Establishment of a Pilot Pediatric Registry for Chronic Vasculitis Is Both Essential and Feasible: A Childhood Arthritis and Rheumatology Alliance (CARRA) Survey

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ABSTRACT. ***Objective***. To identify the need for, and feasibility of, establishing a web-based USA/Canadian registry of children with chronic systemic vasculitis — an otherwise insufficiently studied population.
Methods. Physician members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA; n = 126) were invited to complete 2 surveys exploring vasculitis-related experience, beliefs about childhood versus adult vasculitis, and commitment to contribute patients to a prospective registry. Diagnoses included Wegener's granulomatosis (WG), childhood polyarteritis nodosa, microscopic polyangiitis (MPA), Takayasu's arteritis, primary angiitis of the central nervous system (PACNS), vasculitis, and unclassified vasculitis.
Results. One or both surveys were completed by 102 (81%) physicians. Almost half of first-survey respondents had been in practice for > 15 years. Collective estimated lifetime experience was > 1500 patients (WG and unclassified vasculitis were the most common diagnoses). Three hundred seventeen children with vasculitis were seen in the year preceding the survey, with most physicians seeing only 2–5 patients. The majority of respondents believed that childhood vasculitis differed from adult disease, particularly with respect to classification criteria and disease activity markers. Fifty-nine members committed to contribute 2 years' data (~ 120 patients) to a pilot registry limited to time of diagnosis, focusing on WG, MPA, Churg-Strauss syndrome, PACNS, and unclassified vasculitis.
Conclusion. We obtained overwhelming consensus from an experienced body of pediatric rheumatologists on the need to study childhood-onset vasculitis independently from adult disease, together with commitment from sufficient members to prospectively contribute 2 years' data to a limited pilot registry to answer some basic questions about presenting and diagnostic features and initial treatment practices at disease onset. (First Release Nov 15 2006; J Rheumatol 2007;34:224–6)

Key Indexing Terms:
PEDIATRIC CHRONIC VASCULITIS REGISTRY

To date knowledge of the presentation, management, and prognosis of chronic childhood-onset systemic vasculitis is confined to a few retrospective case series of 10–34 children managed over 1–24 year periods[1-4]. These studies and 2 recent surveys of 110 and 75 patients with small-vessel vasculitis from Turkey[5,6], through direct and indirect comparisons with adult patients, found significant differences in presentation and end-organ damage despite similarities in remission rates and mortality. With the aim of establishing a prospective USA/Canadian diagnostic and therapeutic registry of childhood-onset systemic vasculitis, pediatric rheumatologists were surveyed to identify the extent of vasculitis-related experience, the frequency of new patient referral, their beliefs about the differences between childhood and adult onset disease, and their willingness and ability or otherwise to contribute to a registry.

MATERIALS AND METHODS

All 126 members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) were invited by e-mail to complete 2 successive web-based surveys. The first survey comprised 37 predominantly categorical, non-leading multichoice questions, including a final free field for comment. Questions addressed personal practice and experience, numbers of children with specified vasculitides reviewed during the previous 1 and 5 years (ascertained through "best guess" or a database). Using pediatric Wegener's granulomatosis (WG) as a focus, levels of agreement with statements characterizing beliefs about pediatric-onset versus adult-onset disease, and about the value of a registry were requested using a 5-point Likert scale (beliefs about other diseases surveyed were not explored). The second questionnaire further explored commitment to a registry having fed back the results of the first survey and requested responses to proposals for a limited pilot registry. The definition of chronic vasculitis included WG, childhood polyarteritis nodosa (cPAN), microscopic polyangiitis (MPA), idiopathic crescentic glomerulonephritis, Takayasu's arteritis, primary angiitis of the central nervous system (PACNS), and unclassified primary vasculitis, and excluded Kawasaki disease and Henoch-Schönlein purpura.

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Descriptive analyses were performed with SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The first survey was completed by 83 (66%) physicians from 53 (5 Canadian and 48 USA) centers. Sixty-seven respondents (80%) had been in practice for more than 5 years and 35 (43%) for more than 15 years. Seventy-five (90%) physicians devoted 50% or more time, and 62 (77%) exclusively, to the care of children (≤ 18 years of age) with rheumatic diseases. Over 90% of physicians were in academic hospital settings and 85% in group practice, of which half shared patient care with other physicians within their institution. Of the 43 nonresponding physicians, 23 were not represented by a colleague in their institution who participated in the survey.

Table 1 summarizes physicians' estimated lifetime patient-related experience in Canada and the USA, comprising "best guess" data for 85% of respondents. Collective lifetime experience was of more than 1500 patients, of which WG (24%) and unclassified vasculitis (17%) were the diagnoses most commonly seen. Twenty-two physicians had seen more than 10 patients with WG. Idiopathic crescentic glomerulonephritis and "other" vasculitides were rare. Accounting for duplicate reporting within group-based practices, a total of 317 children with chronic vasculitis were seen in the year preceding the survey, of which 30% were unclassified. The majority were seen by physicians in 5 large institutions and 80% of responders had seen no more than 2 patients of each type of vasculitis. During the preceding 5 years there was an average of 214 patients seen per year, of whom 45 children had WG, 58 had unclassified vasculitis, and between 20 and 27 cases per year of cPAN, Takayasu's arteritis, MPA, and PACNS were seen. Twenty-five percent of respondents reported that some unspecified proportion of patients with chronic vasculitis in their institutions were managed exclusively by other subspecialists without involvement of a rheumatologist.

