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Uveitis and Juvenile Psoriatic Arthritis or Psoriasis

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Abstract

Purpose—To describe the phenotype of the uveitis that accompanies juvenile psoriatic arthritis or psoriasis.

Design—Observational case series

Methods—Setting: Two university based referral clinics, one in England, one in the US

Study population—Five children with uveitis and psoriatic arthritis and one with uveitis and psoriasis

Observational procedure—Retrospective chart review

Main outcome measures—Demographics of subjects such as age and sex; description of ocular and joint disease; surgical and other complications; medical treatment

Results—Five of the six children in this series had the onset of disease at or before age 6 ($p=0.0008$ compared to expected age of onset for psoriatic arthritis in childhood). All children in this series had an inadequate response to topical corticosteroids. Most of the children were treated with systemic corticosteroids for many months, yet all of them went on to require methotrexate. Therapy with systemic methotrexate did not suffice as all the patients also required some form of biologic therapy. Five of six had surgeries such as vitrectomy, cataract extraction, or a procedure for glaucoma control.

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Conclusions—The observations suggest that the uveitis that accompanies juvenile psoriatic arthritis might be a distinct disease which is particularly severe when its onset affects children age six or younger.

INTRODUCTION

Psoriatic arthritis is known to be associated with uveitis. For example, in 1976 Lambert and Wright characterized eye disease among 112 patients with psoriatic arthritis and reported that 7.1% had a history of iritis.¹ A small Norwegian study found that 19% of 31 patients with psoriatic arthritis had uveitis.² A Brazilian study observed that 7.9% of 63 patients with psoriatic arthritis had uveitis³ and a study from Spain reported that 18% or 13 of 71 patients with psoriatic arthritis had uveitis.⁴ Niccoli and colleagues reported on a series of 242 patients with psoriatic arthritis and found that 9% had a history of iridocyclitis.⁵ Psoriatic arthritis has subsets that are distinguished by which joints are involved. In the total series by Niccoli et al., 45% had either axial disease or axial and peripheral disease, while 50% of the patients with uveitis fell into one of these categories.⁵

Several studies have attempted to characterize the uveitis among patients with psoriatic arthritis. For example, our own investigation of 16 patients with uveitis and psoriatic arthritis found that an insidious onset of the uveitis, chronic course, and bilateral eye disease were more common in association with psoriatic arthritis compared to the typical HLA B27-associated uveitis noted in patients with ankylosing spondylitis.⁶ Half of the patients in this series had axial arthritis and 6 of 9 who were HLA B27 typed were positive.⁶ The previously cited Spanish study also noted that bilateral uveitis (39%) and an insidious onset (31%) could be present in association with psoriatic arthritis.⁴ On the other hand, a Japanese study of 13 adults with uveitis and psoriatic arthritis found that all but one had acute anterior uveitis.⁷

Less is known about juvenile onset psoriatic arthritis and the uveitis that may accompany this diagnosis. In a study of 49 children with chronic uveitis, Cabral and colleagues noted that 13% had psoriatic arthritis.⁸ Stoll and colleagues⁹ characterized 139 children with juvenile psoriatic arthritis and astutely divided the children into two groups: those with an early age of onset (before age 5) and those who presented at an older age (after age 5). Uveitis was present in 7.9% of the children in either group.⁹ Twice as many children fell into the older age group as the younger age group. The CARRA (Childhood Arthritis and Rheumatic Disease Research Alliance) recently characterized the joint disease among 361 children with psoriatic arthritis.¹⁰ Eighty-two patients had an early onset with an average age of 3.1 years, while 260 patients had a later age of onset with an average of 11.25 years. Uveitis was noted in 18.8% of children with the early age group and 8.8% of children in the older age group ($p=0.015$).

The uveitis associated with childhood psoriatic arthritis has not been previously characterized to our knowledge. We pooled the experiences of two major referral centers, one in Bristol, England, and one in Portland, Oregon, USA to begin to characterize the uveitis in association with juvenile psoriatic arthritis. Although our series is small, our findings suggest that children with psoriasis or psoriatic arthritis that begins by age 6 or

younger can suffer from a bilateral, chronic, anterior and/or intermediate uveitis that is particularly severe such that biologic therapy was prescribed for all patients in this series.

METHODS

This is an observational case series of six patients who received care at one of two centers. Chart review was conducted on two patients at the Casey Eye Institute (CEI) at Oregon Health & Science University who presented to the uveitis service with severe anterior or anterior and intermediate uveitis associated with a severe psoriatic rash, and four patients who were seen at the Bristol Eye Hospital. Laboratory investigations for these patients were noted, along with medical and surgical therapies. The respective institutional review boards approved the review of patient material for this report. Statistical comparison is based on the chi square test.

