

An original study on Blaschkoid pityriasis rosea – one of the rarest atypical variants of this paraviral exanthem

Running head: Blaschkoid pityriasis rosea

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Abstract

Background: Blaschko's lines are believed to be originated from the migration of mosaic populations of epidermal cells and tissues. Pityriasis rosea (PR) is an exanthem which might be associated with human herpesvirus-7 and -6 infections.

Objective: To evaluate the risk factors, clinical manifestations, co-morbid associations, and complications in patients with Blaschkoid PR, and to determine its relative incidence among all patients with PR.

Methods: Our setting was a skin clinic served by a consultant dermatologist. We searched for and retrieved records of all patients with Blaschkoid PR presented to us during an eight-year period.

Results: Out of 507 patients with PR seen by us, three (0.59%) patients had Blaschkoid PR. All three patients exhibited strictly unilateral distribution of one single group of lesions along Blaschko's lines, as linear or slightly curved stripes. All three patients had prodromal symptoms, herald patches, secondary eruptions, peripheral collarette scaling for some lesions, and spontaneous clinical remission in two to six weeks. We found no risk factor, co-morbidity, and no complications for patients with Blaschkoid PR.

Conclusions: Blaschkoid PR is indeed rare. Apart from the rash distribution, clinical manifestations of this variant are in line with classical PR.

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Introduction

Pityriasis rosea (PR) is an exanthem suspected to be related to primary infection or endogenous reactivation of herpesviruses including human herpesvirus-7 and -6 [1,2]. Lesions in classical PR are discrete, with the distribution being symmetrical involving the trunk and proximal aspects of the limbs. Some of the individual lesions in PR, particularly the larger oval ones, are oriented along lines of skin creases.

Blaschko's lines are believed to be due to migration of mosaic populations of epidermal cells and tissues [3]. Apart from congenital skin diseases, acquired skin diseases conforming to these lines are increasingly being reported. The underlying mechanisms for such associations are still largely unknown.

Blaschkoid PR is a very rare variant of PR. This term notes that the individual lesions conglomerate into a group (or groups), with the entire group(s) following and stretching along Blaschko's lines. The orientation of individual lesions is not embraced in the term. The distribution is unilateral in Blaschkoid PR.

Only one patient with Blaschkoid PR has been reported [4]. We report here the first systematic study for patients with Blaschkoid PR and describe the clinical manifestations of the second to the fourth reported patients with this rare variant.

Aim

Our aim was to evaluate the clinical features of patients with Blaschkoid PR and to determine its relative incidence among all patients with PR.

Materials and Methods

Our setting was a skin clinic served by a board-certified dermatologist. Patients attended our clinics with or without referrals. We searched with the entrez *Blaschko*, *Blaschko's*, *Blaschkoid*, and *pityriasis rosea* for patients who had consulted us over an eight-year period (1 January 2006 - 31 December 2013), and retrieved records of all patients with Blaschkoid PR seen by us during this period. We also searched for all patients with PR seen by us during this period.

For each patient with Blaschkoid PR identified, we hand-reviewed the risk factors, clinical manifestations, co-morbid associations, and complications. Risk factors included demography, family history, congenital abnormalities, neonatal problems, immunisations, hospitalisations, history of PR, history of other viral exanthems and paraviral exanthems, congenital or acquired immunodeficiencies, drug history, travel

history, contact history with other people with viral or paraviral exanthems, smoking, alcohol intake, and sexual history. Co-morbid conditions included atopy, other skin diseases, and chronic diseases. Complications included hyper- or hypo-pigmentations, systemic complications, and adverse effects due to treatments.

We then assessed whether clinical photographs were available to us, and whether consent of the patient or parents/guardians of children under the age of 16 had been given for us to publish the photographs.

If any risk factors, clinical manifestations, co-morbid associations, and complications were found, we would look for such in all patients with PR, and assess the association with the Fisher Exact Probability Test where applicable. Otherwise, we would employ the Chi-square Test. Risk ratios with 95% confidence intervals would also be calculated where applicable.

Results

Five hundred and seven patients with PR were seen by us during these eight years. All patients fulfilled the diagnostic criteria of PR [5]. Clinical records of three (0.59%) patients with Blaschkoid PR were retrieved. Their clinical manifestations are listed in Table 1. We noted no predisposing factor, co-morbid condition, and no complication. Clinical photographs were available for one patient, with written informed consent to publish his clinical photographs. We hereby present the clinical histories and findings of these patients.

