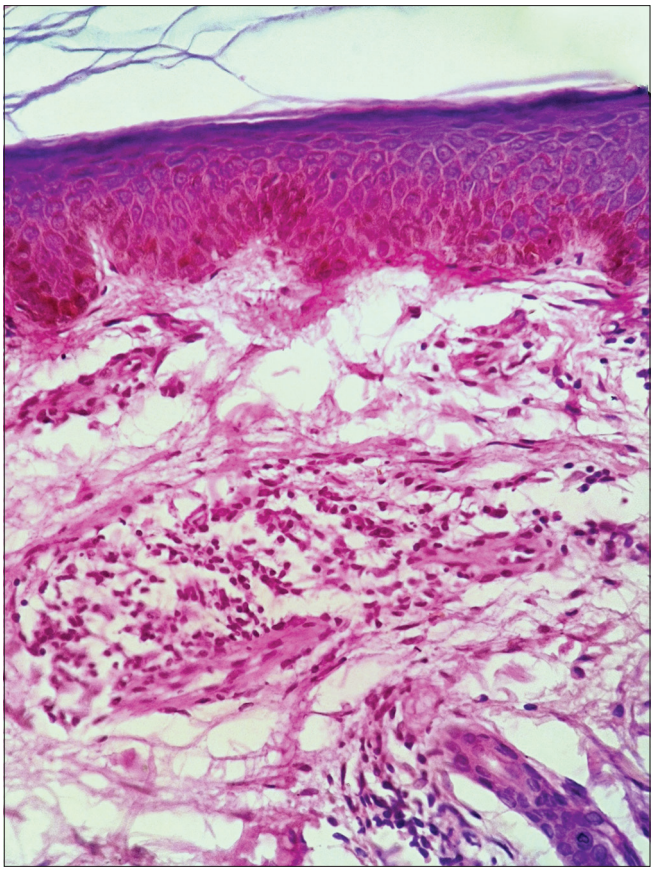

Figure 3b: Normal stratified squamous epithelium with mild to moderate perivascular lymphohistiocytic infiltrate around dilated dermal capillaries with prominent lining (H and E, ×400)

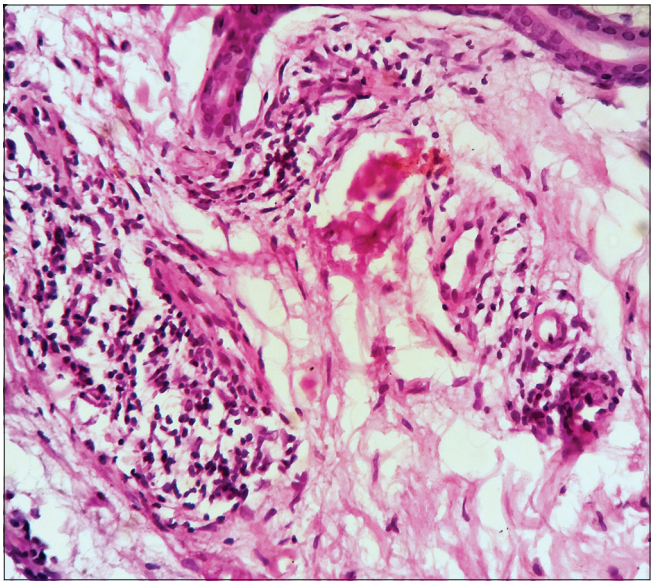

Figure 3c: Dilated capillaries with plump endothelial lining surrounded by mild to moderate lymphohistiocytic infiltrate in dermis (H and E, ×400)

Conclusion

This viral rash is being reported for the first time from the Indian subcontinent. EP is an entity defined by acute onset of multiple