RESULTS

Our series consisted of 4 males and 2 females. The mean age of presentation was 5.7 years, with a range from 2 to 12 years. According to the data from the CARRA study, 76% of children with psoriasis have a late onset around age 11¹⁰, while 83% of the patients with psoriasis and uveitis had an early onset. This difference is statistically significant by chi square testing ($p=0.0008$). This p value should be interpreted cautiously because our definition of early onset is on or before age 6, while the CARRA study used on or before age four.¹⁰ Of the 6 patients, 4 had joint swelling on initial presentation, with one other patient developing joint swelling later in the course of his disease. Joint pain was pauci-articular in all patients. The demographics, joint, and skin disease is described in the Table 1. The one patient without objective joint disease had arthralgias and myalgias.

Skin symptoms (Table 1) were present at initial examination for all of the patients. Four of the six patients presented with a generalized skin rash. Another patient had skin symptoms limited to a plaque-like rash along his left arm, plaques over his scalp, and nail pitting. The last patient had involvement limited to nails only – the right thumb, left index finger, and right great toe.

Uveitis (see Table 1) was initially present in 4 of our 6 patients. In each of the remaining 2 patients, uveitis did not present until 2 years after the initial systemic symptoms. The uveitis was bilateral in 4 of 6 patients, and limited to the right eye in the other 2 patients. Three of the patients had anterior uveitis only, while the remainder also had intermediate uveitis. One of the patients was HLA-B27 positive. Two patients were positive for anti-nuclear antibody (ANA). Presenting visual acuity at the referral center for the 6 patients in involved eyes ranged from 20/20 to 20/200. Of the ten affected eyes, 50% had initial acuity of 20/40 or better and 5 eyes were 20/100 or worse with one of these eyes affected by amblyopia. Medical and surgical treatments are listed in Table 2. Additional details on the medical treatment are provided in Table 3. Initial treatment for the ocular inflammation consisted of frequent topical corticosteroids (usually hourly or every two hours to the affected eye), with inadequate response and persistent inflammation in all patients. Five of the patients were treated with sustained oral prednisone; three received intravenous methyl prednisolone (one

at 1000 mg daily for 3 days; one at 10 mg/kg daily for 3 days for 3 separate courses; one who had two iv courses of methylprednisolone but this was given prior to referral and the dosage could not be ascertained). Another did not receive systemic corticosteroids except around the time of surgical procedures. Only one patient was maintained indefinitely on oral corticosteroids, which was a dose of 5 mg/day of prednisolone. Two of the patients developed both cataract and glaucoma, and required bilateral cataract extraction with anterior vitrectomy, intra-ocular lens placement, and glaucoma surgery, with one of the patients undergoing bilateral trabeculectomy and the other patient undergoing placement of a bilateral Ahmed drainage implant. The patient who underwent trabeculectomy required bleb needling after scarring had occurred. Two additional patients required cataract surgery alone. In total 7 of ten affected eyes required cataract surgery. In addition cataract surgery is planned for the right eye of patient four and patient six has a visually significant cataract but has not had surgery. As shown in Table 2, band keratopathy was present in 4 patients in 5 of ten affected eyes. Two eyes had an epiretinal membrane suspected on clinical examination but not confirmed by OCT. Macular edema was detected by OCT in two of ten affected eyes.

All of the patients were started on methotrexate for control of eye and systemic disease, with 5 of them receiving subcutaneous administration and another receiving only oral therapy. Four of the patients remained on methotrexate for the remaining duration of follow-up, with the exception of one patient for whom methotrexate was discontinued after two years due to nausea and poor tolerance and one who stopped after one year due to lack of efficacy. None of the patients had complete resolution of eye or systemic disease with methotrexate; hence, addition of a biologic was required.

Three of the patients were initially started on infliximab after incomplete response to methotrexate. All three patients were switched to adalimumab after 3 to 4 years. One of these 3 patients was subsequently switched from adalimumab to ustekinumab after 5 years, with a good response to the latter therapy, although topical corticosteroids continued to be needed to control flares. Another patient who had switched from infliximab to adalimumab is planning a switch to ustekinumab due to inadequate control of eye and skin disease on adalimumab. The remaining 3 patients were started on adalimumab as the initial biologic. Two of these patients had a sustained response and were maintained on this therapy with successful control of eye, skin and joint disease. One of the patients who was initially started on adalimumab was switched after five years to infliximab due to recurrent flare-up of anterior and intermediate uveitis, as well as ankle and knee joint symptoms. This change was insufficient, and the patient was switched to treatment with tocilizumab, an IL-6 receptor antagonist. There was persistent inflammation in the right eye, which required additional treatment with an intravitreal dexamethasone implant (Ozurdex) followed by intravitreal fluocinolone (Iluvien).