Patient 1

An 18-year old male student endured coryzal symptoms with no fever. One week later, a skin patch was noted by him on the medial surface of his left thigh. Moderate pruritus was noted. Six days later, daughter lesions appeared on either sides of the herald patch. The secondary lesions stopped progressing five days later.

The patient enjoyed excellent past health. He had no history of allergic or irritant contact dermatitis. Drug history including traditional topical or systemic remedies was unremarkable over the previous month. His family members including his girlfriend had no skin rash known to him.

We saw the patient two weeks after appearance of the herald patch. Examination revealed no pallor and no jaundice. One large oval lesion around 4.5 cm at its longest diameter was noted at the junction of the upper one-third and low two-thirds of his left thigh, in the medial aspect (Figure 1, arrowed). Peripheral collarette scaling configuration with central clearance was noted. Smaller lesions with very similar configurations were noted proximal and distal to the herald patch, in a linear distribution.

Other body surface areas including the palmoplantar surfaces were unaffected. Mucosal surfaces were normal. We noted no inguinal and other regional lymphadenitis. Abdominal examination revealed no hepatosplenomegaly.

His complete blood picture, fasting glucose, and liver and renal function tests were normal. Antibodies against human immunodeficiency virus 1 and 2 and Venereal Disease Research Laboratory test were negative. Antistreptolysin O titre was not elevated. Lesional scrapping from the herald patch and several secondary lesions for potassium hydroxide smear and for fungal culture later came back to be negative for yeasts and for dermatophytes.

Lesional biopsy revealed parakeratosis, epidermal spongiosis, occasional dyskeratotic cells and interface dermatitis with upper dermal lymphocytic infiltrates, involving the perivascular areas. Extravasation of erythrocytes was noted at some places.

We diagnosed PR clinically. As the distribution of lesions was entirely unilateral and along Blaschko's lines for this region (Figure 2), we diagnosed Blaschkoid PR. We prescribed fluticasone cream to be applied twice daily and oral levocetirizine 5 mg nocte for one week. Complete rash resolution with postinflammatory hypopigmentation was noted when he attended us for follow-up 19 days after the appearance of the herald patch. There was no recurrence for the next one year.

Patient 2

Patient 2 was a 32-year-old male office manager. He noted coryzal symptoms but had no fever. Five days later, a solitary skin lesion appeared at the posterior aspect of his right thigh. Another six days later, a group of skin lesions erupted around the primary lesion. The patient enjoyed good past health. Drug history was before rash onset was unremarkable.

We saw Patient 2 two days after the secondary eruption. The herald patch as indicated by the patient was on the posterior aspect of his right thigh, inferior to the right buttock crease. Remnants of peripheral collarette scaling was noted for the herald lesions.

The secondary lesions were seen to be merged into a strap at the posterior and superior aspect of his right thigh. The distribution was strictly unilateral. The larger secondary lesions showed peripheral collarette scaling. As the group of lesions was oriented along Blaschkoid's lines, we diagnosed Blaschkoid PR.

His blood test results were virtually the same as such for Patient 1. Lesional histopathology revealed non-specific spongiotic dermatitis with inflammatory lymphocytic infiltrates in the epidermis.

We prescribed no medication. Complete rash resolution with post-inflammatory hypopigmentation was noted 11 days after the eruption of the herald patch.

Patient 3

Patient 3 is a 12-year-old boy in excellent health. He endured a sore throat, with a slightly pruritic skin lesion noted over his left groin five days later. Multiple lesions appeared around the first lesion six days later.

We saw Patient 3 four days after the eruption of the secondary rash. The herald patch was still intact with clear configuration of peripheral collarette scaling. The group of secondary lesions was a slightly curved strip along the medial aspect of the left groin and the left aspect of the scrotal skin. The distribution was strictly unilateral.

His blood test results were similar to such for Patients 1 and 2. Lesional histopathology revealed spongiosis and perivascular lymphocytic infiltrates.

As there was only a group of lesions unilaterally and the curvature strip of lesions followed Blaschkoid lines, we diagnosed Blaschkoid PR. We prescribed no medication. Complete rash remission with post-inflammatory hypopigmentation was noted 10 days later.

We examined the clinical reports of these three patients meticulously. There was no risk factor, no co-morbid conditions, and no complications.

Discussion

Blaschkoid PR was found by us to be extremely rare. The proportion of this variant was only 0.59% for our patients with definite diagnosis of PR in these eight years.

