Juvenile Idiopathic Arthritis and Uveitis in a Paediatric Sydney Population

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ABSTRACT

Juvenile idiopathic arthritis (JIA) is an inflammatory condition that affects 1 in 1,000 children in Australia. JIA can be defined by inflammation in one or more joints for a period of at least six weeks, with an onset younger than 16 years of age. JIA is sub-classified into different types depending on the number of joints affected, the rheumatoid factor and whether other systemic conditions are present.

JIA can be associated with uveitis, a serious and chronic ocular complication which is often difficult to manage and can result in visual loss. The risk of development of uveitis differs dependent on the type of JIA present. An ophthalmology assessment forms a vital part of the assessment for children with JIA.

The aim of this study was to ascertain the prevalence of visual complications associated with children who have a diagnosis of JIA. A retrospective review of children presenting to the Eye Clinic at The Children's Hospital Westmead with JIA over a twelve-month period between 2009 and 2010 was performed. This paper emphasises the need for ophthalmology review in this cohort of children.

Keywords: juvenile idiopathic arthritis, uveitis, paediatric

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is defined as idiopathic arthritis of greater than six weeks duration with onset before sixteen years of age. It is a chronic inflammatory joint disease and is the most common rheumatic disease in children and adolescents. The incidence of JIA is 10 in 100,000 children worldwide.[1] In Australia at least 5,000 children are affected by JIA at any one time[2] with an incidence of between 1 and 4 cases per 1,000 children.[3] The cause of JIA is currently unknown.

The International League of Associations for Rheumatology (ILAR) sub-classifies JIA into different categories depending on the number of joints involved and associated systemic conditions.

- Persistent or extended oligoarticular arthritis is the most common type of JIA and is defined by the involvement of up to four joints at the onset of the disease.
- Rheumatoid factor positive and rheumatoid factor negative polyarthritis occurs when five or more joints are affected.
- Systemic arthritis is a chronic arthritis, associated with systemic features.
- Enthesitis-related arthritis (previously known as juvenile spondyloarthropathy) is a chronic arthritis associated with enthesitis, or with lower axial skeletal involvement.
- Psoriatic arthritis is a chronic arthritis usually with asymmetrical involvement of small and large joints and evidence of psoriasis or a psoriatic diathesis.
- Undifferentiated arthritis which is arthritis that fulfils criteria in no category or in two or more categories.

The presence of antinuclear antibodies (ANA) is common in inflammatory disease and is detected on a blood sample. JIA may be diagnosed with or without detection of an increased level of ANA (ANA positive or negative respectively).

Symptoms of JIA include swelling of the affected joints, commonly the knee, ankle and wrist, along with pain, joint stiffness and possible joint contracture and joint damage. Extra-articular features are common, such as fever, rash, pleuritis, pericarditis, lymphadenopathy and hepatosplenomegaly. Ocular inflammation and uveitis are the most common extra-articular manifestations. Uveitis occurs when inflammation arising from the iris, ciliary body or choroid is present. It is a serious and chronic condition which is often difficult to manage and can result in severe visual loss and other ocular complications such as glaucoma, cataract, hypotony, cystoid macula oedema, band keratopathy, and amblyopia.[4]

The incidence of JIA-related uveitis is 1 in 100,000 worldwide and it accounts for 80% of all childhood uveitis.[5]

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The severity of uveitis in children with JIA is vast. The risk factors for developing uveitis include an early diagnosis of JIA, female, oligoarticular form and ANA positive. Children developing arthritis below the age of three years are at risk for up to seven years. Children who develop arthritis after the age of six are at risk for up to three years.[1] Chronic anterior uveitis is most commonly associated with JIA. Approximately 20% to 30% of children with JIA and uveitis will have their vision significantly affected.[6]

Clinically, the ocular signs and symptoms associated with JIA-related uveitis can include redness, pain, blurring of vision, and photophobia. It is important to mention that although redness can be a clinical feature of uveitis, the eye is often white, with no obvious sign of inflammation. Some children with mild disease can be asymptomatic. Uveitis can at times be the first sign of JIA.[5]

The severity of the uveitis present and treatment methods used will determine the risk of developing other ocular complications. The use of topical and systemic corticosteroids in the management of this disease can induce adverse ocular effects such as cataract and glaucoma. Surgical intervention is often necessary in these cases. These factors determine the visual prognosis of the patient, which is often poor and can result in irreversible blindness. Children diagnosed with JIA will require regular rheumatology reviews and ophthalmology screening. If uveitis associated with JIA is detected, the frequency of ophthalmology reviews will increase and may be as regular as fortnightly for a duration of years.