The average follow-up was the six patients in this series was 8 years and 8 months with a range from 4 years and 3 months to 11 years and 11 months (Table 1). Final recorded Snellen best-corrected visual acuity in affected eyes ranged from 20/15 to hand motion. Six of ten affected eyes had an acuity of 20/40 or better and 8 of ten were 20/50 or better.

DISCUSSION

We have characterized the uveitis in 6 children with psoriasis or psoriatic arthritis who were managed either in Oregon or in England. Five of the six children developed eye, skin and/or joint disease that began at age 6 or earlier. Most had bilateral eye disease that was vision threatening and often had complications such as glaucoma. All required biologic therapy. Ophthalmic surgery in these children was frequent. One of our patients was HLA B27 positive. All of the patients except one had objective joint disease, five with pauci-articular, asymmetric disease. We included the patient without joint disease in this series because psoriasis is less common in childhood than in adults, and it is especially uncommon in males at a very young age¹¹. Furthermore, the behavior of his eye disease fits well with the others reported in this series and he did experience arthralgias, although the consulting pediatric rheumatologist did not find objective evidence for joint swelling. Since both centers are referral centers, patients with more severe eye and joint disease tend to be seen. Thus, we cannot absolutely confirm the observation from the recent CARRA study that uveitis is more common in children with psoriatic arthritis and an early age of onset. However, our data strongly suggest that children with early onset arthritis and psoriasis are at risk for a severe form of uveitis. We conclude this because the CARRA study shows that psoriatic arthritis is more than 3 times as common in the older age group, while 5 of our 6 children in this series of children with psoriasis, arthritis, and uveitis had disease that began at age 6 or younger.

Our characterization of uveitis in association with psoriatic arthritis in children reveals distinctions from the uveitis noted in adults with psoriatic arthritis. None of the children in this series had axial joint disease, for example. And none of them had unilateral, acute anterior uveitis as is characteristic of HLA B27-associated disease and is also seen in a subset of adults with psoriatic arthritis⁶. Our observations support the hypothesis that juvenile psoriatic arthritis has at least two distinct subsets, one with an onset at age 6 or before and one with an age of onset around age 11. The small size of our series is such that our conclusions should be validated by observations from other centers. We suggest, however, that distinct subsets of disease should correlate with unique aspects of pathogenesis and ultimately with therapy tailored to this pathogenesis.

The differential diagnosis of arthritis associated with psoriasis is extensive. It includes ankylosing spondylitis, reactive arthritis, inflammatory bowel disease, Behcet's disease, pauci-articular early onset juvenile idiopathic arthritis, Kawasaki's disease, sarcoidosis, Blau syndrome, systemic lupus erythematosus, Sweet's syndrome, and even infections such as Lyme Disease or Whipple's Disease. Our observations suggest that early onset juvenile psoriatic arthritis should be added to this list as an entity which is distinct from other forms of psoriatic arthritis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

The uveitis that accompanies juvenile psoriatic arthritis beginning at or before age 6 might be a distinct and severe syndrome.

Table 1

Demographics and Characterization of Eye, Skin, and Joint Disease

Patient	Age at presentation (years)	Gender	Age of presentation of arthritis (years)	Onset	Joint involvement	Skin disease	Age of diagnosis of uveitis (years)	Location of uveitis	Laterality of uveitis	HLA B27	ANA	Initial visual acuity at dx of uveitis (OD, OS)*	Final visual acuity (OD, OS) (duration of follow-up)
1	3	M	7	Sudden	Dactylitis, left fourth toe	Plaque-like rash along left arm and scalp, nail pitting	3	Anterior	OU	Neg	Neg	20/20, 20/20	20/30, 20/40 (5 years 7 months)
2	6	M	8	Sudden	Arthralgias	Diffuse psoriatic rash with nail involvement	6	Anterior and intermediate	OU	Neg	Neg	20/100, 20/20	20/20, 20/15 (5 years, 8 months)
3	5	M	5	Insidious	Left ankle	Nail changes thumb right hand, index finger left hand and First digit right foot	5	Anterior	OD	Neg	Neg	20/120, 20/20	20/50, 20/16 (4 years 3 months)
4	6	M	6	Insidious	Temporomandibular joint, knees, wrists, bilateral PIP, 2 nd toe	Diffuse psoriatic rash	8	Anterior and intermediate	OU	Neg	Pos	20/30, 20/120**	20/40, 20/4 00** (13 years, 8 months)
5	2	F	2	Sudden	Extended oligoarthritis Knees, toes, wrists	Diffuse psoriatic rash	4	Anterior and intermediate	OU	Pos	Pos	20/40, 20/200	20/20, 20/50 (11 years, 11 months)***
6	12	F	12	Insidious	Polyarticular Fingers, toes right shoulder and left knee at presentation	Palmar rash, onycholysis of toenails	12	Anterior	OD	Neg	Neg	20/125, 20/16	HM, 20/20 (10 years, 11 months)

