



REVIEW ARTICLE

Atypical primary varicella rash: Systematic literature review

Calogero Mazzara¹ | Gregorio Paolo Milani^{2,3}  | Sebastiano A. G. Lava⁴ |
 Mario Giovanni Bianchetti⁵  | Gianluca Gualco¹ | Giacomo D. Simonetti^{1,6} |
 Pietro Camozzi⁵ | Lisa Kottanattu^{1,6}

¹Pediatric Institute of Southern Switzerland, Ospedale San Giovanni, Ente Ospedaliero Cantonale, Bellinzona, Switzerland

²Pediatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

³Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy

⁴Pediatric Cardiology Unit, Department of Pediatrics, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland

⁵Faculty of Biomedical Sciences, Family Medicine Institute, Università della Svizzera Italiana, Lugano, Switzerland

⁶Faculty of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland

Correspondence

Gregorio Paolo Milani, Pediatric unit, Foundation IRCCS Ca' Granda, Ospedale Maggiore Policlinico, via della Commenda 9, 20122 Milan, Italy.
 Email: milani.gregoriop@gmail.com

Present address

Sebastiano A. G. Lava, Heart Failure and Transplantation, Department of Pediatric Cardiology, Great Ormond Street Hospital, London, UK

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Abstract

Aim: In previously healthy subjects, primary varicella presents with a distinctive vesicular rash that is more intense on the trunk and head than on the extremities. However, an atypical presentation may occasionally develop. We aimed at systematically assessing the characteristics of cases affected by atypical primary varicella rash.

Methods: The United States National Library of Medicine, Excerpta Medica and Web of Science databases were reviewed, without date or language restrictions. Articles were eligible if reporting previously healthy and immunocompetent subjects with a primary varicella rash (i.e., a photo-localised primary varicella or skin inflammation-associated primary varicella).

Results: Thirty-eight reports providing information on 59 cases of atypical primary varicella were identified. Twenty-four cases (median 8.5 years of age, 19 females) were photo-localised and 35 (median 4.8 years of age, 15 females) were associated with pre-existing skin inflammation (including cast occlusion, diaper irritation, operative sites, burns, insect bites, vaccinations or pre-existing skin disease). The skin rash was monomorphic and without a "starry sky" appearance.

Conclusion: Primary varicella may have a modified presentation in areas of irritation such as sun exposure or pre-existing inflammation. There is a need for a wider awareness of these modulators of varicella rash.

KEYWORDS

atypical rash, chickenpox, primary varicella, varicella

1 | INTRODUCTION

In previously healthy subjects, primary varicella is a self-limited infection characterised by fever and a distinctive vesicular rash lasting

about 5 days that is more intense on the trunk, face and scalp than on the extremities.¹⁻³ The vesicles initially contain clear fluid, rapidly pustulate and subsequently scab. The lesions appear in crops, so that on any one part of the body the rash can be in different stages

[Correction added on 14 May 2022, after first online publication: CRUI-CARE funding statement has been added.]

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of development (“starry sky” or “dew drop on a rose petal” appearance). In the great majority of cases, primary care physicians make a confident diagnosis on a clinical basis. History of recent exposure to varicella supports the diagnosis.¹⁻³ Occasionally, however, the diagnosis is not made because there are only a few lesions.¹

The distribution and characteristics of primary varicella rash may occasionally be atypical.⁴ Sun exposure can predispose to an atypical varicella rash. Localisation of rash to inflamed skin has also been reported. Since textbooks and reviews do not mention the existence of an atypical primary varicella rash,¹⁻³ we systematically reviewed the literature.

2 | METHODS

2.1 | Data source

A systematic search of the literature without date or language limitations was undertaken by two of us (CM and GPM) in accordance with the Preferred Reporting of Systematic Reviews and Meta-Analyses guidelines, using the United States National Library of Medicine, Excerpta Medica and Web of Science in June 2021. The following search terms were used: (“photolocalized” OR “photodistributed” OR “actinic” OR “atypical”) AND (“varicella” OR “chickenpox”).

