Systemic Lupus Erythematosus in the Pediatric North American Native Population of British Columbia

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ABSTRACT. ***Objective.*** To compare the estimated prevalence and the phenotype of pediatric systemic lupus erythematosus (SLE) in a North American Native population with other ethnic groups.

Methods. We performed a retrospective chart review of all patients with SLE currently followed at the single tertiary care pediatric rheumatology clinic in our province. Data collected included demographic characteristics, family history, classification criteria for SLE, laboratory tests at diagnosis, SLE Disease Activity Index (SLEDAI) at presentation, and Systemic Lupus International Collaborating Clinics (SLICC) damage index at 6 months.

Results. The prevalence of SLE in our pediatric Native population is 8.8 per 100,000 (n = 6) compared to 3.3 per 100,000 in the non-NAI population (n = 34) (p = 0.037, Fisher's exact test; OR 2.6, 95% CI 1.1–6.3). Family history of rheumatic disease is more common in our Native children (5/6, 83%) compared to non-Native children (5/34, 15%) (p = 0.002 Fisher's exact test; OR 29, 95% CI 2.8–303.3). The sample size is too small for reliable interpretation of disease phenotype, autoantibodies, disease activity, and disease damage measures.

Conclusion. There is an increased prevalence of SLE and familial autoimmunity among Native children in our population. Public health measures to screen children at risk may detect early disease and may reduce disease morbidity. (J Rheumatol 2006;33:161–3)

Key Indexing Terms:
NORTH AMERICAN NATIVE PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

There is a high prevalence of systemic lupus erythematosus (SLE)[1-5] among several North American Native groups, but phenotype differences are not reported. We compared the prevalence and phenotype of pediatric SLE in Native and non-Native patients in British Columbia, Canada.

MATERIALS AND METHODS

We conducted a retrospective chart review in September 2004 of all patients with SLE who we were actively following through the pediatric rheumatology clinic at British Columbia's Children's Hospital (BCCH), the single tertiary care pediatric rheumatology clinic in our province.

Inclusion criteria. Forty children under age 18 years who fulfilled 4 or more of the revised American College of Rheumatology (ACR) criteria for SLE[6] were included.

Exclusion criteria. Children with SLE previously but not currently followed through our clinic were excluded.

Retrospective chart review. Data collection included demographic characteristics, family history of rheumatic disease in first or second-degree relatives, presence of classification criteria for SLE[6], and results of pertinent laboratory tests at diagnosis and through disease course. Gastrointestinal (GI) involvement was defined as persistent epigastric pain, nausea, or GI reflux disease (GERD) warranting a referral to a gastroenterologist. Pulmonary disease was defined as pleuritis, impaired diffusion with diffusing capacity (carbon monoxide; DLCO) < 70%, or pulmonary hypertension. Disease activity at presentation and disease related damage 6 months after presentation were measured by Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)[7] and Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index (SLICC)[8].

Statistical analysis. Prevalence of SLE was calculated using our patient numbers and Statistics Canada 2001 provincial census data to define the population at risk (the number of children age 0–19 years). Census data defines Native to encompass Natives, Métis, and Inuit. Fisher's exact test was used for comparative statistics. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. Because of the multiple comparisons, a p value < 0.005 was considered significant.

RESULTS

Demographics. The ethnic backgrounds of the 40 patients were, Native: 6; Caucasian: 8; Chinese: 10; East Indian: 4; Filipino: 4; Vietnamese: 4; Taiwanese: 2; Singaporean: 1; and Iranian: 1. All Native patients were female (6/6, 100%); 24/34 (70%) non-Native patients with SLE were female. Mean age at diagnosis in years (range) was 13.9 (7.1–16.9) and 10.6 (4.8–16.1), and at time of data collection was 17.6 (16.0–18.0) and 15.0 (8.2–18.0) for Native and non-Native

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children, respectively. Mean duration of followup in months (range) was 37.3 (6–105) and 47.6 (7–147) for Native and non-Native children, respectively.

Prevalence. The prevalence of SLE in our pediatric Native population was 8.8 per 100,000 (n = 6) compared to 3.3 per 100,000 in the non-Native population (n = 34; p = 0.037; OR 2.6, 95% CI 1.1–6.3). We were unable to estimate prevalence rates for other individual ethnic groups, as accurate age-group census data are not available.

Family history. Family history of rheumatic disease was more common in our Native (5/6, 83%) compared to non-Native (5/34, 15%) children (p = 0.002; OR 29, 95% CI 2.8–303.3) (Table 1).

Clinical and laboratory features, SLEDAI, and SLICC. Arthritis, myositis, and GI symptoms tended to be more frequent in Native children (Table 2). There was no significant difference in disease phenotype, autoantibodies, disease activity, or disease damage measures between Native and non-Native patients.

DISCUSSION

We estimate the prevalence of SLE in our pediatric Native population to be 2.5 times greater than in the non-Native population. There are no accurate prevalence data for pediatric SLE, but conservative estimates from older studies cite 15% to 17% of patients as having childhood onset of disease[9,10]. US population studies report SLE prevalence ranging from 15 to 130 per 100,000, with increased prevalence in recent series, and incidence ranging from 2 to 8 cases per 100,000[11]. High prevalence rates are reported in several Native tribes[2-5], the highest in the Nuu-Chah-Nulth Native Indians on Vancouver Island (300–500 per 100,000)[2]. Estimating prevalence figures for children based on adult data is not possible, but we have the impression that Native children have an excessively high incidence of SLE.