Table 1: Details of the patients

Serial number	Age/sex	Prodrome	Time since onset of lesions	Course	Lymphadenopathy	Total leukocyte count and Differential leukocyte count (neutrophils/ lymphocytes/ monocytes/ eosinophils)	Time taken for resolution	Associated pruritus
				Children				
1	4/male	Mild fever with diarrhea 2 days prior to onset of lesions	3 days	Angioma like lesions started from dorsum of hands and feet, spread to involve neck and trunk in 2 days	-	TLC - 3700 DLC - 51/47/1/1	5 days	
2	14/female	History of sore throat 1 week back, malaise for 4 days	4 days	Lesions started from hands and feet, spread to calves, face and neck over a day	Left cervical lymph node - 1 cm, firm, nontender, freely mobile	TLC - 2900 DLC - 42/55/0/3	7 days	Mild to moderate
				Adults				
3	20/female	Malaise for 3-4 days	2 days	Started from legs and arms, spread with a day to involve trunk, neck and face	Bilateral cervical 0.6 cm × 0.8 cm - 1 cm, nontender, firm, mobile	TLC - 5200 DLC - 50/47/1/2	10 days	Mild to moderate
4	46/female	Malaise	7 days	Started from extremities spread to involve trunk, face and neck	-	TLC - 7200 DLC - 46/48/2/4	14 days	Mild to moderate
5	26/male	-	3 days	Started from neck, spread to trunk within a day, extremities in 2 days from onset	-	TLC - 6900 DLC - 67/33/0/0	15 days	Minimal
6	50/male	Diarrhea for 2 days. Sore-throat, fever and malaise a week prior to onset of lesions	1 day	Started from legs and forearm, spread to neck, trunk, face within a day	Bilateral cervical and axillary, 0.8-1 cm, nontender, firm, mobile	TLC - 2600 DLC - 38/59/1/2	20 days Resolved within 9 days from onset, recurred after 4 days	Moderate to severe
7	21/female	Fever, malaise	5 days	Forearms and legs, few lesions on trunk and neck	Bilateral cervical nodes, 0.8-1 cm in diameter, nontender	TLC - 3870 DLC - 54/45/0/1	25 days Resolved in 7 days after onset, recurred in 9 days	Mild to moderate
8	20/male	Sore throat a week back	2 days	Started from feet and legs, thighs spread to involve arms, forearms and neck in 2 days	-	TLC - 7800 DLC - 56/43/1/0	6 days	-
9	19/female	Fever and malaise×1 week, history of insect bite 3 weeks back	3 days	Started from feet, spread to forearms face and hands in a day	-	TLC - 5600 DLC - 62/36/1/1	11 days	Mild to moderate
10	45/female	Malaise and sore throat for a week	7 days	Started from feet and legs, spread to forearms, face and hands in a day	-	TLC - 3930 DLC - 56/44/0/0	12 days	-
11	24/female	-	3 days	Lesions on forearms and legs	-	TLC - 8100 DLC - 67/32/0/1	10 days	-
12	40/female	Sore throat 1 week back History of insect bite 4 weeks back	4 days	Lesions started on forearms, spread over 2 days to involve arms, forehead and neck	-	TLC - 2700 DLC - 42/51/2/5	18 days, resolved in 5 days after onset, recurred within 4 days after resolution	Moderate to severe