2.2 | Study selection

Eligible were original articles and letters reporting previously healthy and immunocompetent subjects with a primary varicella rash occurring preferentially or exclusively in body areas recently exposed to sun. The term photo-localised (or actinic) primary varicella was used to denote these cases. Cases of primary varicella localised to previously inflamed skin caused among others by abrasion, trauma or operation, diaper irritation, insect bites, pre-existing skin disease or vaccination were also included. The term skin inflammation-associated primary varicella was used to denote these cases. Cases with second varicella, breakthrough varicella or herpes zoster infection were excluded.^{2,3}

Data were extracted using a predefined dedicated database. The information sorted from each case included demographics, distribution and characteristics of rash, the underlying cause and the microbiological work-up including history of recent exposure to varicella, absence of prior varicella, Tzanck smear and test for varicella zoster virus.¹⁻³ The diagnosis of primary varicella rash made by the authors of the original report was carefully re-evaluated by two experienced paediatric hospitalists.

2.3 | Analysis

Categorical data are shown as counts and were analysed using the Fisher's exact test.⁵ Continuous data are presented as medians, ranges and interquartile ranges and were compared using the

Key Notes

- Twenty-four cases of photo-localised (median 8.5 years) and 35 cases of skin inflammation-associated primary varicella (median 4.8 years) were reported between 1927 and 2021.
- The skin rash was monomorphic and without a “starry sky” appearance.
- Previous sun exposure or inflammation may occasionally predispose to an atypical varicella rash.

Mann–Whitney–Wilcoxon test.⁵ Two-sided *p*-values of < 0.05 were regarded as statistically significant.⁵

3 | SYNTHESIS

3.1 | Search output

The study flowchart is shown in [Figure 1](#). For the final analysis, we retained 38 communications published between 1927 and 2021 in English (*N* = 33), French (*N* = 3) or Spanish (*N* = 2).⁶⁻⁴³ The articles were reported from the United States of America (*N* = 16), France (*N* = 6), Spain (*N* = 6), Turkey (*N* = 3), Japan (*N* = 2), Belgium (*N* = 1), Brazil (*N* = 1), Canada (*N* = 1), South Africa (*N* = 1) and United Kingdom (*N* = 1).

3.2 | Clinical data

The 38 reports provided information on 59 cases ([Table 1](#)) of atypical primary varicella rash. The clinical diagnosis of primary varicella was supported by history of recent exposure to varicella and absence of prior varicella in all cases, by a Tzanck smear in 21 cases and by a positive test for varicella zoster virus in 7 cases. Twenty-four cases were photo-localised^{8-18,20,21,23,24,28,30,31,33,38,41,43} and 35^{6,7,14,16,19,21,22,25-27,29,30,32,34-37,40,42} skin inflammation associated. Females (79%) predominated in the cases with photo-localised varicella, males (57%) in the group with skin inflammation-associated varicella (*p* < 0.01). Finally, subjects with photo-localised varicella were slightly but significantly (*p* < 0.01) older than subjects with inflammation-associated varicella ([Table 1](#)).

The distribution of photo-localised primary varicella is given in [Figure 2](#). Following body regions were especially often affected: back, trunk, face, extremities and neck. Interestingly, nine reports explicitly stated that the skin rash was monomorphic and without a “starry sky” appearance.^{10,13,15,21,28,31,39,41} The rash was not described in detail in the remaining cases. In 35 cases, the rash was preferentially or exclusively localised in areas of inflammation, as depicted in [Table 2](#). The upper limbs and palms or soles were the most commonly affected body regions. Interestingly, varicella

FIGURE 1 Atypical varicella. Selection process for articles included in the systematic review

