Clinical Findings in Cryptococcoid Neutrophilic Dermatosis: A Review of the Literature and Single-Center Retrospective Study

Michael Tang, MD,[1] Grace C. Herron, MD [2], Anne Ning, MD[3], Yolanda Helfrich, MD[4], Lori Lowe, MD[4], Severine Cao, MD[4]

[1]Trinity Health Ann Arbor; [2] Santa Clara Valley Medical Center; [3]University of Cincinnati; [4]Department of Dermatology, University of Michigan, Ann Arbor, MI, USA

Background

- Cryptococcoid neutrophilic dermatosis (CND) is a recently described dermatologic entity characterized histologically by a neutrophilic infiltrate with acellular, vacuolated bodies that mimic Cryptococcus infection
- CND has been attributed to various causes in the literature (iododerma, Sweet syndrome, vasculitis) and displays variable clinical features including chronic kidney disease (CKD), iodine and hydralazine exposure, and perinuclear antineutrophil cytoplasmic antibodies (p-ANCA)[1-2]

Objectives

- To provide a systematic characterization of the clinical presentation of CND, with focus on comparing cases attributed to iododerma versus other causes

Methods

- **Study Type/Inclusion Criteria (a):** Single-center retrospective study of patients with CND seen at the Michigan Medicine (MM) from 2012-2024
- **Study Type/Inclusion Criteria (b):** Systematic literature review. Search terms: “Cryptococcoid neutrophilic dermatosis” and “Cryptococcal Sweet Syndrome.”
- **Primary Outcomes:** Lesion characteristics, associated clinical features, treatment and course. Cases were designated as iododerma-induced CND (I-CND) and non-iododerma CND (N-CND)

Table 1. Demographics & Lesion Characteristics

	Literature Review		MM Cohort	
	I-CND (n=10)	N-CND (n=26)	I-CND (n=7)	N-CND (n=3)
Demographics				
Age	58.7	66.2	63.3	71.7
Sex (F)	8 (80%)	20 (77%)	4 (57%)	2 (67%)
Lesion Characteristics				
Lesion Morphology				
Papules/Plaques	7 (70%)	23 (88%)	4 (57%)	2 (67%)
Vesicle/Bullous	9 (90%)	11 (42%)	6 (86%)	1 (33%)
Purpuric	1 (10%)	5 (19%)	1 (14%)	0 (0%)
Nodule	0 (0%)	5 (19%)	1 (14%)	0 (0%)
Pseudovesicular/pseudobullous	0 (0%)	3 (12%)	0 (0%)	0 (0%)
Vegetating	1 (10%)	0 (0%)	0 (0%)	0 (0%)
Lesion Features				
Hemorrhagic	8 (80%)	14 (54%)	7 (100%)	3 (100%)
Ulcerated/Erosive	3 (30%)	9 (35%)	2 (29%)	0 (0%)
Umbilicated	5 (50%)	6 (23%)	1 (14%)	0 (0%)
Necrotic/Eschar	1 (10%)	3 (12%)	0 (0%)	0 (0%)
Pustular/Purulent	1 (10%)	1 (4%)	1 (14%)	1 (33%)
Location				
Head/Neck	8 (80%)	20 (77%)	6 (86%)	2 (67%)
Upper Extremities	6 (60%)	22 (85%)	7 (100%)	1 (33%)
Trunk	5 (50%)	14 (54%)	5 (71%)	1 (33%)
Lower Extremities	2 (20%)	16 (62%)	3 (43%)	1 (33%)
Mucosal	4 (40%)	13 (50%)	3 (43%)	1 (33%)

Table 2. Risk Factors & Clinical Course

	Literature Review		MM Cohort	
	I-CND (n=10)	N-CND (n=26)	I-CND (n=7)	N-CND (n=3)
Risk Factors				
Hydralazine exposure (+)	2 (20%)	5 (19%)	6 (86%)	1 (33%)
CKD	8 (80%)	13 (50%)	6 (86%)	0 (0%)
P-ANCA (+)	3 (30%)	11 (42%)	5 (71%)	1 (33%)
Contrast Exposure	9 (90%)	7 (27%)	7 (100%)	3 (100%)
>2/4 of Above Features	*8 (80%)*	*12 (46%)*	*7 (100%)*	*1 (33%)*
>3/4 of Above Features	*3 (30%)*	*7 (27%)*	*6 (86%)*	*1 (33%)*
4/4 of Above Features	*0 (0%)*	*0 (0%)*	*4 (57%)*	*1 (33%)*
Clinical Course				
Resolution of symptoms	7 (70%)	15 (58%)	6 (86%)	2 (67%)
Time Course:				
Rapid resolution	6 (60%)	6 (23%)	3 (43%)	1 (33%)
Prolonged resolution	0 (0%)	3 (12%)	1 (14%)	0 (0%)
Unknown time course	1 (10%)	6 (23%)	2 (29%)	1 (33%)
Worsening or non-resolution	0 (0%)	1 (4%)	0 (0%)	0 (0%)
Deceased during Hospitalization or <30 days of Onset	3 (30%)	7 (27%)	1 (14%)	0 (0%)
Unknown	0 (0%)	3 (12%)	0 (0%)	1 (33%)

Results

Literature Review (I-CND: 10, N-CND:26)

- Reported causes: 10 (28%) iododerma, 17 (47%) Sweet Syndrome, 9 (25%) other (e.g. drug-induced vasculitis, HIV)
- I-CND and N-CND typically presented with hemorrhagic papules/vesicles on the head/neck & upper extremities. N-CND also involved lower extremities
- CKD and contrast exposure were observed in most I-CND cases and were common among N-CND cases. Hydralazine exposure and positive p-ANCA were also frequently noted in both groups
- Mortality rate was similar for both I-CND (30%) and N-CND (27%)

MM Cohort (I-CND: 7, N-CND 3)

- I-CND and N-CND commonly presented with hemorrhagic papules and vesicles on the head/neck. I-CND cases also involved the upper extremities and trunk
- CKD, positive p-ANCA, contrast and hydralazine exposure were frequently observed in I-CND. Among N-CND patients, all had contrast exposure, one was exposed to hydralazine, and one was noted to have positive p-ANCA
- Mortality rate was 14% in I-CND, and 0% in N-CND

Conclusions

- Notable overlap exists between I-CND and N-CND: despite being attributed to different causes, they exhibit similar clinical features, including CKD, hydralazine/contrast exposure, and p-ANCA antibodies
- Contrast exposure was reported in most cases of I-CND, but also in cases of N-CND, suggesting an underrecognized role for iodine. Cases of CND may all fall within the same syndrome
- When CND is identified on biopsy, renal function, iodine levels, ANCA serologies, and medications should be evaluated
- Management should include discontinuation of iodine exposure & hydralazine. Close monitoring and consideration of early systemic steroids is warranted, given high mortality rates

References

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Correspondence and/or reprints: Michael Tang (mijitang@umich.edu)