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Pityriasis Rubra Pilaris Treatment Options: a Retrospective Case Series from a Tertiary Hospital

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Acknowledgements:
None to list

Keywords:
Pityriasis Rubra Pilaris, therapy - systemic, therapy – biology, erythroderma, pharmacology

Running Short Title:
PRP treatment options

Conflicts of Interest:
None to declare

Authors contribution:
Ringin, S: main writer, data collector and reviewer
Baker, C: review of article
Foley, P: review of article
Daniel, B: review of article

Funding:
No Funding Sources

Data Availability:
All data generated or analysed during this study are included in this published article (and its supplementary information files).

Abstract:

Background: Pityriasis Rubra Pilaris (PRP) is a group of uncommon chronic inflammatory skin conditions with unclear pathophysiology and aetiology. To date there is limited published literature and no clinical guidelines for the management of PRP. Infliximab, alone or in combination, is the most widely published successful treatment for adults and etanercept for paediatric populations. We present a case series of patients diagnosed with PRP.

Method: Retrospective data were collected from a tertiary Australian dermatology department between January 2010 and December 2019 on patients with PRP. Electronic medical records and pathology database were searched.

Results: A total of thirteen patients were included. Twelve of the thirteen patients used topical agents and three patients attempted narrow-band ultraviolet B phototherapy. All patients received acitretin as first line systemic agent with the dose varying from 10-50mg daily. Six patients treated with acitretin reported adverse events, requiring dose reduction or cessation. Of the nine patients who did not receive a biologic agent, complete clearance of PRP was achieved in five cases. At least one biologic agent was used in four cases with two experiencing a marked improvement. Overall, complete clearance was achieved in six patients.

Conclusion: PRP continues to be a challenge to treat with many treatment options used with variable efficacy.

Pityriasis Rubra Pilaris (PRP) is a group of uncommon chronic inflammatory skin conditions with unclear pathophysiology and aetiology,[1] characterised by palmoplantar keratoderma and varying degrees of erythematous keratotic papules tending to confluence, with islands of uninvolved skin, 'sparing'.[2] There are 6 subtypes described, known as Griffith's Classification.[3] The natural history is variable and the condition presents more frequently in patients of male sex and white race.[4]
There is limited published literature and no clinical guidelines for the management of PRP, though some have described various treatment options in case series.[5] Infliximab, alone or in combination, is the most published successful treatment for adults and etanercept for paediatric populations.[6] We present a case series of patients diagnosed with PRP.

Retrospective data were collected from St Vincent's Hospital Melbourne, Australia (SVHM) between January 2010 and December 2019 on patients with a diagnosis of PRP. Data were gathered through electronic medical and pathology records, private dermatologists and general practitioners, as well as the patient or family member. Patient demographics, PRP subtype, management, clinical response and duration of disease were determined. Management was further divided to separate topical, physical, systemic and biologic agents used.
Clinical response was defined as follows: marked improvement (75 - 100%), partial improvement (30 - 75%) or poor improvement (< 30%). These definitions were for direct comparison to a similar case series by Eastham et al.[5] Complete clearance was defined as no further clinical presentation of PRP. The geographic location of each patient was categorised into either 'metropolitan' or 'rural' determined by the Australian Government allocation of the patient's home postcode.[7]

Electronic medical record coding searched for 'Erythroderma' and 'Pityriasis Rubra Pilaris' collated a total of forty patients; ten of whom had a diagnosis of PRP. A further thirty-five cases were identified searching the SVHM pathology biopsy request forms for PRP. Eight cases had at least one biopsy with features supporting PRP. With the removal of patient duplications, a total of thirteen patients were included for this case series.
One patient had an unclear duration of disease, having deceased, with limited medical or family information available. Another patient was lost to follow up and a further patient was continuing treatment as of December 2019.
Patient demographic information, treatment agents, clinical response and clearance, as well as disease duration were recorded in Table 1.
Of the thirteen patients, 77% were male, mean age of 62 years at diagnosis and 54% resided in a rural location. Twelve patients had PRP type 1 with only one patient diagnosed with type 2. Ten patients were hospitalised for PRP management. No information on the weight of six patients could be found.
Twelve of the thirteen patients were prescribed topical agents, with nine using two or more. Eight patients used betamethasone dipropionate 0.05% ointment with a further two using betamethasone valerate 0.02%. Four patients used methylprednisolone aceponate 0.1% ointment and another four patients used mometasone furoate 0.1%. Three patients attempted narrow-band ultraviolet B (nbUVB) phototherapy therapy, without success.
All thirteen patients received acitretin as first line systemic agent with the dose varying from 10-50mg daily. Other systemic agents used were isotretinoin, prednisolone, methotrexate and ciclosporin. Four patients reported adverse events

from acitretin, which included blurred vision, hearing loss, tinnitus and hepatitis; resulting in dose reduction or cessation. A further two patients had unspecified side effects to acitretin. (Supplementary Information)

Of the nine patients who did not receive a biologic agent, six had a marked improvement to acitretin, two had a partial response and one had a poor response to treatment. Complete clearance of PRP was noted in five patients treated with acitretin, which was achieved between 3 months and 2.5 years.

