

# Pediatric Dermatology Instructive Cases

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## Disclosures

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*Discussion is based on evidence-based recommendations and public presentations/publications.*

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## History

- 13 yo girl with CRMO and psoriasiform dermatitis that developed PG.

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## TNFa inhibitor paradoxical "psoriasis"

- Multicenter retrospective case series of <18 yo who developed new-onset psoriasiform eruption while taking a TNF inhibitor for a non-dermatologic disorder

**JAMA Dermatology | Brief Report**  
**Paradoxical Psoriasiform Eruptions in Children Receiving Tumor Necrosis Factor α Inhibitors**

Joshua Eickstaedt, MD; Amy S. Paller, MD; Emily Lund, MD; Morgan Murphy, MD; Heather Branding-Bennett, MD; Megan Maurano, MD; Estaban Fernandez Faith, MD; Kristen E. Holland, MD; Erin Ibbler, MD; Marlynn G. Liang, MD; Patricia S. Todd, MD; Elaine Siegfried, MD; Sean Iqbalwan, MD; Kelly M. Corbero, MD; Meghan M. Tollesford, MD

Location	Patients, No. (%) (N = 103)
Scalp	85 (83)
Ear	32 (31)
Postauricular	35 (34)
Face	27 (26)
Trunk	48 (47)
Extremities	17 (17)
Upper extremities	31 (30)
Hands or fingers	10 (10)
Fingernails	4 (4)
Lower extremities	40 (40)
Foot or toes	15 (15)
Toenails	2 (2)
Intertriginous	22 (21)
Perianal or buttocks	16 (16)
Genitals	10 (10)

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## TNFa inhibitor paradoxical "psoriasis"

103 Patients with TNF-induced psoriasiform eruptions

65 Patients continued initial TNFi				12 Patients discontinued initial TNFi and did not start second line TNFi				26 Patients switched to second line TNFi			
Treatment	Resolved or improved, %	No improvement, %	Not documented, %	Treatment	Resolved or improved, %	No improvement, %	Not documented, %	Treatment	Resolved or improved, %	No improvement, %	Not documented, %
Topicals alone	43 (66)	1 (2)	5 (8)	Topicals alone	3 (25)	2 (17)	1 (8)	Topicals alone	14 (54)	1 (4)	1 (4)
Methotrexate	12 (18)	0	0	Methotrexate	2 (17)	2 (17)	0	Methotrexate	5 (19)	1 (4)	0
Synthetic steroids	1 (2)	1 (2)	0	Acute response	1 (8)	0	0	Synthetic steroids	2 (8)	0	0
Phototherapy ± acitretin	1 (2)	0	0	Ustekinumab	2 (17)	0	0	Phototherapy ± synthetic steroids	1 (4)	0	0
Phototherapy	1 (2)	0	0					Phototherapy ± methotrexate	1 (4)	0	0

18 Patients continued second line TNFi without psoriasiform eruptions  
8 Patients developed a second TNFi-induced psoriasiform eruption  
2 Patients discontinued second line TNFi  
6 Patients discontinued second line TNFi and did not start another biologic

Eickstaedt et al. JAMA Derm 2023.

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### TNF $\alpha$ inhibitor paradoxical “psoriasis”

- Systematic review of 4564 pediatric patients on TNF $\alpha$  inhibitors, 4.6% developed paradoxical psoriasis
  - Infliximab 8.3% vs adalimumab 3.3%
- CRMO most highly associated, more likely pustular

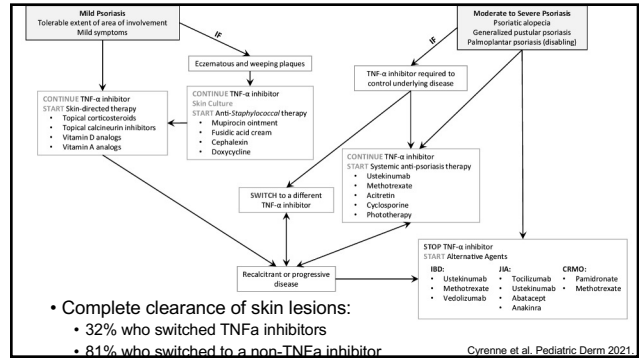
**TABLE 1** Prevalence of drug-induced psoriasis by underlying disease and biologic therapy