We identified an increased familial occurrence of rheumatic disease among our Native pediatric patients with SLE; this has also been reported in adult Native populations with SLE[1].

Native children were more likely to have arthritis, myositis, and GI symptoms than non-Native patients, but the incidence of arthritis in our non-Native population is lower than other reports. GI symptoms were also strikingly more frequent in Native patients, although it was difficult to differentiate disease or treatment effect. The importance of eliciting abdominal symptoms is supported by the recent SLICC suggestion that abdominal serositis (manifest by either diffuse abdominal pain, with rebound or guarding, and/or ascites or bowel wall edema in the absence of other causes) be added to the existing serositis criterion.

In adult SLE populations, increased morbidity and mortality has been reported for non-Caucasians. An association between poor outcome and ethnicity has not been confirmed in the pediatric population. Disease activity and disease damage as measured by SLEDAI and SLICC scores did not differ between Native and non-Native children in our study.

There are several drawbacks to our retrospective study, including potential errors in case identification (although Native patients are likely to be underidentified), small patient numbers, and the unknown validity of self-report ethnicity. Our sample size is too small for reliable interpretation of disease phenotype, autoantibodies, disease activity, and disease damage measures. Finally, there is a paucity of literature on pediatric SLE in Native populations with which to compare our results.

We identified an increased prevalence of SLE and familial autoimmunity in our pediatric Native population. The increased frequency of arthritis, myositis, and GI symptoms is somewhat atypical, thus increasing the potential for alternative or late diagnosis. Education and screening of this high-risk population may facilitate early diagnosis and treatment, ultimately resulting in decreased morbidity in this unique population.

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Table 1. Family history of rheumatic disease in NAI and non-NAI children with SLE or mixed connective tissue disease.

Patient	Family History SLE	RA	JIA	SSc	TA	Thyroid Disease
1 NAI		2 aunts (p)		1 aunt (p)		
2 NAI	1 aunt (p)	1 aunt (p)				
3 NAI			1 aunt (p)			
4 NAI		1 aunt (m)				
5 NAI						
6 NAI	Mother				Grandmother (m)	
Non-NAI (n = 34)	Female cousin (p) (n = 1)	Father (n = 1), grandmother (m) (n = 1)	2 female siblings (n = 1)			Mother (n = 1), female cousin (p) (n = 1)

RA: rheumatoid arthritis; JIA: juvenile idiopathic arthritis; SSc: systemic scleroderma; TA: Takayasu's arteritis; p: paternal; m: maternal; female cousin (p): same individual.

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Table 2. Clinical features, autoantibodies, SLEDAI and SLICC scores. Because of the multiple comparisons, $p < 0.005$ was considered significant (Fisher's exact test). Low complement: C3 < 0.90 g/l, C4 < 0.10 g/l; positive anti-ds-DNA: > 55 kU/l by ELISA; positive SSA > 46 u/ml, SSB > 14 u/ml, Smith > 40 u/ml, RNP > 40 u/ml.

	NAI, n = 6 (%)	Non-NAI, n = 34 (%)	p	OR (95% CI)
Encephalopathy* Seizures Psychosis	1 (17)	4 (12)	0.58	1.5 (0.1 to 16.3)
Nephritis* Proteinuria > 0.5 g/day Cellular casts	2 (33)	18 (53)	0.33	0.4 (0.1 to 2.8)
Malar rash*	5 (83)	21 (62)	0.30	3.23 (0.5 to 20.2)
Nonerosive arthritis*	6 (100)	11 (32)	0.003	Infinity (0–infinity)
Myositis	2 (33)	0 (0)	0.019	Infinity (0–infinity)
Pulmonary involvement (pleuritis* or DLCO < 70% normal, pulmonary hypertension)	4 (67)	13 (38)	0.20	3.2 (0.5 to 20.2)
Gastrointestinal symptoms (persistent epigastric pain, nausea or gastrointestinal reflux disease)	5 (83)	3 (9)	0.0005	51.7 (4.4 to 600.2)
Anti-ds-DNA* antibodies	3 (50)	26 (76)	0.20	0.31 (0.05 to 1.8)
SSA	6 (100)	18 (53)	0.035	Infinity (0–infinity)
SSB	2 (33)	6 (18)	0.34	2.3 (0.34 to 15.8)
Smith* antibody	3 (50)	9 (26)	0.24	2.8 (0.47 to 16.3)
RNP	5 (83)	15 (44)	0.09	6.3 (0.67 to 60.2)
SLEDAI at presentation	15.2 (range 6–29) SD 8.0	13.4 (range 0–49) SD 9.3		
SLICC at 6 mo**	0 (n = 4), 1 (n = 1)	0 (n = 22), 1 (n = 7), 2 (n = 1), 4 (n = 1)		

* SLE ACR criteria[6]. ** Data missing for one NAI patient and 3 non-NAI patients.

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