METHODS

A retrospective analysis of the medical records of patients with a diagnosis of JIA, seen in the eye clinic at The Children's Hospital at Westmead over a twelve-month period, between June 2009 and June 2010 was performed. Ethical approval was obtained for this study.

The data retrieved from medical records included age, gender, presenting symptoms, diagnosis and sub-classification of JIA, age at onset of JIA, presence of antinuclear antibodies, presence and classification of uveitis, age at onset of uveitis, secondary ocular complications and final visual acuity.

Children presenting with uveitis without a diagnosis of JIA were excluded from the study.

RESULTS

A total of 57 patient files were included in the study, with the characteristics presented in Table 1. JIA was more prevalent in females than males with 65% of patients reviewed being female.

Table 1. Characteristics of children with juvenile idiopathic arthritis

	All JIA patients (N = 57)	Patients with JIA and uveitis (N = 20)	Patients with JIA without uveitis (N = 37)
Patients, %	100	35.7	64.3
Female Number (%) {% of all female patients}	37 (64.9)	8 (40) {21.6}	29 (78.4) {78.4}
Age at diagnosis of JIA (years) Mean (range)	3.9 (1-13)	4.7 (1-13)	3.5 (1-10)
Age at diagnosis of uveitis (years) Mean (range)		5 (3-13)	N/A
ANA positive* Number (%)	39 (68)	18 (90)	21 (57)

* Five patients did not have an ANA analysis available

Oligoarticular JIA was the most prevalent subtype, being identified in 30 patients (53%). Polyarticular JIA was present in seven patients (12%), systemic JIA in four patients (7%) and one patient reviewed had psoriatic JIA (2%). Fifteen patients (26%) were identified as having undifferentiated arthritis or nonspecific JIA, and no patients reviewed were diagnosed with enthesitis-related arthritis (Figure 1).

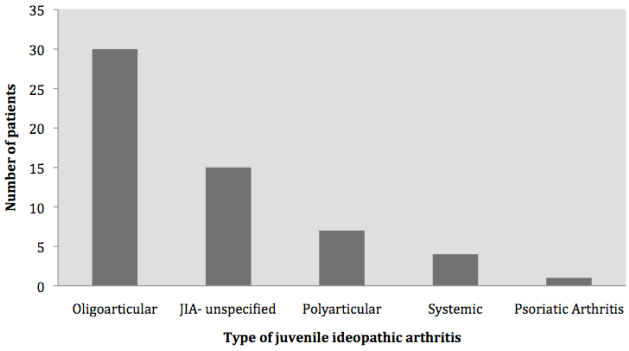

Figure 1. The distribution of the sub-classifications of JIA (N = 57).

A positive ANA factor was prevalent across the group. Thirty-nine patients (68%) were identified as ANA positive and 18 patients (32%) ANA negative. The age of patients at onset of JIA ranged from 12 months to 13 years with a mean of 47 months (SD ±32.06), showing no apparent pattern in the age of diagnosis (Figure 2).

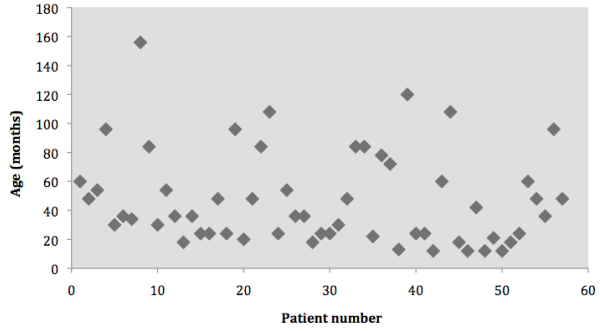

Figure 2. The age of patients at the time of diagnosis of JIA (N = 57).