Drug	Any disease		IBD		JIA		CRMO	
	n (%)	N	n (%)	N	n (%)	N	n (%)	N
Any TNF $\alpha$ inhibitor	210 (4.6)	4564	158 (6.1)	2591	40 (3.8)	1053	3 (8.6)	35
Infliximab	123 (8.3)	1478	112 (10.0)	1122	9 (4.2)	214		
Etanercept	2 (0.3)	705			1 (0.5)	213		
Adalimumab	15 (3.3)	454	4 (3.2)	124	3 (3.2)	94		
Golimumab	0 (0)	15						
Certolizumab	0 (0)	5	0 (0)	5				

Abbreviations: CRMO, chronic recurrent multifocal osteomyelitis; IBD, inflammatory bowel disease; JIA, juvenile inflammatory arthritis; KD, Kyrle's disease.

Cyrenne et al. *Pediatric Derm* 2021.

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### Chronic Recurrent Multifocal Osteomyelitis (CRMO)

- Rare, primary autoinflammatory bone disease
- Typically children (most 7-9 yo at diagnosis)
- Female to male ratio 2:1
- Chronic, recurrent episodes of symptomatic osteolytic sclerotic bone lesions
- Pro-inflammatory cytokines (TNF $\alpha$ , IL-1b, IL-6, IL-20) overexpressed, decreased anti-inflammatory mediators
- Maybe SAPHO syndrome presenting in pediatric patient patients or distinct disorder on the same spectrum
- Dermatologic associations: psoriasis, palmoplantar pustulosis, acne, Sweet syndrome, pyoderma gangrenosum (rarely)

Moreno-Mateo et al 2021; Beck et al 2022; Romagnuolo et al 2023.

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### Canakinumab treatment in a young girl with refractory chronic recurrent multifocal osteomyelitis associated with pyoderma gangrenosum

Sabrina Aciermo<sup>1</sup> | Francesca Angrisani<sup>1</sup> | Achille Marino<sup>2</sup> | Roberto Felice Caporali<sup>1,4</sup> | Rolando Cimaz<sup>2,3</sup> | Teresa Gian<sup>1,4</sup>

- 13 yo F with CRMO, ulcer 2 mo after adalimumab start
- Bx: necrotic epidermis, carcinomatous hyperplasia on epidermal reactive neoangiogenesis with fibrosis, dense neutrophilic infiltrate compatible with PG
- Adalimumab switched to canakinumab, prednisone 2 mo, topical steroid
- 1 year later – disease well-controlled

Aciermo et al 2022

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### Pyoderma gangrenosum following anti-TNF therapy in chronic recurrent multifocal osteomyelitis: drug reaction or cutaneous manifestation of the disease? A critical review on the topic with an emblematic case report

Maurizio Romagnuolo<sup>1,2</sup>, Chiara Moltrasio<sup>1</sup>, Claudia Iannone<sup>1</sup>, Maurizio Gattinara<sup>1</sup>, Stefano Cambiaghi<sup>1,2</sup> and Angelo Valerio Marzano<sup>1,2</sup>

- 16 yo pt, 2 mo after adalimumab for CRMO
- Bx: pseudo-carcinomatous epidermal hyperplasia w admixed inflammatory infiltrate
- Tx: adalimumab switched to anti IL-1 canakinumab, prednisone, clobetasol
- 3 mo later – partially healed

Romagnuolo et al 2023

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### 8 cases of PG in patients with CRMO

- 6/8 cases PG onset after CRMO dx, 2/8 cases with both occurring at the same time
- 6/8 on legs, 2/8 on arms
- 50% of cases had PG ulceration in same location as bone inflammation
- 3 cases at bone biopsy site, suggestive of pathergy
- Only 1 case on TNF $\alpha$  inhibitor (etanercept) – discontinued due to good control of CRMO
- All cases, PG lesions resolved w conventional therapy

Romagnuolo et al 2023; Katsuo et al 2020; Wurm et al 2016.