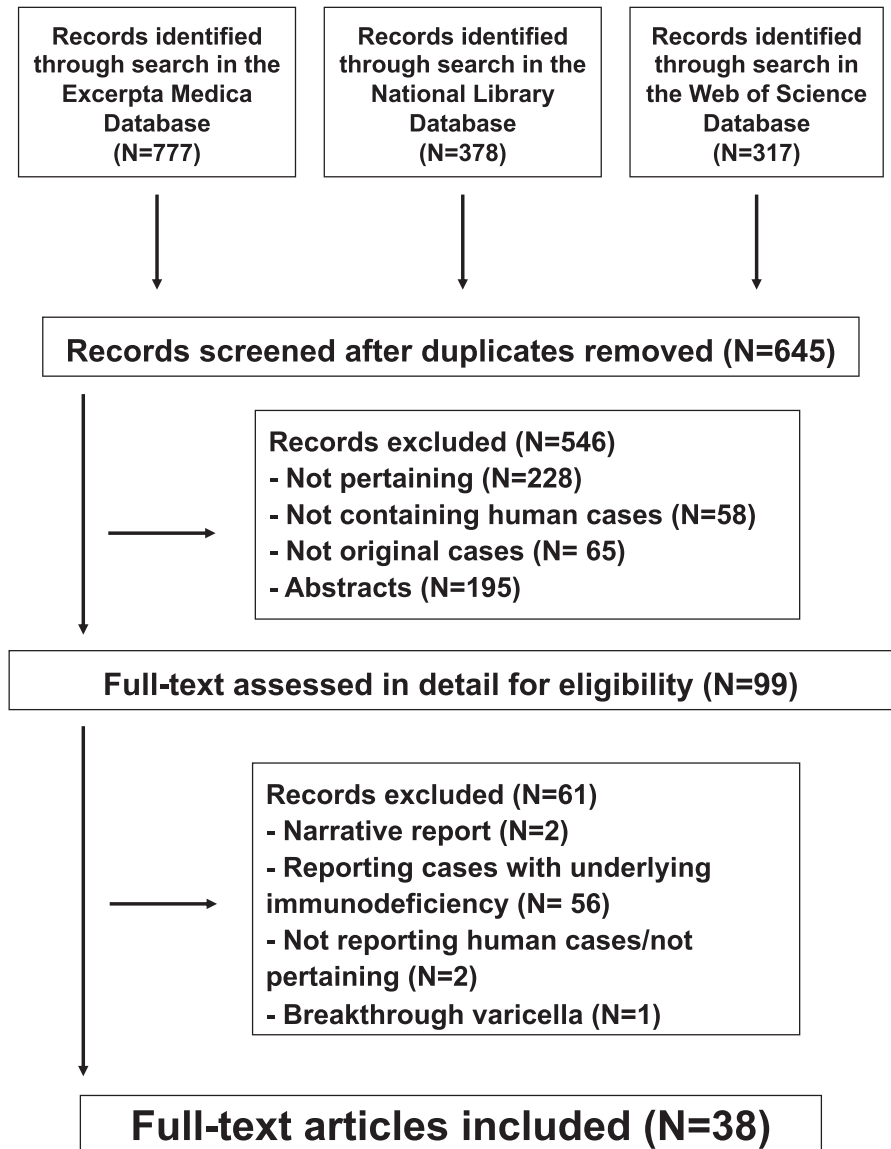


TABLE 1 Baseline characteristics of previously apparently healthy and immunocompetent subjects with atypical primary varicella rash

	All	Photo-localised	Skin inflammation associated	p-Value
N	59	24	35	
Females: males (N)	34: 25	19: 5	15: 20	<0.01
Age (years)				
Median	5.8	8.5	4.8	0.01
Ranges	0.7–59	2.0–59	0.7–41	
Interquartile range	3.6–12	4.9–19	3.1–8.8	
≤18 years of age (N)	49	16	33	0.01

skin eruptions on the scalp were not specifically mentioned in the 59 cases.

4 | DISCUSSION

This review of the literature points out that irritants such as sun exposure or a pre-existing skin inflammation may modulate the

distribution of varicella rash in previously apparently healthy subjects. The results also indicate that the usually heteromorphic rash of varicella is often monomorphic in these cases.