For these three patients, the prodromal symptoms, herald patch, secondary eruption of multiple lesions, collarette scaling, and remission without active treatment all substantiated a diagnosis of PR. The histopathological changes were fairly specific for PR for Patient 1, and less specific for PR for Patients 2 and 3. However, lesional histopathological features for PR are non-specific, and are mainly used to exclude important differential diagnoses only. Histopathological changes of all three patients are therefore compatible with diagnoses of PR.

There has only been one report on Blaschkoid PR as indexed in *PubMed* [4]. That female aged 42 years, and the authors stated that her eruption fulfilled the diagnostic criteria of PR [4,5].

We have previously proposed a new classification for typical and atypical PR [6]. Despite Blaschkoid PR having been reported for one patient only [4], we incorporated *Blaschkoid pityriasis rosea* in the classification. At that time, we were unsure about whether this variant was singular only, with no further reports in the future. To the best of our knowledge, this article is thus the first reported systematic study on Blaschkoid PR.

Blaschko's lines originate from physiological development of the skin during embryogenesis [3]. It is postulated that mutation leads to the formation of mosaic cell populations. Migration of these cell populations causes these lines. These lines are "V" shaped on the back, inverted "U" shaped on the upper anterior chest and breasts, "S" shaped with whirls on the lower anterior chest and abdomen, as complicated curves on the face, wavy on the head, and longitudinal on the upper and lower limbs

(Figure 2). These lines do not cross the midline, and thus skin diseases along these lines are characteristically asymmetrical or unilateral [3,7,8]. When a skin disease is said to be *Blaschkoid*, usually only one group of lesions is seen, with multiple lesions being involved along these lines, in linear or curved manner.

We believe that our three patients demonstrated Blaschkoid PR due to four reasons. Firstly, there was only one group of lesions present for all three patients. Other skin surfaces were not affected. These were definitely not classical PR for which the distribution of the secondary lesions should be on the trunk and proximal aspects of limbs. Secondly, the **distribution** was strictly unilateral for all three patients, a feature shared by many other skin diseases with distribution along Blaschko's lines.

Thirdly, the distribution of the lesions was linear or as curved stripes for all three patients, which is the pattern of Blaschko's lines for the corresponding body regions. For **Patient 1**, the distributions were vertical down on the thighs, directly corresponding to Blaschko's lines on the thigh. For Patient 2, the lesions were at the posterior and superior aspect of the right thigh. The distribution was semi-circular, directly corresponding to the directions of Blaschko's lines for this region. For Patient 3, the lesions were at the medial aspect of the left groin, involving the left aspect of the scrotal skin as well. The curving distribution of the lesions conformed to Blaschko's lines in that region. Fourthly, the **distribution of lesions for all three patients does not** correspond with other dermatological linear or curved patterns, such as dermatomes or lines of skin cleavage [8,9].

We might compare the distribution of lesions with the dermatomes. For Patient 1, the lesions inferior to the left inguinal crease lie at dermatome L2. However, the lesions jump to medial aspects of the thigh which would correspond to L3. L3 covers the anterior aspects of the lower thigh, but no lesion is there. For Patient 2, the lesions seem to be lying at the right S3 region. However, S3 covers some of the anterior surface of the scrotal skin, but no lesions are there. For Patient 3, the lesions jump from S3 (and probably S4) to L1.

Many skin diseases exhibiting Blaschkoid distributions are congenital [10,11] such as hypomelanosis of Ito, linear and whorled naevoid hypermelanosis, inflammatory linear verrucous epidermal naevus, and congenital milia *en* plaque [12]. Acquired skin diseases associated with Blaschko's lines include lichen striatus [13], lichen planus [7,14], seborrhoeic keratosis, fixed drug eruption, segmental vitiligo [15], linear trichilemmoma [16], and morphoea [17,18]. More intriguing are the associations of Blaschko's lines and infections, including pityriasis versicolor [19] and tuberculoid leprosy [20], suggesting immunopathogenetic elements of the lines in these diseases.

For some conditions such as Becker's naevus, both congenital and acquired patterns are seen [21]. **For lichen planus, both Blaschkoid-types** and Köebner phenomenon-types are seen [14]. However, Blaschko's lines *per se* is not related to Köebner phenomenon [3,14]. The nosology of lichen striatus and Blaschkitis [22] and the classification of *Blaschko-linear manifestations of multifactor polygenic diseases* [23] are still being explored.

A particular strength of this study is that all patients consulted us directly without referrals. Patients with all variants and severities of PR could thus consult us. **We**

thus believe that our data should be representative of PR in the community. If this study was performed in a hospital-based setting, only patients with extensive rashes or severe pruritus might be seen. This would lead to biased sampling from all patients with PR.

