



ORIGINAL RESEARCH

A comparative study of childhood psor asis and atopic dermatitis and greater understanding of the overlapping condition, psoriasis-dermaticis

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ABSTRACT

Background and Objectives: Psoriasis (Pso) in children may be confused clinically with atopic der matitis (AD) and, indeed, the two conditions may co-exist. The aim of this study was to determine historical and clinical features that are different in paediatric Pso and AD and to describe children who have features of both: psoriasis-dermatitis overlap (PD). **Methods:** Children with features of psoria eczema, or both, who were referred to paedia ric out patients and/or private rooms were evaluate. Data were collected from 170 consecutive chil as 1 less than 12 years between July 2011 ar 1 November 2011. Participants were classified by described criteria as having Pso (n = 64), AD (n = 62) U (n = 44). **Results:** Only 9.4% of children with Pso in recorrectly diagnosed by the referring do not Children with Pso relative to AD were more likel; have had a history of scaly scalp and na, w rash in infancy, a family history of psoriasis, current scalp and periauricular rashes, defined, patch, p. 1e morphology and papulosquamous rasheart, vical of adult psoriasis on extensor elbows and knees. Children with PD had features of bot ' but he sented most often as typical paediatric psorias's combined with flexural eczema. Children vun . and PD responded well to specific treatment 'rategies for psoriasis, including potent topica. steroids (TCS), calcipotriol

an into the rapy. Both Pso and PD tended to by ire more potent TCS than AD to achieve disease surpression.

Conclusion: We found that Pso and PD in children both differ clinically from AD and have identified historical and clinical features that characterise childhood Pso.

Key words: atopic dermatitis, childhood, diagnosis, paediatric, psoriasiform dermatitis, psoriasis.

INTRODUCTION

Psoriasis (Pso) is a clinical diagnosis based on history and morphology. Unlike atopic dermatitis (AD), no accepted diagnostic criteria have been established. In the paediatric population, it is the authors' experience that Pso is commonly confused with AD. This led us to identify a need to determine their differentiating features.

We considered this important because of implications for treatment, prognosis and advice to the family. While both AD and Pso are chronic skin diseases and often share a parallel treatment regime in the acute flare stages, maintenance therapy for the two conditions differs, with phototherapy and classical Pso treatment modalities such as calcipotriol and tar-containing preparations being useful in Pso in children.² Additionally, the prognosis of AD is good and it is possible to reassure parents that most children, particularly those with mild to moderate disease, will recover spontaneously. However the prognosis for childhood Pso must be more guarded as there are no long-term follow up studies.

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Abbreviations:

AD atopic dermatitis
PD psoriasis-dermatitis overlap
Pso psoriasis
TCS topical corticosteroids

While differences in adult and childhood Pso are described in the literature, there is little information about how to differentiate childhood Pso from AD in children. Beyond this, it has be estimated that approximately 5% of paediatric patients show an overlap of both eczema and psoriasis⁵ and greater understanding of this condition is required.⁴

The aims of this study were to identify the diagnostic features of Pso in childhood that enable the disease to be differentiated from AD, and to investigate the nature of the intermediate or overlap condition, psoriasis-dermatitis (PD).

MATERIALS AND METHODS

A prospective comparative observational study was performed, in which historical and morphological data were collected from 170 consecutive patients aged less than 12 years presenting to a paediatric dermatology clinic in a tertiary referral centre or the private dermatology rooms of one of the authors between July 2011 and November 2011. All patients during this period gave their informed consented study was approved by the Human Research Ethics Committee of the Northern Sydney Central Coast A1 a Health Service.

All patients in the study were referred for the diagnons and management of acute, chronic or subacute papulosquamous rashes. The presence, or absence, of disease conteristics was noted for each patient. Each point was classified as Pso (n = 64), AD (n = 62) or PD (n = 14), as described below. Disease severity was classified a visual analogue scale.

A literature review was performed us. the search engines including Medline, PubMed and hogle under search teams, 'childhood psoriasis', 'aediatric psoriasis', 'psoriasis', 'childhood' and 'paediatric'.

The results of this literature review have been tabulated to demonstrate the main features of Pso described in the current literature (Table 1). Bas are this, it is seen that well-demarcated psoriatic plaque, guidate disease, nail pits, acral fingertip eruptions napediate of and pustular Pso were used most commonly when diagnosing Pso in the paediatric population. Although the current literature and were not mought reliable enough to diagnose patients with Ps. As no definitive criteria exist, the presence of at leas one of these features was chosen to classify a patient in the Pso group.