Table 2 lists the four patients who received biologic agents. Infliximab, adalimumab, ustekinumab, secukinumab and tidrakizumab were used after failing to achieve an adequate response to acitretin and methotrexate. The duration of systemic therapy prior to a biologic agent ranged from 3 months to 48 months. Patients numbers 11 and 12 had a single biologic agent while patients numbers 10 and 13 received a second biologic agent. Patients 10 and 12 had a marked improvement; however only patient 12 experienced complete clearance. Disease duration varied between 16 months and 5 years. Patient number 11 developed polymyalgia rheumatica, potentially associated with adalimumab, resulting in cessation of treatment. Overall, six of the thirteen patients achieved completed clearance of PRP.

A previous case series by Eastham et al described the effectiveness of systemic and biologic agents for treatment of PRP in forty patients. The authors found no sex predominance, majority white race, with a mean age of 57 years for adults. Our case series had a predominantly male population (10 of 13 patients) with a mean age of 62 years. Seven of the thirteen patients lived in a rural location compared to patients residing in the city. This could be attributed to referral patterns or decreased dermatology services available outside of the city, though not statistically conclusive. Interestingly, the majority of our patients were hospitalised, potentially due to the department of dermatology having initial contact while the patient was already admitted to hospital, whereas Eastham et al only had six.

Our population were all treated with acitretin with doses ranging from 10-50mg/d and 66.6% achieving a marked improvement. Similarly, Eastham et al reported 62.5% achieved a marked improvement on acitretin (25-50mg/d). Our patients were prescribed similar non-biologic systemic agents as the published literature. Eastham et al, like our findings, had approximately two-thirds of patients achieving complete clearance and unsurprisingly the duration of disease ranged from months to multiple years. The unclear PRP pathophysiology and limited evidence based treatments potentially the cause of such discrepancy in duration.

Four patients received further biologic agents for managing PRP (Table 2). There were no identifiable predictors indicating a patient who required a biologic agent. Patterns of male sex, middle age and hospitalisation were noted, with differences in geographic location, adverse reactions, and systemic agent durations. Similar biologic agents were used to those in the Eastham et al case series, except for etanercept or alefacept. Eastham et al, did not highlight the reason for requiring a second biologic agent, with no further suggestion of disease clearance noted. Removing paediatric patients, Eastham et al had a marked improvement in two-thirds of their patients with the majority requiring maintenance therapy. Our study did not determine maintenance therapy requirements, only achievement of complete clearance, which took place in two of the four cases. Again, disease duration varied dramatically between months and years in both studies.

Limitations of this case series include a small sample size, retrospective nature of study, potential for spontaneous resolution, limited documented adverse events and

death or lost to follow up data challenges. It is also difficult to compare our findings accurately to Eastham et al due to the different sample sizes and change in biologics available.

Between 2010 and 2019, we report thirteen PRP patients from a tertiary dermatology department, all of whom were treated with systemic agents while four received additional biologic agents. Complete resolution was documented in six patients. PRP continues to be a challenging disease to treat with many treatment options used with variable efficacy. We recommend commencing acitretin prior to escalating to a biologic agent.

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Tables:

Table 1: Patient Demographics and Overview of Treatment Agents

Patient No/Sex	Age at onset[y]	Loc*	PRP type	Weight (kg) ^	Hosp	Topical Agent	Physical Therapy	Systemic Agent	Biologic Agent	Clinical Response	Complete Clearance	Disease Duration
1/M	75	M	1	N	Yes	1. Betamethasone valerate 0.02% 2. Methylprednisolone aceponate 0.1%	No	1. Acitretin 10mg/d	No	Marked	Yes	Unk, pt deceased
2/F	61	M	1	N	Yes	1. Betamethasone dipropionate 0.05% oint 2. Methylprednisolone aceponate 0.1%	No	1. Isotretinoin 10-25mg 2. Acitretin 20mg/d	No	Marked	Yes	3 months
3/M	76	R	1	76	Yes	1. Betamethasone dipropionate 0.05% oint 2. Hydrocortisone 1% to face	No	1. Acitretin 10-35mg/d	No	Partial	No	36 months
4/F	56	M	1	66	Yes	1. Betamethasone dipropionate 0.05% oint 2. Methylprednisolone aceponate 0.1% 3. Mometasone furoate 0.1%	No	1. Acitretin 25mg/d	No	Marked	Yes	22 months
5/M	70	R	1	N	Yes	1. Mometasone furoate 0.1% 2. Betamethasone dipropionate 0.05% oint 3. WSP 50% and LP 50%	No	1. Acitretin 25mg/d 2. Prednisolone 2.5-25mg/d	No	Partial	Unk	Unk
6/F	54	M	1	N	Yes	1. Betamethasone dipropionate 0.05% oint 2. Salicylic acid	nbUVB	1. Acitretin 25-35mg/d	No	Marked	Yes	30 months
7/M	57	R	1	80	No	1. Betamethasone dipropionate 0.05% oint	No	1. Acitretin 25-37.5mg/d	No	Marked	No	11 months
8/M	50	R	2	N	No	1. Mometasone furoate 0.1%	No	1. Acitretin 10-35mg/d	No	Poor	No	24 months
9/M	73	R	1	N	No	No	No	1. Acitretin 25mg/d	No	Marked	Yes	12 months
10/M	58	M	1	74	Yes	1. Betamethasone dipropionate 0.05% oint 2. Salicylic acid 10% with WSP 3. Clobetasol propionate for hands and feet 4. 15% lactic acid and 10% propylene glycol in AC	nbUVB	1. Acitretin 25-50mg/w or d 2. Methotrexate 10mg/w	1. Infliximab 400mg 2. Secukinumab 300mg	Marked	No	60 months
11/M	64	R	1	74	Yes	1. Betamethasone valerate 0.02% 2. Methylprednisolone aceponate 0.1% 3. Mometasone furoate 0.1%	nbUVB	1. Acitretin 10-50mg/d 2. Methotrexate 10mg/w	1. Adalimumab 40mg/bw	Partial	No	4 years
12/M	52	M	1	120	Yes	1. Betamethasone dipropionate 0.05% oint	No	1. Acitretin 25-50mg/d 2. Methotrexate 10-25mg/w	1. Ustekinumab 90mg/w	Marked	Yes	48 months
13/M	65	R	1	88	Yes	1. Betamethasone dipropionate 0.05% oint 2. 10% WSP, 10% glycerol, 10% LP in SC	No	1. Acitretin 10-35mg/d 2. Methotrexate 10-20mg/w 3. Ciclosporin 100mg/bd	1. Secukinumab 300mg/m 2. Tildrakizumab 200mg/w	Partial	No	6 months #

***Loc (Location):** Metropolitan [M], Rural [R] ^ Weight: N = No weight recorded # Treatment continuing as of December 2019

Abbreviations: Hosptalisation, Hosp; White Soft Paraffin, WSP; Liquid Paraffin, LP; Aqueous Cream, AC; Sorbolene Cream, SC; Narrow Band Ultraviolet B, nbUVB; Daily, d; Twice daily, bd; Weekly, w; Twice weekly, bw; Monthly, m; Unknown, Unk; Patient, pt; Treatment, Tx.

Table 2: Biologic Agents used for PRP Treatment

Patient No/Sex	Systemic Agent	Duration	Systemic duration prior to Biologic	Biologic Agent	Duration
10/M	1. Acitretin 25-50mg/w or d	25mg/d: 2014-2015 25mg/d and 50mg/d alternate days: 2015 25mg/d: Oct 2015 50mg/d then 25mg/d then 25mg bw: 2016	12 months	1. Infliximab 400mg/fn	4 months: Oct 2015
	2. Methotrexate 10mg/w	4 months: 2015		2. Secukinumab 300mg/m	11 months: 2016-2017
11/M	1. Acitretin 10-50mg/d	15 months: 2009-2010	48 months	1. Adalimumab 40mg/bw	14 months: 2012-2013
	2. Methotrexate 10mg/w	4 months: 2012			
12/M	1. Acitretin 25-50mg/d	25mg/d, 14 days: 2016 50mg/d, 3 months: 2016 then ceased Restarted 50mg/d, with MTX 2016-2017	3 months	1. Ustekinumab 90mg/12 weekly	18 months: 2017-2018
	2. Methotrexate 10-25mg/w	10mg/w, increased to 25mg/w, over 1 month: then reduced to 10mg/w with acetretin 50mg: 2016-2017			
13/M	1. Acitretin 10-35mg/d	25mg/d, 1 month 2018 35mg/d, 2 months 2018 10mg/d, with secukinumab	8 months	1. Secukinumab 300mg/m	4 months, 2018-2019
	2. Methotrexate 10-20mg/w	10mg/w, 2 weeks 2018 20mg/w, 4 months 2018 then ceased 10mg/w, with secukinumab 20mg/w, with tildrakizumab		2. Tildrakizumab 200mg/week 0,4	2 months, 2019
	3. Ciclosporin 100mg/bd	2 months, 2018			

Abbreviations: Methotrexate, MTX; Daily, d; Twice daily, bd; Weekly, w; Twice weekly, bw; Fortnightly,fn; Monthly, m; Unknown, unk;