* Visual acuity based on initial evaluation at referral center;

** Visual acuity attributed to amblyopia;

*** follow up time is given based on time seen at University of Bristol; patient was followed for another 11 years prior to referral

Table 2

Medical and Surgical Therapies

Patient	Topical corticosteroids	Systemic Steroids	Age methotrexate started	Route of methotrexate	Initial biologic	Successive biologics (in order)	Cataract surgery	Glaucoma surgery	Additional locally injected steroids	Band keratopathy
1	Yes	Oral, up to 2 mg/kg for one year, iv methylprednisolone	3	Subcutaneous	Infliximab	Adalimumab	OU	No	No	No
2	Yes	Oral, mostly limited to short postoperative courses	6	Subcutaneous	Adalimumab	None	OU	Tube shunt OU; pars plana vitrectomy OD	No	OD
3	Yes	Oral	5	Oral	Adalimumab	None	OD	No	No	OD
4	Yes	Intravenous	8	Oral then subcutaneous	Adalimumab	Infliximab, tocilizumab	No	No	dexamethasone implant OU; fluocinolone injectable intravitreal implant OD	No
5	Yes	Oral	9	Oral then subcutaneous	Infliximab	Adalimumab, Ustekinumab	OU	Trabeculectomy OU, bleb needling OU	No	OU
6	Yes	Oral, intravenous	12	Oral	Infliximab	Adalimumab	No	No	Orbital floor OD, Intravitreal triamcinolone OD	OD

Table 3

Details on Medical Therapies

Patient	Topical Corticosteroids	Systemic Corticosteroids	Additional Immunosuppressive	Age Methotrexate Started (Years)	Methotrexate dose/duration	Initial Biologic	Subsequent Biologic
1	Prednisolone Difluprednate	Oral prednisolone up to 2mg/kg for 1 year; IV methylprednisolone, course over 3 days on 3 occasions	Cyclosporine 4mg/kg/day divided dose for 5 months combined with methotrexate	3	Up to 20 mg/week SQ for 2 years	Infliximab 5 mg/kg for 6 mos.	Adalimumab 2 mg EOW up to 40 mg/week for 3 yrs. 9 mos. Ustekinumab 0 planned but not yet instituted.
2	Prednisolone Difluprednate	Brief oral prednisone taper only immediately after ocular surgeries		6	Up to 25 mg/week SQ for one year	Adalimumab 20 to 40 mg EOW to 40 mg every 4 wks for 4 yr. 6 mos.	
3	Prednisolone	Prednisolone, up to 40 mg/day for 5 weeks. Prednisolone for 1 week after cataract surgery		5	Up to 15 mg/week orally for 3 yrs. 11 mos.	Adalimumab 20 to 40 mg EOW for 3 yrs. 1 mos.	
4	Prednisolone	Prednisolone up to 25 mg/day for 7 weeks. IV methylprednisolone 1 gm/day for 3 days	Mycophenolate up to 1 gm bid for 5 yrs. 5 mos.	8	Up to 20 mg/week for 12 yrs. 4 mos. orally then SQ	Adalimumab 40 mg EOW 6 yrs. 10 mos.	Infliximab 6 mg/kg Q 8 wks. ×4 mos. Tocilizumab, 162 mg/week SQ ×10 mos.
5	Prednisolone Dexamethasone	Prednisolone up to 40 mg/day for 6 yrs. 9 mos. Current maintenance is 5 mg/day		9	Up to 12.5 mg/week orally and then SQ for 6 years	Infliximab up to 5 mg/kg Q 6 wks. for 8 yrs.	Adalimumab 40 mg EOW 3 yrs. 8 mos. Ustekinumab 45 mg Q 3 mos. for 3 yrs.
6	Prednisolone	Prednisolone up to 10 mg/day for 11 mos. 2 courses IV methylprednisolone prior to referral. IV methylprednisolone 2 courses		12	Up to 20 mg/week oral for 11 years	Infliximab 3 mg/kg up to 6 wks. for 5 yrs. 2 mos.	Adalimumab 40 mg EOW 3 yrs. 8 mos.

IV=intravenously; SQ=subcutaneously; EOW=every other week; wks=weeks; mos=months; yrs=years