The UK Working Diagnostic Group for the diagnosis of AD was used for the diagnosis of patients in the AD group, whereby patients must have an itchy skin eruption or parental report of scratching or rubbing in a child in conjunction with three of the following: a history of flexural involvement, a personal history of atopy in a child under 10 years of age or in their relative or parent, a history of generalised dry skin in the last year or visual flexural eczema and onset in a child under the age of 2 years (Table 2). Excoriated skin seen on examination was used to confirm parental reports of scratching by the child.

 Table 1
 Summary of childhood psoriasis literature review

| | Well | | Palmar | | | | | | | |
|--|------------|---------|---------|-----------|-----------|-----------|---------|--------------|--------------|------------|
| | demarcated | Guttate | plantar | | Napkin | Pustular | Family | epto, cca1 | . soriatic | Koebner |
| | plaques | disease | disease | Nail pits | psoriasis | psoriasis | history | prec oits it | e ythroderma | phenomenon |
| Altobelli <i>et al.</i> (2007); 1420 patients ⁵ | X | X | X | X | X | X | X | | | |
| Morris <i>et al.</i> (2001); 1262 patients ⁴ | X | X | X | X | X | X | X | | | |
| Kumar et al. (2004); 419 patients ⁶ | X | X | X | X | | X | | | X | |
| Lewkowicz and Gottlieb (2004); Review ² | X | X | | X | | X | | | X | |
| Rogers (2001); Review ⁷ | X | X | X | X | X | X | X | X | | |
| Burden (1999); Review ⁸ | X | X | X | | X | X | | | | |
| Hogan <i>et al.</i> (2011); Textbook ⁹ | X | X | | X | X | | | | | |
| De Waard-van der Spek et al. (2006); Textbook ¹⁰ | X | X | | X | X | X | | | X | |
| Cohen (2005); Textbook ¹¹ | X | X | X | X | X | | X | | | X |
| Patel et al. (2009); Textbook ⁵ | X | X | | X | X | X | | X | | |
| Holm and Helm (2004); Textbook ¹² | X | X | | | X | X | | X | | X |
| Patrizi et al. (1999); 5 patients ¹⁵ | X | | X | X | | | | | | |
| Dogra and Handa (2004); 1 patient ¹⁴ | X | | | X | | X | | | | |
| Wardrop et al. (1998); 1 patient ¹⁵ | | | | | | | | X | | |
| | | | | | | | | | | |

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Table 2 The UK Working Group to establish diagnostic criteria for the diagnosis of $\mathrm{AD^{16}}$

Atopic eczema should be diagnosed when a child has an itchy skin condition plus three or more of the following:

- visible flexural dermatitis involving the skin creases, such as the bends of the elbows or behind the knees (or visible dermatitis on the cheeks and/or extensor areas in children aged 18 months or under)
- a personal history of flexural dermatitis (or dermatitis on the cheeks and/or extensor areas in children aged 18 months or under)
- 3. a personal history of dry skin in the last year
- a personal history of asthma or allergic rhinitis (or history of atopic disease in a first-degree relative of children aged under 4 years of age)
- 5. onset of signs and symptoms under the age of 2 years (this criterion should not be used in children aged under 4 years)

Patients with features of both groups, classified by displaying features consistent with each group, were considered to be in keeping with PD and thus were removed f. m. Pso and AD groups, respectively. These data were entered in an Excel 2007 database (Microsoft, Redmond, Washing on USA).

Statistical methods

Data were analysed using descriptive statistics of the valuables studied. Statistical analysis was calculated with SPSS statistical software (ver. 16.0; SPSS 2010 IBM, where, NY, USA). Significant differences between the Lso, Ab and PD groups were calculated using χ^2 and wish who considered significant.

RESULTS

Participants were classified by the desc. bed criteria as having Pso (n = 64), AD (n = 62) PI (n = 44). The results are summarised in Table 3.