Table 2: Summary of previous case reports

Case report/ number of cases	Age	Gender	Viral prodromes	Season	Duration of the clinical signs	Biopsy results	Recurrences
1969, Cherry *et al*. (4 cases)	8-11 months	One female infant Three male infants	High grade fever	-	4-7 days	Biopsy not performed Suggested ECHO virus infection (ECHO 25 in two and ECHO 32 in other two) related endothelial cell insult or immune complex deposition as a cause	-
1993, Prose *et al*. (3 cases)	Three children (two 6-month-old-male infants, one 6-year-old male child)	Three male infants	Two infants – onset coinciding with resolution of an upper respiratory infection 6-year-old boy-fever, headache, vomiting, and malaise, tonsillitis	-	7-14 days	Performed a skin biopsy in one patient and found dilation of the dermal vessels, lined by plump endothelial cells and a discrete perivascular infiltrate without vascular proliferation. The epidermis showed no pathologic changes	-
2000, Navarro *et al*. (1 case)	37 years	One female	Infection of the upper airways, evidence for Epstein–Barr virus (immunoglobulin) IgM and IgG	-	10 days	The epidermis showed no pathologic changes Perivascular lymphocytic infiltrate in the dermis with dilatation of the capillaries; vessels not increased in number. The capillaries showed endothelial cellular edema with protrusion of these cells into the lumen	-
2000, Guillot *et al*. (9 cases)	Mean age - 63 years	Eight females One male	One patient had history of flu-like illness	-	Average duration: 1-3 months	Histological examination showed dilated blood vessels with plump endothelial cells but no evidence of an increased number of vessels. A sparse perivascular infiltrate with lymphocytes and polymorphonuclear neutrophils, more rarely eosinophils, was present in the superficial dermis. The epidermis remained normal. There was no vasculitis	-
2003, Joung and Kim (3 cases)	Mean age - 52 years	Three females	Asymptomatic in two One had fever with recurrences	Summer-autumn	Average duration: 2-3 weeks	Oedema and lymphocytic infiltration around the telangiectatic capillaries in the upper dermis in all and erythrocyte extravasation in one biopsy	One patient had recurrences in summer-autumn

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Table 2: Contd...

Case report/ number of cases	Age	Gender	Viral prodromes	Season	Duration of the clinical signs	Biopsy results	Recurrences
2004, Ban *et al*. (26 cases) hospitalized patients	Mean age - 70 years	19 females Seven males	-	Late autumn/ autumn-spring	Average duration: 3 weeks	Histopathology revealed dilated blood vessels in dermal papillae and/or lymphocytic infiltration in the dermis	-
2007, Barrio *et al*. (7 cases)	Mean age - 62 years	Six females One male	One patient gave history of mosquito bite 6-asymptomatic	Spring/summer	Average duration: 18 days	Vascular dilation in all seven cases, endothelial cells protruded slightly towards the lumen of the vessel, surrounded by a predominantly lymphohistiocytic infiltrate	In five patients in spring/ summer season
2013, Kim *et al*. (32 cases)	Mean age - 50 years		No prodromal or systemic symptoms	Summer (56%), spring (23%), autumn (19%) and winter (1% cases)	Mean duration: 1.64 months	Dilated dermal blood vessels and slight to moderate perivascular lymphocytic infiltration in the superficial capillary plexus Plump endothelial cells, intravascular neutrophils, and a few eosinophils were observed in 100%, 78%, and 22% of patients, respectively	-
2016, Alcántara-Reifs *et al*. (1 case)	73 years	Female	None	-	-	The epidermis was unaffected and there was no vascular proliferation dilated capillaries with plump endothelial cells and a mild lymphocytic infiltrate surrounding the affected vessels in the dermis	-
Present study (12 cases)	Mean age - 27.4 years	Eight females Four males	Malaise, sore throat and diarrhoea in seven, five and two patients respectively with overlapping of prodromal symptoms Two patients gave history of insect bite prior to the onset of lesions	Spring/summer	Mean duration: 12.7 days	Normal epidermis with mild perivascular lymphohistiocytic infiltrate surrounding dilated capillaries with prominent, plump endothelial cell lining in the dermis	In three adult patients-two females and one male

ECHO: Enteric cytopathic human orphan

millet-sized asymptomatic-pruritic erythematous, discrete spots with a halo distributed mainly on exposed skin; the halo may not appear around the spots on the face. In adults, females are more commonly affected and the eruption lasts for more than 1 week, with recurrences being more common than in children. Though very rare, this benign, self-limiting exanthema should be considered as a differential diagnosis for various cutaneous eruptions, with which the concerned patients present to health care professionals. Cases of EP may not seek medical help because of benign nature of disease and spontaneous remission or may go unrecognized. It might an underreported entity and may be more cases will be reported once we start considering it as a differential for various exanthemas in India.

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Conflicts of interest

There are no conflicts of interest.

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