The majority (99%) of responders agreed (82% strongly) that a prospective registry was integral to any meaningful study of pediatric chronic vasculitis and 98% indicated (78% strongly) that childhood onset vasculitis should be studied independently from adult onset. All respondents indicated that an adult-based registry would not meet the needs for understanding pediatric disease. Fewer respondents, 59% (8% strongly), indicated a belief that the natural history of childhood WG differs significantly from adult disease, whereas 70% believed that diagnostic criteria and 76% that disease activity markers have not been adequately characterized in children. Potential barriers for participation in a proposed registry were: limited financial resources, personnel, and support for institutional review board (IRB) submission or data entry (11 respondents); personal time constraints and commitments to other registries (10 respondents); and lack of compensation in terms of authorship (3 respondents). One respondent stated that the registry was unnecessary.

In the second survey, 59 of 67 respondents corroborated commitment to contribute prospective data for 2 years to a web-based registry limited to patients with small-vessel antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (WG, MPA, Churg-Strauss syndrome, and unclassified vasculitis) and time of diagnosis. In such a registry, workload would be minimized to an estimated annual contribution of 2–5 patients per physician and supplied templates for IRB submission.

DISCUSSION

This survey of CARRA members corroborates that the rarity of childhood chronic vasculitis is such that no single physician or institution is likely to have sufficient or timely patient-related experience to characterize or prospectively study any of these diseases. The survey, focusing on the beliefs of CARRA members about WG, determined that this was an insufficiently characterized group of patients and

Table 1. Estimated number of patients with childhood onset vasculitis in North America seen by responding Childhood Arthritis and Rheumatology Research Alliance members during lifetime and over the last 1 and 5 years. Figures have been modified to account for duplicate data arising from group practices.

	No. of Patients Seen								
	Lifetime Experience				Last Year		Last 5 years		
Specific Diagnosis	Total	Median	Mode	≥ 10 pt*	Total	Median	Total	Median	Mean
Wegener's granulomatosis	452	5 (0–6)	5 (23)	22	63	1 (0–6)	223	3 (1–20)	45
Childhood polyarteritis nodosa	290	4 (0–19)	2 (17)	9	34	0 (0–3)	137	2 (0–15)	27
Microscopic polyangiitis	222	2 (0–15)	0 (23)	6	27	0 (0–3)	99	1 (0–10)	20
Interstitial crescentic glomerulonephritis	102	0 (0–16)	0 (54)	4	12	0 (0–2)	43	0 (0–7)	9
Takayasu's arteritis	246	3 (0–20)	2 (22)	5	34	0 (0–4)	106	1 (0–15)	21
Primary angiitis of the CNS	234	2 (0–20)	2 (16)	5	35	0 (0–5)	110	1 (0–15)	22
Unclassified vasculitis	327	5 (0–20)	0 (36)	27	96	1 (0–8)	290	3 (0–20)	58
Other**	19	1 (0–15)	1	3	16	0 (0–6)	66	0 (0–20)	11
Total	1892				317		1074		

* Number of physicians who have seen ≥ 10 patients; ** Churg-Strauss syndrome, Cogan's syndrome, urticarial vasculitis. CNS: central nervous system.

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that the questionable differences between adult versus pediatric onset WG would be best addressed through a prospectively collected registry of pediatric patients. It is envisaged that physicians from about 50 centers will participate in a proposed work-limited pilot registry with a one-year recruitment potential well in excess of total populations of previous studies.

The preponderance of patients who were "unclassified" in this survey supports 2 previous population studies where, after excluding the acute self-limited vasculitides (Henoch-Schönlein purpura and Kawasaki disease), two-thirds of children with "chronic" vasculitis were "unclassified"[7,8]. The difficulty in adults of distinguishing WG from PAN, MPA, Churg-Strauss syndrome, and idiopathic crescentic glomerulonephritis[9] is even greater in children, in whom it is not known how many with "unclassifiable" vasculitis ultimately develop a named vasculitis such as WG. Moreover, one-third of children with a rheumatologist diagnosis of WG do not fulfil adult-derived classification criteria[1]. The relative frequencies of the different childhood vasculitides may also differ from adult populations, and further argues the need to review the classification of vasculitis and spectrum of disease in children through a patient registry.

Such an effort will provide prompt information to clinical presentation, time to diagnosis, and the scope of initial treatment practices for WG and other small-vessel ANCA-associated vasculitides. This registry will also provide an opportunity to test the veracity of existing adult-derived classifications[10,11] versus newly proposed pediatric-specific classification criteria[12]. An expanded registry with improved case-capture methodology at each center will enable an estimation of the frequency, geographic distribution, and ethnic variation of each type of chronic vasculitis throughout Canada and the USA. As with other registries[13-15], the challenge of this proposal will be to ensure continued enthusiasm and commitment of participants by engaging them from concept to execution while maintaining accurate, complete, and confidential data sets. Survey participants have already collaborated in hypothesis-setting and database content. Efficient web-based data entry and retrieval by each center will be maintained if it can become part of their normal practice for audit. The major limitation of this pilot registry is that the cohort will be selected for those patients who see pediatric rheumatologists. Success, additionally assessed by the number of "recruited" centers (or physicians), will facilitate an expanded scope to include other diagnoses, sites beyond the USA and Canada, and, to ensure complete and valid data sets, participation of non-rheumatology subspecialists.

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