In the Pso group, there were 2000 and 41 girls while in the AD group there were 37. The system and 25 girls. This is a significant difference in the properties of girls with child-hood Pso in comparisor with "D, which is in keeping with the current literature. The makes age of onset of disease was 2.7 years in the Psogroup, 0.6 years for AD and 1.18 years for PD, which is in the Psogroup, 0.6 years for AD and 1.18 years in the Psogroup, 1.6 years for AD and 2.19 years for PD. There were significantly more severe and more sub-acute AD patients in our cohort compared to severe and sub-acute Pso patients, respectively (P = 0.05, P = 0.01).

Comparing Pso and AD, there were statistically more patients with a scaly scalp, history of nappy rash, a family history of Pso and the requirement for potent topical corticosteroids (TCS) to achieve objective disease suppression in the Pso group than in the AD group (P = 0.002, P = 0.0001, P = 0.0001, P = 0.003). Itch, itch worse at night, a family history of atopy and the requirement of only moderate steroids for response to treatment (P = 0.003, P = 0.0001,

P = 0.0005, P = 0.004, respectively) was more prevalent in AD than Pso. Steroid classification was based upon guidelines from Therapeutic Guidelines Australia.¹⁷

When comparing P(J and PD, itch-disturbing sleep, a family history of Ps a family history of atopy, well-demarcated pink planes, attate psoriasis, the presence of genital rash, disease at a resal hands and ankles, disease periorbitally, perior that a face occurred at significantly different rates between these groups (P = 0.001, P = 0.007, P = 0.0001, P = 0.007, P = 0.001, P = 0.001, P = 0.003, P = 0.01, respectively) This inflects 10 of 28 clinical end-points for which patients with 2D differ from those with Pso.

When ome ling AD and PD, scaly scalp, nappy rash, a prior diagnosis of AD, a family history of Pso, a family history of AD, a family history of Pso, a family history of AD, a family history of Pso, a family history of AD, a family history of Pso, and soles, perioral ase and the presence of post-auricular disease occur edit statistically significant different rates between less approximately likely approximately P = 0.0001, P = 0.05, P = 0.0001, P = 0

In terms of treatment response we found that 81.3% of 150, 95.2% of AD and 95.2% of PD had remitted with the nitial prescribed treatment at 4–6 weeks follow up. In the Pso and PD groups, this included the use of betamethasone dipropionate 0.05% plus calcipotriol 0.5% (Daivobet, Leo Pharma, Brisbane, Queensland, Australia), topical liquor picis carbonis, in 2% aqueous cream for the face or 4% for the body) and narrow band UVB phototherapy. In the AD group potent TCS were used only for initial management and flares, with moderate to mild TCS used for maintenance with moisturisers and environmental modification.

DISCUSSION

Unlike Pso, diagnostic criteria for AD have been established^{16,18} (Table 2) The diagnosis of Pso is clinical and depends on typical morphology and distribution, coupled with family history and supported by a biopsy. The latter is rarely practical in children.

In adults the clinical diagnosis of Pso is usually straightforward; however the morphology of childhood Pso has previously been recorded to differ from adults and may resemble atopic dermatitis or discoid eczema, as plaques in children are thinner, lack white scale and are less well defined.⁴ (Fig. 1) In our study Pso was more patchy and well defined than in AD, spared the flexures and genital or nappy area, was more likely to involve the scalp and periauricular skin and less likely to be associated with xerosis and significant itch and it is also less likely to be generalised. (Fig. 2)

It appears from our data that Pso is difficult for non-dermatologists to identify. In our series, only six children with Pso (9.4%) were referred with the correct diagnosis, while 51 (79.9%) of patients with Pso were referred with a diagnosis of AD. The establishment of features that support a diagnosis of childhood Pso may reduce misdiagnosis in the paediatric population and enable clinicians to institute