The presence of uveitis was reviewed. Twenty patients (36%) had uveitis, while 37 patients (64%) had not developed uveitis at the time of the review. Bilateral uveitis was most prevalent and identified in 85% (n = 17) of patients while only 15% (n = 3) had unilateral disease. The age of onset of uveitis ranged from 3 years to 13 years with a mean of 65 months (SD ±27.39). Fifteen patients (75%) had an onset of uveitis before 7 years of age. Two patients reviewed with uveitis did not have an age of onset documented (Figure 3, Table 1).

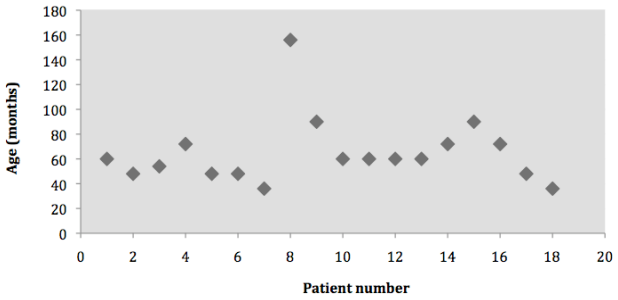

Figure 3. The age of patients at the time of diagnosis of uveitis (N = 18).

The type of uveitis present was reviewed. Anterior uveitis was most common, and was detected in 18 patients (90%) and panuveitis was identified in two patients (10%). No cases of intermediate uveitis were identified.

Patients with oligoarticular JIA had a high incidence of ANA positivity (76%, n = 23) and uveitis was present in 23% (n = 7). Unclassified JIA also had a high incidence of ANA positivity at 60% (n = 9) and uveitis at 67% (n = 10) (Table 2).

Table 2. Relationship of ANA factor and uveitis to type of JIA

JIA sub-classification	Number of patients	ANA positive N (%)	Patients with uveitis N (%)
All subgroups	57	39 (68.4)	20 (35.1)
Oligoarticular	30	23 (76.7)	7 (23.3)
Polyarthritis	7	3 (42.9)	1 (14.2)
Systemic	4	1 (25.0)	2 (50)
Psoriatic	1	1 (100)	0
Enthesitis-related	0	0	0
Unclassified	15	9 (60.0)	10 (66.7)

The initial symptoms of uveitis varied across the group. Interestingly, eight patients (40%) were asymptomatic. Ocular symptoms included red eyes 35% (n = 7), photophobia 15% (n = 3) and reduced vision 5% (n = 1). In one patient the initial symptoms were not documented as this patient had been transferred from another eye care centre (Figure 4).

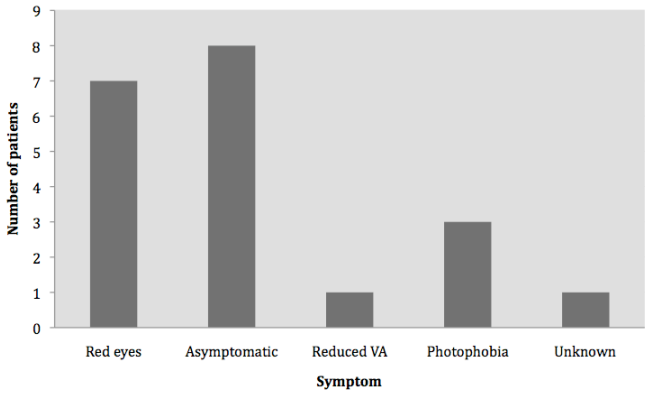

Figure 4. The distribution of the initial presenting symptoms of uveitis (N = 20).

Visual outcome in patients with JIA and uveitis ranged from 6/4.5 to no light perception. Of the 37 eyes with uveitis 62% (n = 23) had visual acuity of 6/9.5 or better, 11% (n = 4) had visual acuity of 6/12 to 6/18, 11% (n = 4) had visual acuity of 6/18 to 6/60 and 16% (n = 6) had visual acuity worse than 6/60.

Associated ocular complications in these patients were diverse. Commonly, glaucoma (60%, n = 12) and cataracts (40%, n = 8) were identified. Other complications identified in the group were band keratopathy (15%, n = 3), and anterior or posterior synechiae (15%, n = 3). 50% (n = 10) of these patients with ocular complications required surgical intervention.

