#AAD2019

Highlights AEDV

In 77TH AAD Congress

1-5 March 2019

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Dermatopathology

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Scientific Initiative of:

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SURVIVAL OF PATIENTS WITH EARLY INVASIVE MELANOMA DOWN-STAGED UNDER THE NEW 8TH AJCC EDITION

- In the 8th edition of AJCC, classification of T1 melanomas was modified, and mitotic rate is no longer a staging criterion and 0.8mm not 1.0mm becomes the thickness boundary
- Follow-up study in Australia from 2010 to 2014, of 208 T1b melanomas according to te 2017 AJCC classificacion
- 111 (53%) remained T1b
- 97 (47%) decreased to T1a under the 8th edition
- <0.8mm thick, without ulceration and with mitotic rates:
  - 1-3/mm2 (n=87)
  - >3/mm2 (n=10).
- 5 recurrences in 3 years (95% DFS):
  - 1-3/mm2: DFS 96%
  - >3/mm2: DFS 80%
- DFS of patients down-staged to T1a under the 8th AJCC edition remains comparable to the 93% DFS of T1b melanomas

Survival of patients with early invasive melanoma down-staged under the new eighth edition of the American Joint Committee on Cancar staging system
J Am Acad Dermatol 2019;80:272-4.

ATYPICAL INTRAEPIDERMAL MELANOCYTIC PROLIFERATION

- Proliferation of predominantly single melanocytes in the epidermis without a developed nevus or melanoma
- Other names: atypical junctional melanocytic lesion, proliferation of solitary units of melanocytes, atypical melanocytic hiperplasia, lentiginous junctional melanocytic proliferation

- Mohs for AIMP. Etzkorn et al.
  - Retrospective review, single institution, 223 lesions of the head, neck, hand, foot, or pretibial, treated with Mohs surgery
  - 42 (18,8%) of all lesions upstaged to unequivocal melanoma in situ or invasive melanomas
- Mohs for AIMP. Blank et al.
  - Retrospective review, 1127 biopsies reported as AIMP subsequently excised, one academic instituion
  - Melanoma (in-situ, stage 1A) was diagnosed after excision in 8.2% (92/1127) of AIMP samples

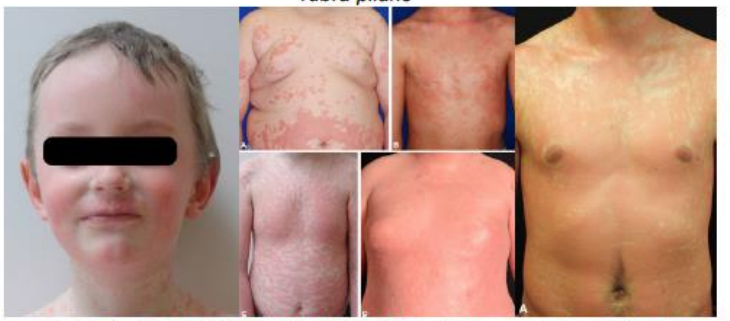
- Take-home message: Perform complete excision in incompletely removed AIMP. A subset represent MIS/MM

Etzkorn et al. JAAD 2018;79:1109-16
Blank NR et al. JAAD 2019, Jan 14. doi: 10.1016/j.jaad.2019.01.005

CARD14-ASSOCIATED PAPULOSQUAMOUS ERUPTION: A SPECTRUM INCLUDING FEATURES OF PSORIASIS ANS PITYRIASIS RUBRA PILARIS

- They identify 15 families with CARD14-associated papulosquamous eruption (CAPE).
- Characteristic features of CAPE include early age of onset; prominent involvement of the cheeks, chin, and ears; family history of psoriasis or PRP; minimal response to conventional topical and systemic psoriasis therapies
- Improvement with ustekinumab
- The possibility of CARD14 mutation should be considered in subjects with papulosquamous eruptions characterized by features of both psoriasis and PRP, especially those who present with early onset of disease, facial involvement, and family history of psoriasis or PRP

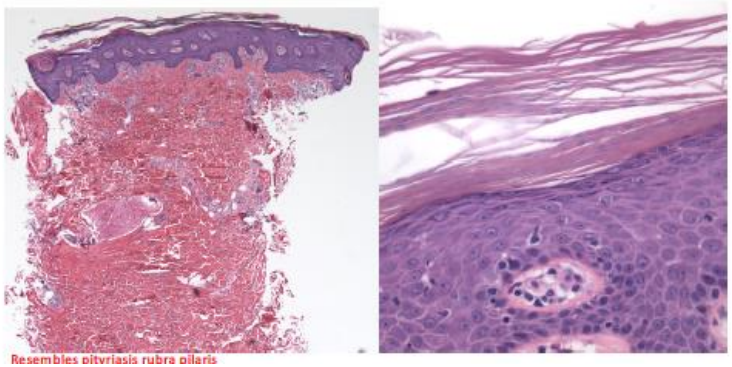
CARD14-associated papulosquamous eruption: A spectrum including features of psoriasis and pityriasis rubra pilaris