Table 3 Summary of details

| | Psoriasis | Atopic dermatitis | | P | P | P |
|---|------------------------|------------------------|-----------------------|--------------|----------------|----------------|
| | (Pso) (%) | (AD) (%) | PD (%) | 7,00 | Pso & PD | AD & PE |
| General | | | | | | |
| Total | 64 (37.6) | 62 (36.4) | 44 (25.9) | | | |
| Sex | | | | | | |
| Male | 23 (35.9) | 37 (59.7) | 19 (45.2) | 0.01 | 0.55 | 0.12 |
| Female | 41 (64.1) | 25 (40.3) | 25 (56.8) | 0.01 | 0.55 | 0.12 |
| Age at onset (average) | 2.7 years | 0.6 years | 1.18 years | 0.52 | 0.004 | 0.03 |
| Age at diagnosis (average) | 5.6 years | 1.6 years | 2.19 years | 0.60 | 0.02 | 0.14 |
| Degree | 24 (72.9) | 45 (24.2) | 0 (46) | 0.77 | 0.40 | 0.40 |
| mild moderate | 21 (52.8) 18 (28.1) | 15 (24.2) 15 (24.2) | 8 (18 ') 19 (43.2, | 0.53 0.69 | $0.12 \\ 0.14$ | $0.49 \\ 0.06$ |
| severe | 2 (3.1) | 15 (24.2) | 7 (15.9) | 0.09 | 0.14 | 0.00 |
| Nature | 2 (3.1) | 15 (24.2) | (13.9) | 0.001 | 0.05 | 0.54 |
| acute | 14 (21.9) | 19 (30.6) | 40 (22.7) | 0.31 | 0.46 | 0.39 |
| chronic | 22 (34.4) | 13 (21.0) | 24 (5) | 0.86 | 0.05 | 0.004 |
| sub-acute | 6 (9.4) | 17 (27.4) | 3 (6.8 | 0.01 | 0.74 | 0.01 |
| History | () | , | | | | |
| Scaly scalp in first year of life | 43 (67.2) | 24 (38.7) | J5 (79.5) | 0.002 | 0.19 | 0.0001 |
| Nappy rash | 40 (62.5) | 8 (12.9) | 26 59.1) | 0.0001 | 0.84 | 0.0001 |
| Itch | 47 (73.4) | 58 (93.5) | 37 (84.1) | 0.003 | 0.24 | 0.19 |
| Itch-disturbing sleep | 29 (45.3) | 51 (82.3) | o4 (7.5) | 0.0001 | 0.001 | 0.62 |
| Prior diagnosis of psoriasis | 6 (9.4) | 5 (8.1) | 7 (15.9) | 1.00 | 0.37 | 0.23 |
| Prior diagnosis of atopic dermatitis | 51 (79.7) | 54 (87.1) | 31 (70.5) | 0.34 | 0.36 | 0.05 |
| Steroid requirement | | | | | | |
| Mild | 2 (3.1) | 7 (11.3) | 3 (6.8) | 0.09 | 0.40 | 0.52 |
| Moderate | 12 (18.8) | 27 (43.5 | 11 (25.0) | 0.004 | 0.48 | 0.06 |
| Potent | 39 (60.9) | 25 (40. | 27 (61.4) | 0.03 | 1.00 | 0.05 |
| Family history of psoriasis | 42 (65.6) | 10 (16.1, | 17 (38.6) | 0.0001 | 0.007 | 0.01 |
| Family history of atopy | 29 (45.5) | 47 (75.8) | 42 (95.5) | 0.0005 | 0.0001 | 0.007 |
| Personal/family history of | 40 (20 4) | 25 (4() | 27 (72.7) | 0.40 | 0.02 | 0.24 |
| asthma | 18 (28.1) | 25 (4(3) | 25 (52.5) | 0.19 | 0.02 | 0.24 |
| eczema bay foyon | 12 (18.8) | 9 (1 | 26 (59.1) | 0.03 | 0.0001 | $0.05 \\ 0.14$ |
| hay fever Atopic dermatitis: accepted features | 5 (7.8) | 9 (1 | 12 (27.1) | 0.27 | 0.01 | 0.14 |
| Generalised dry skin | 13 (20.3, | (80.6) | 41 (93.2) | 0.0001 | 0.0001 | 0.09 |
| Visible flexural eczema | 7 (10.9) | 51 (2.3) | 37 (84.1) | 0.0001 | 0.0001 | 1.00 |
| History of flexural eczema | 3 (4.7) | (66.1) | 14 (14.0) | 0.0001 | 0.0001 | 0.0007 |
| Diffuse non-localised disease | 6 (9.4) | 34 (54.8) | 32 (72.7) | 0.0001 | 0.0001 | 0.07 |
| Excoriated | 1 (3) | ^3 (41.9) | 12 (27.3) | 0.0001 | 0.0001 | 0.15 |
| Psoriasis: accepted features | , | (1213) | () | | | |
| Well demarcated plaques | 51 (70.7) | | 41 (93.2) | | 0.06 | |
| Colour of plaque | | | ` / | | | |
| Red | 30 () | | 13 (29.5) | | 0.08 | |
| Pink | 19 (29.7) | | 27 (61.4) | | 0.002 | |
| Skin | 1 (1.6) | | 5 (6.8) | | 0.30 | |
| Colour of scale | | | | | | |
| White | 5 7.8) | | 4 (9.1) | | 1.00 | |
| Gray | 15 (5) | | 4 (9.1) | | 0.18 | |
| Nil | ? (3.1) | | 5 (11.4) | | 0.12 | |
| Guttate | (25.4) | | 4 (9.1) | | 0.03 | |
| Acral fingertips | 6 (9.4) | | 9 (20.5) | | 0.16 | |
| nail pits | 17 (26.6) | | 15 (34.1) | | 0.52 | |
| Napkin psoriasis Pustular psoriasis | 16 (25.0) 0 (0.0) | | 11 (25.0) 1 (2.5) | | 1.00 0.41 | |
| Genital rash | 13 (20.5) | 7 (11.3) | 1 (2.3) | 0.22 | 0.007 | 0.14 |
| Degree of scalp scale | 15 (20.5) | 7 (11.5) | 1 (2.5) | 0.22 | 0.007 | 0.17 |
| 0 | 36 (56.3) | 49 (79.0) | 24 (57.1) | 0.008 | 1.00 | 0.01 |
| 1 | 15 (23.4) | 11 (17.7) | 13 (29.5) | 0.51 | 0.51 | 0.17 |
| 2 | 10 (15.6) | 2 (5.2) | 7 (15.9) | 0.03 | 1.00 | 0.03 |
| 3 | 2 (3.1) | 0 (0.0) | 0 (0.0) | 0.50 | 0.51 | 1.00 |
| Other features identified | ` ' | ` / | ` / | | | |
| Dorsal elbows/knees rashes | 30 (46.9) | 9 (14.5) | 29 (65.9) | 0.0001 | 0.08 | 0.0001 |
| Dorsal hands/ankles rashes | 10 (15.9) | 6 (9.7) | 23 (52.3) | 0.42 | 0.0001 | 0.0001 |
| Umbilicus involved | 7 (10.9) | 5 (8.1) | 8 (18.2) | 0.76 | 0.40 | 0.14 |
| Palms and soles rash | 7 (10.9) | 2 (5.2) | 8 (18.2) | 0.16 | 0.40 | 0.02 |
| Eye lid involvement | 13 (20.3) | 20 (52.5) | 20 (45.5) | 0.15 | 0.01 | 0.22 |
| Lip dryness, fissuring and perleche | 13 (20.3) | 8 (12.9) | 21 (47.7) | 0.34 | 0.003 | 0.0001 |
| Ear involvement | 28 (43.8) | 14 (22.6) | 20 (45.5) | 0.01 | 1.00 | 0.02 |
| Face involvement | 25 (39.1) | 44 (71.0) | 29 (65.9) | 0.0004 | 0.01 | 0.67 |