Of the patients reviewed, six had a diagnosis of uveitis that preceded a diagnosis of JIA. For these patients, the visual outcome was poorer than those initially diagnosed with JIA who then went on to develop associated uveitis. Two of patients initially diagnosed with uveitis had a final visual acuity of no light perception in at least one eye, one had 6/18 or worse vision and three had a visual acuity of 6/9.5 or better. Five had an associated ocular complication, which included glaucoma (n = 4), cataract (n = 3), posterior or anterior synechiae (n = 2), and band keratopathy (n = 1). Surgical intervention was required in four patients with associated ocular complications required surgical intervention.

DISCUSSION

Early presence of uveitis in JIA is an important prognostic factor associated with adverse visual outcomes.[7] Early detection and treatment of uveitis is mandatory in enabling the best possible visual outcome for these patients. Regular follow-up and review for the duration of their childhood, and sometimes into the adult years, is required due to the chronic nature of the condition. While not all children with uveitis will go on to develop JIA, it is important that it is investigated throughout the course of the disease.

Uveitis can be the initial presentation of JIA. Children with signs of uveitis preceding signs of arthritis may have a poorer visual outcome.[8] Patients reviewed in this study with a diagnosis of uveitis prior to a diagnosis of JIA showed a poorer visual outcome and majority of these patients had an associated ocular complication, such as glaucoma or cataract. A poorer visual outcome in these patients may be a result of later presentation to an ophthalmologist, and therefore further progression of the disease.

Symptoms of uveitis may be nonspecific, such as intermittent red eyes, epiphora and reduced vision. Some children may even be asymptomatic. Interestingly, in this study 40% of patients reviewed were asymptomatic. It is imperative that all children with idiopathic uveitis are screened for JIA and early treatment is commenced to achieve the best visual outcome.

The type of subclassification of JIA and the ANA factor determine the risk of development of uveitis. Oligoarticular and unclassified JIA with an ANA positive factor are at high risk for the development of uveitis. In this study 23% of patients with oligoarticular JIA were ANA positive and had a diagnosis of uveitis, and 67% of patients with unclassified JIA were ANA positive and had a diagnosis of uveitis.

The exact visual prognosis of children with JIA is not known. Rates of visual impairment ranging from 6% to 25% have been published for JIA-associated uveitis.[9,10] In this study visual acuity ranged from 6/4.5 to no light perception. This emphasises the importance of regular eye reviews for patients with JIA and the significance of comorbidity in children with JIA. All patients included in this study required frequent ophthalmic review over the twelve-month period. Review periods included fortnightly, monthly, three-monthly, six-monthly and yearly. The frequency of review depended upon the type of JIA, level of uveitis and current ocular associations and varied for patients throughout the course of their disease. The Royal College of Ophthalmologists and the British Paediatric Association have compiled a summary of recommendations regarding the frequency of eye review for these patients. The recommended schedule ranges from three to twelve months depending on whether the patient is considered high or low risk.[11]

The disease course of JIA is prolonged and can continue into adulthood. Although JIA becomes less inflammatory with age, it has been reported that up to 50% of adults who suffered JIA in childhood will continue to experience the effects of the disease, such as joint deformity, growth abnormalities, osteoporosis, pain and difficulties with daily living.[12] They may also suffer a visual impairment as a result of uveitis, or the secondary complications of cataract and glaucoma. The transition from paediatric health services to appropriate adult health services must be considered for these patients.

CONCLUSION

Juvenile idiopathic arthritis is a serious and chronic condition that has a known association with uveitis. It is more common in females than males. The type of sub-classification of JIA and the ANA factor determine the risk of development of uveitis with oligoarticular and unclassified subgroups with ANA positivity being the highest risk factor.

Uveitis is an ocular condition that can be difficult to manage and results in visual loss and other ocular complications such as glaucoma and cataract, which often require surgical intervention. Visual prognosis in children with JIA is influenced by the age at which uveitis is detected. Children with a diagnosis of uveitis preceding a diagnosis of JIA have a poorer visual outcome.

All children who are diagnosed with JIA will require a full ophthalmology screening as well as regular eye reviews. Similarly, all children who present with uveitis will require a full rheumatology assessment as uveitis may be the first sign of juvenile idiopathic arthritis.

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