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### Conclusions

- CRMO is associated with neutrophilic dermatoses, PG could be a cutaneous manifestation
- Anti-TNF therapies may aggravate neutrophilic disease, possibly an additive risk factor
- Paradoxical "psoriasis" is also associated with anti-TNF, discontinuing and switching to a new biologic may improve psoriasis and PG

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### History

- 15 mo boy with hepatoblastoma diagnosed at 14 months, on cisplatin/5-FU/vincristine/doxorubicin that developed varicella reactivation and measles

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### Primary Varicella

- Usually benign, self-limited in immunocompetent children
- Develop ~15 days after exposure with prodrome (fever, loss of appetite, malaise) => Generalized vesicular rash within 24 hours



Straus et al. Ann Int Med 1988.

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### Varicella "Breakthrough Disease"

- Varicella infection after receiving VZV vaccine
- ~20% of children after one dose of vaccine
- Milder with less skin lesions and complications, including in pediatric cancer patients
- Rash more atypical



Chavez et al. J Infect Dis 2008. Weimann et al. J Infect Dis 2008. Takahashi et al. Pediatrics 1986. Levin et al. J Infect Dis 2008.

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### Herpes Zoster in Children

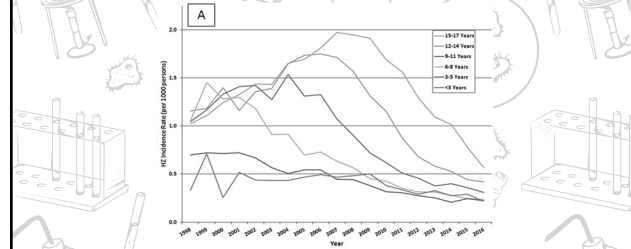
- Incidence <1/1000 in children <10 years old annually
- Risk factors:
  - Exposure to VZV infection in utero
  - Immunocompromised state
  - Infection during first year of life
  - Postherpetic neuralgia rare



Gunnar et al. Ped Inf Dis J 1998. Guess et al. Pediatrics 1985. Feder et al. Ped Inf Dis J 2004.

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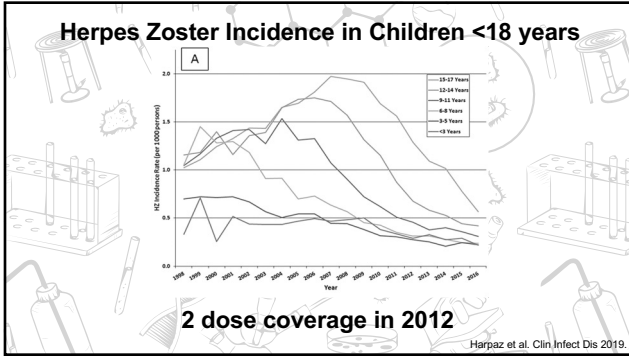
### Herpes Zoster Incidence in Children <18 years



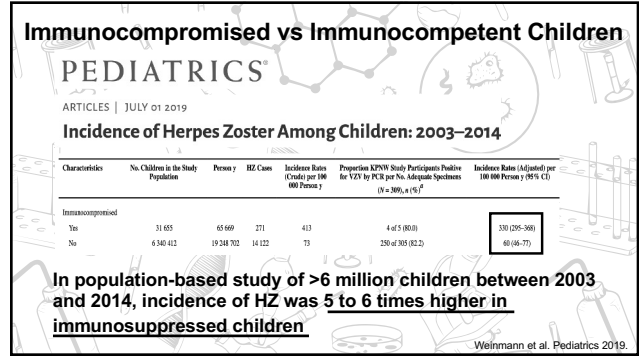
Varicella Vaccine Introduced in 1996

Harjapaz et al. Clin Infect Dis 2019.