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Figure 1 Psoriatic plaque in a child is thinner, paler and less we defined than in an adult and may resemble discoid eczema.

specific treatment. In our cohort, 81.3% of Pso, 95.2% of AD and 93.2% of PD remitted with the initial prescribed treatment at 4–6 weeks follow up. As expected, Pso was the most difficult of the three conditions to manage.

Moreover, we foul that many children who were referred with a dismostant of AD and who had failed to respond to mild or noder to topical corticosteroids, in fact, had Pso or PD and absendently improved with treatment with potent TCS combined with topical calcipotriol, tars and phototherapy and control that the proportion of patients requires strong corticosteroid therapy was significantly bight in the Pso group than in the AD group while moterally strong corticosteroids were sufficient in more AD patient, than Pso patients.

Tre tme is resistance may explain the relatively high prevalence of patients with Pso in our cohort, which is well ably to hat expected for the normal population. Pso represence 37. '% of all papulosquamous diseases presenting at our paratric dermatology referral clinic and practice. Moreover, as can be seen by the proportion of misdiagnoses in the so group, patient referrals are typically the clinically conflicted in primary care settings is less often a pierred to a specialist paediatric dermatology centre. This is also evidenced by a significantly higher rate of the clinically challenging severe AD (24.2%) and sub-acute AD (27.4%), when compared to equivalent categories in the Pso group.