Clinical gestalt: Pityriasis rubra pilaris (PRP; type IV or V; "familial") >> psoriasis

Craiglow et al, JAAD 2018;79:487

Histopathology – most common pattern

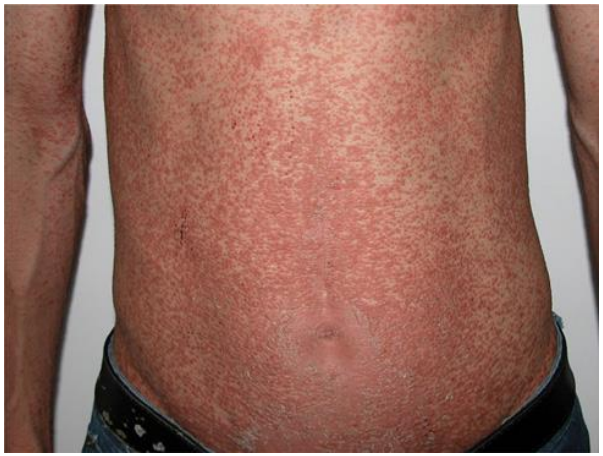


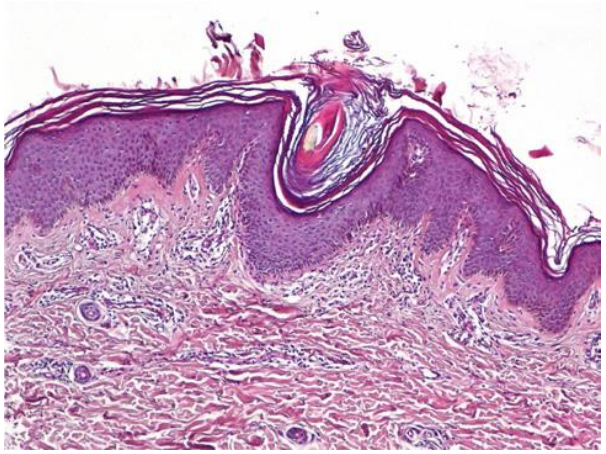
Resembles pityriasis rubra pilaris

CARD14-associated papulosquamous eruption: A spectrum including features of psoriasis and pityriasis rubra pilaris. JAAD 2018;79:487-94

CHECKPOINT INHIBITOR REACTIONS SUPPORT THAT INFLAMMATORY REACTION PATTERNS ARE NOT SPECIFIC TO GIVEN DISEASE

- Example: Lichenoid reaction, psoriasis-like, bullous pemphigoid-like, sarcoidal, and also pityriasis rubra pilaris like:
- Pembrolizumab
- Sorafenib, bevacizumab, ponatinib, Imatinib
- Sofosbuvir, telaprevir
- Insulin
- Topical imiquimod
- Simvastatin





Pityriasis rubra pilaris-like eruption following insulin therapy initiation
Dermatol Pract Concept 2016;6:19-21

PD-1 ASSOCIATED LICHENOID REACTIONS

- Despite having different clinical diagnosis, many PD-1 reactions have lichenoid histological features
- Delayed cutaneous adverse reactions to PD-1 inhibitors are frequently observed
- Cutaneous adverse reactions may also occur after PD-1 inhibitor therapy has been discontinued

Table 1. Summary of Patients and Drug Reactions After PD-1 Inhibitor Therapy

Patient No./Sex/Age, y	Malignant Neoplasm	PD-1 Inhibitor Used	Cutaneous Adverse Reaction	Time From Treatment to Reaction, mo	No. of Treatment Cycles Completed	Timing of Cutaneous Reaction Relative to Treatment[a]	Tumor Response	CTCAE Grade[b]
1/M/60s[c]	Melanoma	Pembrolizumab	Sarcoidosis	12.0	10	After (4.7 mo)	CR	1
2/M/80s	Melanoma	Pembrolizumab	Eczema	0.5	1	During	PD	1
3/M/50s[d]	Melanoma	Pembrolizumab	Lupuslike reaction	7.4	7	During	CR	1
4/F/60s	Melanoma	Pembrolizumab	Lichenoid dermatitis	3.7	5	During	CR	3
5/M/60s[e]	Melanoma	Pembrolizumab	Bullous pemphigoid	20.4	30	During	CR	2
6/F/80s	Melanoma	Pembrolizumab	Lichenoid dermatitis	3.9	4	After (2.0 mo)	PR	2
7/M/70s	Melanoma	Nivolumab	Bullous pemphigoid	1.5	3	During	CR	2
8/M/70s	SCC	Pembrolizumab	Bullous pemphigoid	2.0	3	During	PD	2
9/M/60s[f]	Melanoma	Nivolumab	Lichenoid dermatitis	4.4	9	During	CR	2
10/F/80s	SCC	Pembrolizumab	Erythema multiforme	3.0	4	During	PD	1
	SCC	Pembrolizumab	Bullous pemphigoid	8.2	4	After (6.0 mo)	PD	2
11/M/50s	RCC	Nivolumab	Eczema	16.7	20	During	PD	1
12/M/80s	RCC	Nivolumab	Bullous pemphigoid	19.9	22	During	CR	2
13/M/60s	SCC	Pembrolizumab	Lichenoid dermatitis	2.4	3	During	PR	2
14/M/40s	Melanoma	Pembrolizumab	Lichenoid dermatitis	3.0	3	After (1.0 mo)	CR	2
15/F/70s	Melanoma	Nivolumab	Lichenoid dermatitis	0.5	1	During	CR	2
16/F/60s[g]	Melanoma	Pembrolizumab and nivolumab	Lichenoid dermatitis	4.7	6	After (1.0 mo)	PD	3
17/M/70s	Melanoma	Pembrolizumab	Erythema multiforme	38.0	35	During	PD	3