Moreover, we could see patients at an earlier phase of PR, enabling us to document the clinical manifestations as text and images in the active phase of PR. PR is a self-limiting disease. A delay in referrals might be accompanied by partial remission of the rash, and clinical photographs might only capture remitting rashes without active earlier features.

The major limitation of this report is that owing to the retrospective methodology, we had little to no virological, histopathological, immunohistochemical, and serological results for our patients. However, given the classical clinical features of coryzal phase, herald plaque, secondary eruptions, peripheral collarette scaling, typical course, and the compatible histopathologies, we leave no doubt that *Blaschkoid pityriasis rosea* is the most appropriate diagnostic label for our three patients.

Another limitation is that owing to the small number of patients with Blaschkoid PR found, the estimated proportional incidence of 0.59% incurs low validity and low reliability. Studies on larger scales would be needed to determine the incidences of this and other variants of this paraviral exanthem.

Conclusion

Blaschkoid PR is a very rare variant of PR. The proportion was only 0.59% for all patients with PR which we have seen over eight years. Apart from the rash distribution, clinical features of this variant are in line with classical PR, with coryzal symptoms, herald patch, secondary eruption, peripheral collarette scaling, and spontaneous remission over two to four weeks.

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Figure 2 were modified from a figure published in the DermNet (www.dermnetnz.org/). We thank Associate Professor Amanda Oakley, the managing dermatologist of the webpage, for her generosity in waiving the fees for us to reproduce the figures for academic use.

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Table 1

Patient number	Age and sex	Prodromal symptoms	Herald patch	Number of groups of lesions	Symmetry	Skin areas with Blaschkoid pityriasis rosea	Linear or slightly curved strip	Peripheral collarette scaling	Treatments given	Clinical course
1	18 years, male	Present	Present, clearly documented	One	Strictly unilateral, left	Medial aspect of left thigh	Yes	Present	Oral levocetirizine, topical fluticasone	Clinical remission 19 days after the appearance of the herald patch
2	32 years, male	Present	Present, clearly documented	One	Strictly unilateral, right	Posterior and superior aspect of right thigh	Yes	Present	None	Clinical remission 10 days after appearance of the herald patch
3	12 years, male	Present	Present, clearly documented	One	Strictly unilateral, left	Medial aspect of left groin and left scrotal skin	Yes	Present	None	Clinical remission 14 days after appearance of the herald patch

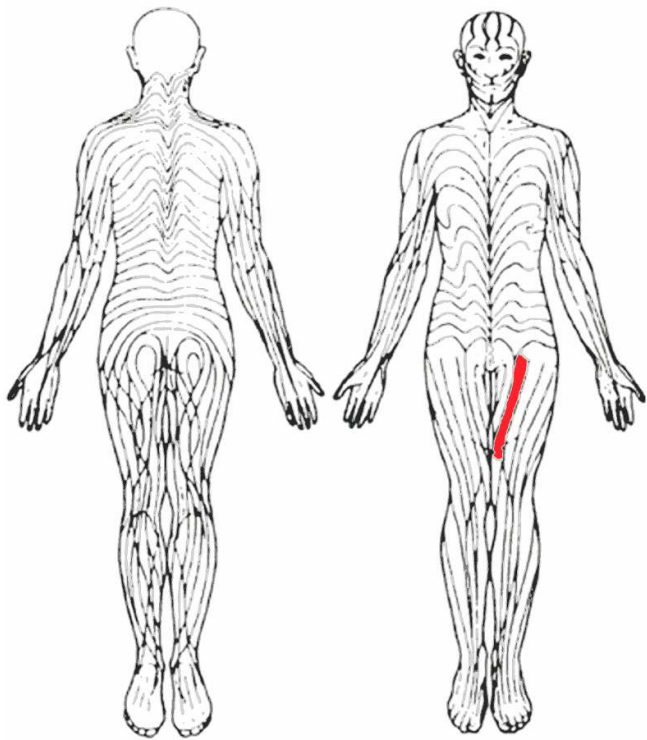
Table legend

Table 1: Clinical data of three patients with Blaschkoid pityriasis rosea

Figure 1



Figure 2



Figures legends

- Figure 1: Lesions of Patient 1 with Blaschkoid pityriasis rosea in a linear distribution along the medial aspect of his left thigh. The herald is arrowed black.
- Figure 2: This figure was modified from a figure published in the *DermNet* (www.dermnetnz.org/). Classical Blaschko's lines with the affected area of Patient 1 colour-filled in red.