

Pseudoporphyrias: A Systematic Review and Meta-Analysis

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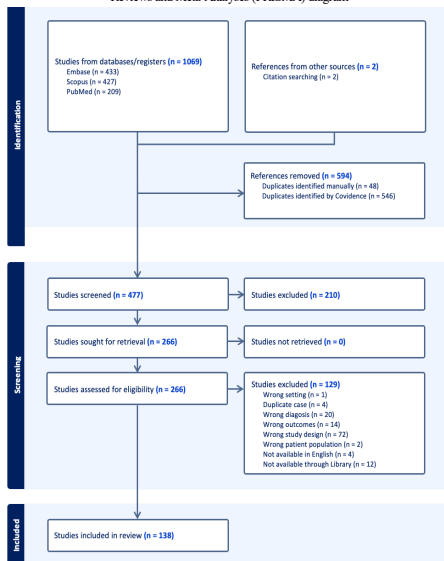
Introduction

- Pseudoporphyria is a phototoxic reaction. It is characterized by photodistributed bullae which present clinically and histologically similarly to porphyria cutanea tarda (PCT) but distinguished by normal levels of porphyrins, lack of hypertrichosis and hyperpigmentation, and sclerodermoid features.^{1,2}
- Pseudoporphyria is most commonly induced by medications and chronic renal failure on dialysis. Less commonly reported causes include ultraviolet A (UVA) radiation as well as other miscellaneous household and environmental substances.
- Studies suggest that the accumulation of medication or other substances in the basement membrane leads to injury and subsequent formation of bullae.^{3,4}
- This review analyzed causes of pseudoporphyria, trialed treatments, and their efficacy across different patient demographics.

Methods

- PubMed, Scopus, and Embase databases were searched for articles regarding pseudoporphyria.
- Of the 477 articles screened, 138 articles describing 191 patients were analyzed.
- The 2009 Oxford Levels of Evidence criteria were used for quality of evidence assessment.

Figure 1: Article selection performed via the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram



Results & Discussion

- Reported cases of pseudoporphyria were induced by medications (136), renal insufficiency (38), UV exposure (14), and miscellaneous triggers (3; including lime juice, brewer's yeast, and Coca-Cola). On average, cases resolved with trigger discontinuation after 3.2, 2.5, 1.5, and 1.5 months, respectively.
- The hands were the most commonly affected body area (78.5% of cases).
- Of the renal insufficiency-induced cases, 97.4% were on dialysis, predominantly hemodialysis. Therapy was discontinued in only 7.9% of patients, but full resolution occurred in 73.7%. More patients in this group were given treatment (75.8%) compared to those with medication-induced causes (8.1%), likely due to the inability to stop dialysis.
- Of the 14 UV-induced cases, 13 were due to tanning bed use and one resulted after phototherapy treatment for psoriasis. All UV-induced cases were biopsy proven. Interestingly, two of the patients were 22-year-old female monozygotic twins who had been using tanning beds for 8 months.⁵ No other cases reported a family history of porphyrias.
- Of the medication-induced cases, a total of 36 medications were identified as probable triggers. NSAIDs were most commonly implicated (58.8%), followed by antineoplastics (8.1%), antifungals (7.4%), and diuretics (6.6%). Naproxen was the leading offending agent, with 54 total cases reported (39.7%), most commonly prescribed for various immune and non-immune mediated arthropathies.
- Therapy was discontinued in most medication-induced cases (90.4%), leading to complete symptom resolution in 80.1%. Most patients (91.9%) did not receive any specific treatment for pseudoporphyria. In those who did receive treatment, topical steroids (2.9%) were most commonly used.

Table 1: Demographics and Clinical Characteristics of Patients with Pseudoporphyria stratified by associated cause