It is difficult to obtain an accurate age of disease onset for childhood Pso and AD from parents because the question is



Figure 2 This child with typical guttate psoriasis also demonstrates periauricular rash but does not have xerosis and was only mildly itchy.

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Figure 5 Severe scalp scale in this baby was associated wi^t a family history of psoriasis in the child's mother.

usually asked retrospectively (as was the case in this riudy) and may be subject to recall bias. The problem is compounded when there is more than one cosease process involved, such as for the PD cases that the results in the preschool-age population. In our study where was no significant difference between the age of opened and the age of diagnosis among the Pso, AD and AD groups and this may be reflected by the relatively large standard deviation around the means (AD 1.05 and 1.75 and Fro 3.15 and 3.44, respectively). The results may some that AD begins at a younger age than Pso and presents partier for medical consultation. It is also possible that AD y occur early and be supplanted by Pso later.

The risk of developing by a "" and AD are increased in first-degree relatives of ration," however neither of the conditions has been show to row w an obvious Mendelian patterns of inheritance. 19 close genetic link between the conditions is apparent trow alkage studies that have identified numerous compositions are susceptibility loci (chromosome 1q21, 3q21, 17q25 and 2op) for AD and Pso. 20 Common genetic factors may be involved in the immunopathophysiology of both conditions, which feature a similar inflammatory cytokine pathway and the predominance of T-cell infiltrates in the dermis. 19

Historical features demonstrated that scaly scalp (Fig. 3) and nappy rash (Fig. 4) in the first year of life occurred more commonly in the Pso group than the AD group, while itch and itch-disturbing sleep were more common in the AD than Pso group. This could be used to differentiate Pso and AD.



Fig. w 4 7 pical psoriatic nappy rash.



Figure 5 Typical genital psoriasis.

Clinical features diagnostic of AD, including generalised dry skin, visible flexural eczema and history of flexural eczema, were all significantly more prevalent in the AD group than the Pso and PD groups as these end-points were criteria used for defining the AD group. Excoriations were also significantly more frequent in the AD group than in Pso and PD, in keeping with historical itch factors and the diffuse, non-localised disease.

Patients diagnosed with AD who had any of the Pso diagnostic symptoms were reclassified as PD and thus analysis of prevalence of the Pso diagnostic symptoms in the AD group is not possible. There were no cases of Pso with signs of pustular psoriasis however this rare presentation was missed by the small cohort. Genital rash was more common in Pso than PD group (Fig. 5)

Having defined the diagnostic groups, further clinical end-points were examined. It was seen that the presence of a papulosquamous rash (as opposed to typical psoriatic plaques which are uncommon in the paediatric population) over the dorsal knees and elbows, or both (Fig. 6) and

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rare 6 Papular and papulosquamous rashes were commonly found in children with classic signs of childhood psoriasis on other parts of the body.



Figure 7 Well-defined facial plaques on this ba. y with a very well demarcated extensor plaque on the thow and a family history of psoriasis.

post-auricular and infra validation are rash and splitting occurred more commor win the Pso group than in the AD. These could also be used as acquarcts to clinical diagnosis and should be looked for in making a diagnosis of Pso. Moreover, facial involvement was more prevalent in our AD group than the Postago in the Postago involvement is relatively common in children with Pso. Further, we noted that the clinical appearance in the Pso group differed from AD in that it presented as defined plaques rather than diffuse facial involvement. (Fig. 7)

With 10 of 28 (35.7%) clinical end-points statistically different from Pso group versus 10 of 16 (62.5%) for AD, PD patients generally appear to have more in common with patients with Pso than those with AD. These patients most often presented as typical childhood Pso with the addition of typical itchy flexural AD and a family history of atopy as well

as psortions. The most significant of their features was their response to the strong treatment than AD patients, suggestive of the restment requirements of PD in comparison to AD. The ist the in the literature on the condition PD and turther studies are required.

CONCLUSION

o and PD in children both differ clinically and historically fom typical adult Pso and from childhood AD and children with the overlap condition PD appear to be closer clinically to patients with Pso in terms of clinical features and treatment requirements. Both Pso and PD respond well to the addition of tar, calcipotriol and phototherapy.

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