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### Complications in Immunocompromised Children?

The Journal of Infectious Diseases

#### Immunocompetent Children Account for the Majority of Complications in Childhood Herpes Zoster

Veit Grote,<sup>1,2</sup> Rüdiger von Kries,<sup>1</sup> Eva Rosenfeld,<sup>1</sup> Bernd H. Belohradsky,<sup>2</sup> and Johannes Liese<sup>2</sup>

<sup>1</sup>Institute of Social Pediatrics and Adolescent Medicine, and <sup>2</sup>Dr. von Hauner Children's Hospital, Ludwig-Maximilian University of Munich, Munich, Germany

Grote et al. J Infect Dis 2007.

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### Proportion of Complications By Immune Status

Children, no. (% in category)	Children, no. (% in category)		P
	Immunocompetent (n = 95)	Immunocompromised (n = 19)	
Skin infectious complications	42 (33.26)	7 (37)	> .999
Ophthalmic zoster	29 (26.27)	2 (10)	.234
Zoster oticus	12 (11.11)	1 (5)	.336
Zoster oticus with facial paralysis (Ramsay Hunt syndrome)	11 (10.10)	1 (5)	.638
Meningoencephalitis	22 (20.21)	2 (11)	.522
Generalized herpes zoster (shingles)	9 (4.4)	5 (26)	.074
Other complications	8 (5.15)	9 (47)	.125
Pneumonia	5 (4.4)	1 (5)	> .999
Upper respiratory tract, ear/nose/throat	5 (5.15)	0 (0)	.539
Other neurological complications	4 (4.4)	0 (0)	> .999

NOTE: The presence of multiple complications in a child is possible. The table does not include 129 children in whom no complication was reported.

Except for generalized HZ, no statistically significant complications in immunocompromised children

Grote et al. J Infect Dis 2007.

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### Vaccine-Induced Herpes Zoster

Pediatric Dermatology

ORIGINAL ARTICLE | Full Access

Pediatric vaccine-strain herpes zoster: a case series

> J Child Neurol. 2019 Mar;34(4):164–168. doi: 10.1177/0883207318821468. Epub 2019 Jan 10.

#### Severe Herpes Zoster Following Varicella Vaccination in Immunocompetent Young Children

Amaran Moodley <sup>1</sup>, Jack Swanson <sup>2</sup>, Charles Grose <sup>3</sup>, Daniel J Bonthuis <sup>4</sup>

Case Reports | > J Pediatr. 2022 Dec;231:219–219. doi: 10.1016/j.peds.2022.08.032. Epub 2022 Aug 23.

#### Varicella Vaccine-Induced Infantile Zoster-Like Skin Rash

Numerous cases reported in the literature

Sugal, J Pediatr. 2022; Moodley, J Child Neurol. 2019; Dreyer, Ped Derm. 2017.

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### Vaccine-Induced Herpes Zoster

Can occur in the same dermatome as the vaccine injection

Sugal, J Pediatr. 2022.

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## Management

- Limited efficacy evidence of antiviral therapy in patients <50 years
- Antiviral therapy for symptoms within 72 hours of onset
- Can consider conservative management given rare post-zoster neuralgia (except HZ ophthalmicus)
- IV acyclovir in immunocompromised children

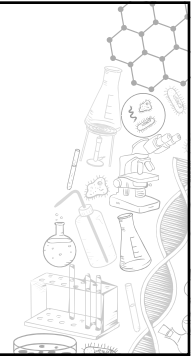


Arvin, Semin Pediatr Infect Dis, 2002.

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## Summary

- Varicella infection after vaccination can occur and generally presents milder and atypical
- Herpes Zoster is rare in children
- Clinical presentations of Herpes Zoster can be similar regardless of immune status
- Vaccine-strain VZV may establish latency and later reactivate in children



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