	Drug-Induced	Renal Insufficiency-Induced	UV-Induced
Sex (n, %)			
Male	58 (42.6)	18 (47.3)	1 (7.1)
Female	70 (51.5)	20 (52.6)	13 (92.9)
Not reported	8 (5.9)	0 (0.0)	0 (0.0)
Average age (years)	41.9	47.1	34.6
Average duration of therapy (months)	17.9	76.6	25.6
Average duration of lesions prior to presentation (months)	6.4	11.0	15.8
Location affected (n, %)			
Generalized	13 (9.6)	1 (2.6)	0 (0.0)
Head	38 (27.9)	15 (39.4)	3 (21.4)
Neck	6 (4.4)	0 (0.0)	0 (0.0)
Chest	1 (0.7)	0 (0.0)	1 (7.1)
Back	1 (0.7)	0 (0.0)	0 (0.0)
Arms	22 (16.2)	10 (26.3)	2 (14.2)
Hands	104 (76.5)	32 (84.2)	12 (85.7)
Legs	18 (13.2)	1 (2.6)	2 (21.4)
Feet	21 (15.4)	4 (10.5)	4 (28.6)
Trigger discontinued (n, %)			
Yes	123 (90.4)	3 (7.9)	5 (35.7)
No	9 (6.6)	35 (92.1)	2 (14.3)
Not reported	4 (2.9)	0 (0.0)	7 (50.0)
Resolution (n, %)			
Yes	109 (80.1)	28 (73.7)	5 (35.7)
No	9 (6.6)	4 (10.5)	0 (0.0)
Not reported	4 (2.9)	6 (15.8)	9 (64.3)
Avg. time to resolution after discontinuation (months)	3.2	2.5	1.5
Skin biopsy performed (n, %)	90 (66.2)	31 (81.6)	14 (100)
Treatment* (n, %)			
None	125 (91.9)	13 (34.2)	10 (71.4)
Topical Steroids	4 (2.9)	3 (7.9)	0 (0.0)
Antibiotics	1 (0.7)	4 (10.5)	0 (0.0)
Hydroxychloroquine	2 (1.4)	4 (10.5)	0 (0.0)
Topical antiseptic	1 (0.7)	3 (7.9)	0 (0.0)
Dasatinib	1 (0.7)	0 (0.0)	0 (0.0)
N-acetylcysteine	0 (0.0)	20 (52.6)	0 (0.0)
Vitamin D	0 (0.0)	2 (5.3)	0 (0.0)
Outcome after treatment (n, %)			
No resolution	23 (16.9)	5 (13.2)	7 (50)
Partial resolution	22 (16.2)	5 (13.2)	0 (0.0)
Full resolution	87 (64.0)	28 (73.7)	5 (35.7)
Not reported	4 (2.9)	0 (0.0)	2 (14.3)
Scarring reported (n, %)			
Yes	36 (26.4)	16 (42.1)	6 (42.9)
No	47 (24.6)	10 (26.3)	3 (21.4)
Not reported	53 (39.0)	12 (31.6)	5 (25.7)

*One patient may have received more than one type of treatment, therefore total value may not equal n

Table 2: Medications Associated with Inducing Pseudoporphyria

Medication Name	# of patients	Average Total Medication Duration (months)	Average Symptom Duration Before Presentation (months)	Reason for Medication Use
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) (58.8%)				
Naproxen	54	23.6	9.23	Ankylosing spondylitis, juvenile chronic arthritis, osteoarthritis, cervical spondylitis, rheumatoid arthritis, pauciarticular juvenile chronic arthritis, factor VIII deficiency arthropathy, systemic lupus erythematosus
Nabumetone	15	16.9	6.6	Rheumatoid arthritis, fibromyalgia
Oxaprozin	6	5	1.92	Juvenile rheumatoid arthritis, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, cervical spine disease
Celecoxib	1	1.5	NR	Pauciarticular juvenile Chronic arthritis
Aspirin	1	18	12	Back pain
Ketoprofen	1	9	3	Rheumatoid arthritis
Rofecoxib	1	0.5	NR	Guillain-Barre syndrome
Diflunisal	1	3	3	Osteoarthritis
Antineoplastics (8.1%)				
Imatinib mesylate	6	23.3	10	Chronic myelogenous leukemia, acute lymphocytic leukemia
Cyclosporine	2	31	1	Liver transplant, acute kidney graft rejection
Olaparib	1	12	12	Ovarian cancer
Sunitinib	1	6	NR	Gastrointestinal stromal tumor
5-Fluorouracil	1	2	NR	Adenocarcinoma
Antifungals (7.4%)				
Voriconazole	10	9.7	6.67	Fungal infections (coccidioidomycosis meningitis, aspergillosis, candida parapsilosis),

Conclusions

- While rare, pseudoporphyria is important to keep on the differential for vesiculobullous eruptions.
- It is important to review all patient medications at the time of diagnosis, including chronic medications as reactions do not always occur closely following medication or dialysis initiation.
- For drug-induced or UV-induced pseudoporphyria, prompt discontinuation of the offending agent is key for symptom resolution.
- Further research regarding a genetic component, mechanisms behind triggering agents, and diagnostic standards may aid in developing targeted preventive strategies and treatments.
- Limitations of this study include heterogeneity of metric reporting within published studies.

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