The mechanisms by which sun exposure or skin inflammation may modulate the distribution and the characteristics of varicella rash remain unclear. It has been postulated that sun exposure and skin trauma increase the capillary permeability and activate the local inflammatory cycle. Furthermore, sun radiation favours the

Photo-localised Atypical Varicella Rash

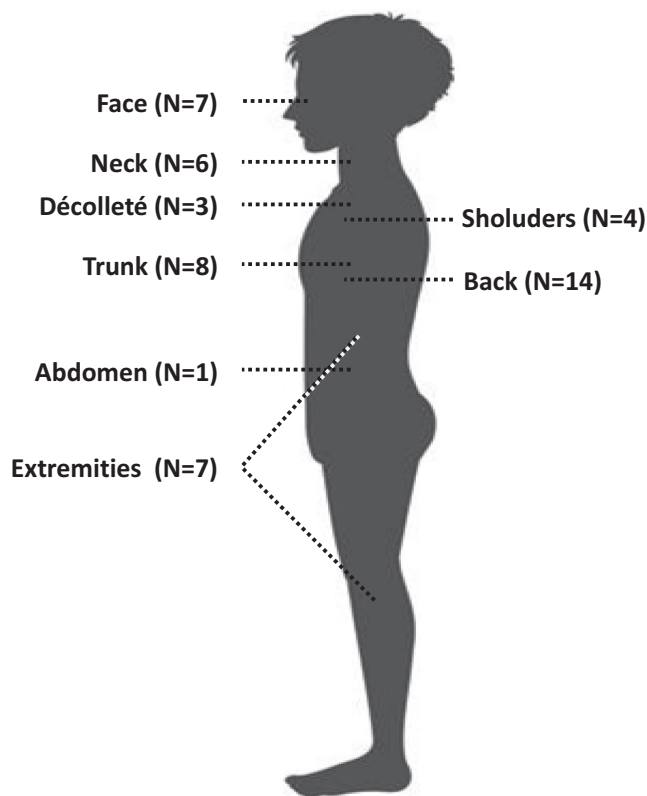


FIGURE 2 Distribution of photo-localised varicella rash occurring after recent sun exposure in 24 patients. The total number indicated in the figure exceeds the number of patients because more than one localisation was observed in some patients

secretion of cytokines, which may modulate the distribution and the type of rash. Similar observations have been made in the context of skin rashes associated with Herpes simplex, Morbillivirus, Picornaviruses and Rubella-virus.^{9,26}

Two further conditions predispose to an atypical varicella rash in previously apparently healthy subjects, including breakthrough varicella and second varicella.^{1-3,44,45}

Breakthrough varicella,⁴⁴ that is, the disease that occurs despite vaccination, is customarily mild, often atypically distributed and predominantly maculopapular (without vesicles). Similarly, recurrence of varicella after the natural disease, which is more common than is generally accepted, is typically mild and sometimes with an atypical distribution and morphology of rash.⁴⁵

Results of this review must be viewed with an understanding of the inherent limitations of the analysis, which included a small number of case reports and data from sometimes not very well documented cases published between 1927 and 2021.

In conclusion, this review confirms that viral skin diseases including varicella may have a modified presentation in areas of irritations such as sun exposure or inflammation caused by cast occlusion,

TABLE 2 Distribution of rash in 35 cases of skin inflammation-associated primary varicella

Distribution	Underlying skin inflammation	N
Diffuse	Contact dermatitis	1
	Diffuse psoriasis	1
	Scarlet fever	1
Face - scalp	Tinea	1
	Skin wound	1
Upper limbs	Cast application	3
	Bracelet rub	1
	Skin test	1
	Skin wound	1
	Vaccination	1
	Wasp sting	1
Lower limbs	Atopic dermatitis	1
	Burns	1
	Cast application	1
	Trauma	1
	Vaccination	1
Palms or soles	Unknown irritant	3
	Hand-foot-mouth disease	1
	Prolonged walking	1
	Walking on stones	1
Anogenital region	Diaper dermatitis	8
	Lichen sclerosus	1
	Streptococcal dermatitis	1
	Surgery	1

diaper irritation, operative sites, burns, insect bites, vaccinations or pre-existing skin disease. There is a need for a wider awareness among clinicians of these modulators of viral skin diseases.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

ORCID

Gregorio Paolo Milani  <https://orcid.org/0000-0003-3829-4254>
 Mario Giovanni Bianchetti  <https://orcid.org/0000-0003-4827-6973>

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