Abbreviations, CR, complete response; CTCAE, common terminology criteria [d] Described by Shao et al.[5]

Table 2. Summary of Reactions That Occurred After Discontinuation of PD-1 Inhibitor Treatment

Patient No./Sex/Age, y	Malignant Neoplasm	PD-1 Inhibitor	Cutaneous Adverse Reaction	Time to Onset After PD-1 Inhibitor Discontinuation, mo	Tumor Response	Associated Extracutaneous irAE
1/M/60s	Melanoma	Pembrolizumab	Sarcoidosis	4.7	CR	Lung sarcoidosis
6/F/80s	Melanoma	Pembrolizumab	Lichenoid dermatitis	2.0	PR	None
10/F/80s	SCC	Pembrolizumab	Bullous pemphigoid	6.0	PD	None
14/M/40s	Melanoma	Pembrolizumab	Lichenoid dermatitis	1.0	CR	None
16/F/60s[a]	Melanoma	Pembrolizumab and nivolumab	Lichenoid dermatitis	1.0	PD	None

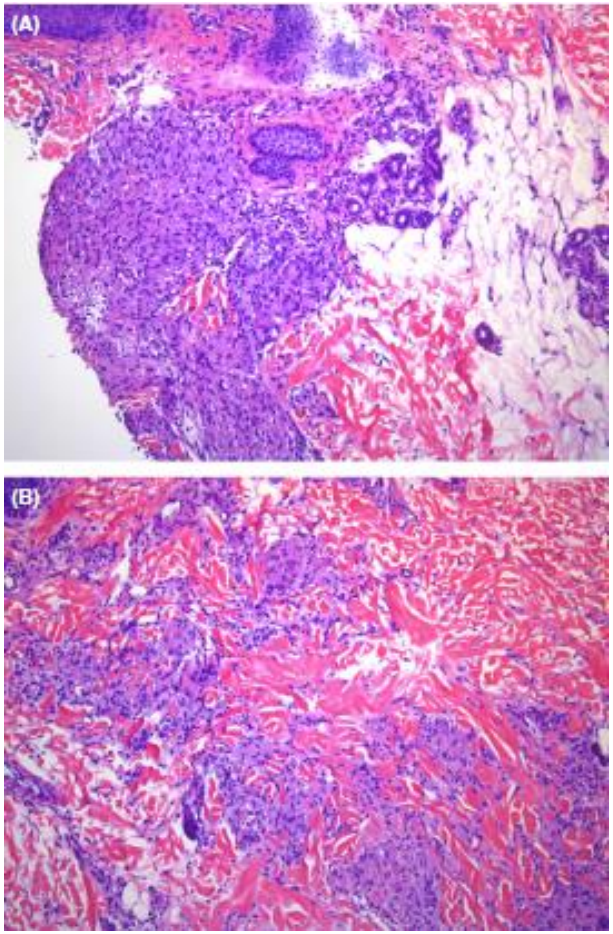
Abbreviations: CR, complete response; irAE, immune-related adverse event; PD, progression of disease; PD-1, programmed cell death protein 1; PR, partial response; SCC, squamous cell carcinoma.

[a] Received 3 cycles of pembrolizumab followed by 3 cycles of ipilimumab and nivolumab.

Timing of Onset of Adverse Cutaneous Reactions Associated With Programmed Cell Death Protein 1 Inhibitor Therapy
JAMA Dermatol;154:1057-1061

VEMURAFENIB CUTANEOUS SIDE EFFECTS

- Expanding role of BRAF-inhibitors: melanoma, thyroid , colorectal, non-small cell lung, brain tumors
- Recent discoveries of BRAF V600E in more than half of tested Langerhans cell histiocytosis lesions have prompted clinical trials of vemurafenib therapy for children with refractory, multisystem Langerhans cell histiocytosis
- Vemurafenib-induced neutrophilic panniculitis
- Granulomatous dermatitis with features resembling granuloma annulare in addition to sarcoidal granulomas



Chen, et al. Granulomatous dermatitis secondary to vemurafenibin a child withLangerhanscell histiocytosis. PediatrDermatol. Nov 2018.