Influence of Age, Sex, and Place of Residence on Clinical Expression of Giant Cell Arteritis in Northwest Spain

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ABSTRACT. ***Objective.*** To investigate the epidemiology of giant cell arteritis (GCA), we examined whether differences in clinical and laboratory features exist in patients with biopsy-proven GCA from Northwest Spain according to sex, place of residence, and age at disease onset.

Methods. Retrospective study of biopsy-proven GCAdiagnosed from January 1, 1981, to December 31, 2001, at the single hospital for a well defined population of 250,000. A comparative analysis was conducted of clinical and laboratory features according to sex, place of residence (rural or urban), and age at the onset of symptoms (< 70 yrs; ≥ 70 yrs).

Results. Between 1981 and 2001, 210 patients from the Lugo region were diagnosed with biopsy-proven GCA. In urban areas GCAwas significantly more common in women (rate ratio 1.58, 95% CI 1.00–2.53, p = 0.05). Women presented manifestations of polymyalgia rheumatica (PMR) more commonly than men. However, no statistically significant difference in the frequency of visual manifestations or permanent visual loss were observed between the sexes. GCA was slightly more common in rural than in urban areas (annual adjusted incidence rate in rural areas 10.4/100,000 in people age ≥ 50 years vs 9.1/100,000 in urban areas; p = 0.34). GCAwas more common among men in rural areas (rate ratio 1.73, 95% CI 1.10–2.70, p = 0.02). Patients younger than 70 years at the time of diagnosis (20%) had a trend to a longer delay to diagnosis and a marginal increase in the frequency of PMR compared with those with disease onset at age ≥ 70 years. A higher inflammatory response was observed in the patients younger than 70 years.

Conclusion. In patients with biopsy-proven GCA from Northwest Spain PMR manifestations are more commonly observed in women. The higher inflammatory response and the longer delay to diagnosis in younger patients call for a higher physician awareness of this vasculitis among individuals younger than 70 years. (J Rheumatol 2003;30:1548–51)

Key Indexing Terms:
GIANTCELL(TEMPORAL) ARTERITIS SEX AGE OF ONSET PLACE OF RESIDENCE

Giant cell arteritis (GCA) (temporal arteritis) constitutes the most frequent vasculitic syndrome in Western countries[1,2]. It involves large and middle-size blood vessels, with a predisposition to the involvement of cranial arteries[1,2]. Its frequency increases with aging and peaks in patients older than 70 years[3]. Patients with GCA often present clinical manifestations of polymyalgia rheumatica (PMR). As with series of patients with isolated PMR, nearly all epidemiological studies on GCA have shown a higher incidence of GCA in women[1]. An exception to this was observed in the Lugo region of Northwest Spain during the period 1981–90[4]. Former studies had disclosed more severe inflammatory response in women with PMR[5]. Recently, Israeli investigators assessed clinical differences according to sex in patients with temporal arteritis[6]. In Germany an increased prevalence of GCA was observed in urban areas[7].

To further investigate the epidemiology of GCA we examined whether differences in clinical and laboratory features exist in biopsy-proven GCA in Northwest Spain according to sex, place of residence, and age at the time of disease onset.

MATERIALS AND METHODS

Population characteristics. This was a retrospective study of patients diagnosed with GCA in the Department of Medicine of the Hospital Xeral-Calde, Lugo, Spain, from January 1981 to December 2001. This is the only referral center for a mixed urban and rural population of almost 250,000 people. The main characteristics of this population have been reported[8,9]. In 1996, almost 48% lived in urban areas, most of them in the city of Lugo. The population in rural areas is older than in urban areas. However, the distribution of the population 50 years and older is similar (p = 0.25). Also, the population structure is very similar for men and women.

A temporal artery biopsy procedure was performed as described[4,10]. Clinical and laboratory data at the time of diagnosis of the patients with biopsy-proven GCAwere assessed.

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Statistical analysis. Comparisons were made using Student t or the chi-square test. When required, Fisher's exact test was used. Statistical significance was defined as $p \leq 0.05$. Rates were adjusted by age and sex.

RESULTS

Between 1981 and 2001, 210 patients were diagnosed with biopsy-proven GCA.

Differences between men and women. In urban areas the incidence of GCA was significantly higher in women (rate ratio 1.58, 95% CI 1.00–2.53, p = 0.05). Women also presented PMR manifestations more commonly than men did (Table 1). Hemoglobin was lower in women. However, the importance of this result is uncertain, as women generally have lower hemoglobin values than men. No significant differences in the frequency of visual manifestations were observed between the sexes.

Differences in GCAaccording to place of residence. Biopsy-proven GCA was slightly more common in people living in rural than in urban areas (annual adjusted incidence rate of GCAin rural areas 10.4/100,000 people 50 years and older, vs 9.1/100,000 in urban areas; p = 0.34). GCA incidence was higher among men in rural areas (rate ratio 1.73, 95% CI 1.10–2.70, p = 0.02). Other differences are summarized in Table 2.

Differences according to age of onset. We assessed whether the age of onset might influence the clinical spectrum of the disease. We compared the clinical manifestations of patients younger than 70 years at time of diagnosis (n = 42; 20%) with those observed in patients with disease onset at age ≥ 70 years (Table 3). In the younger age group there was a nonsignificant longer delay to diagnosis. Clinical manifestations of PMR were marginally increased in patients with disease onset before the age of 70 years. More severe inflammatory response, manifested by higher frequency of constitutional syndrome, higher erythrocyte sedimentation rate, platelet count and alkaline phosphatase values, and lower hemoglobin levels, was observed in this younger age group.

DISCUSSION

Investigators from Catalonia, in Northeast Spain, did not observe significant clinical differences in GCAaccording to sex[5]. In Lugo the age at the onset of symptoms was similar in both sexes. In contrast, French investigators found an older age at diagnosis in women compared to men[11]. Unexpected differences in the frequency of GCA between men and women according to place of residence were observed in Lugo.

In Rochester, Minnesota, headache was more common in women[12]. This was not observed in our larger series. We previously reported a slightly increased frequency of headache and more remarkable reduction of ischemic manifestations, in particular in jaw claudication, in our series of biopsy-negative GCA compared with biopsy-proven cases[13]. Thus, it is possible that the increased frequency of headache in the report by Machado, *et al*[12] might be

Table 1. Comparison of clinical and laboratory features and site of residence between men and women with biopsy-proven GCA.

Variable	Men, n = 97 (46.2%)*	Women, n = 113 (53.8%)*	p
Age at diagnosis, yrs± SD	74.5 ± 6.6	74.7 ± 7.3	0.42
Patients living in urban areas, n	26 (26.8)	52 (46.0)	0.004
Delay to diagnosis, weeks**	9.7 ± 12.6	11.0 ± 10.4	0.20
Headache	87 (89.7)	96 (85.0)	0.31
Scalp tenderness	33 (34.0)	39 (34.5)	0.94
Constitutional syndrome#	65 (67.0)	70 (62.0)	0.45
Abnormal temporal arteries on examination	82 (72.6)	76 (78.4)	0.33
Jaw claudication	35 (36.1)	51 (45.1)	0.18
Dysphagia	3 (3.1)	8 (7.1)	0.16
Polymyalgia rheumatica	32 (33.0)	55 (48.7)	0.021
Fever (temperature ≥ 38° C)	8 (8.3)	13 (11.5)	0.44
Visual manifestations	25 (25.8)	24 (21.2)	0.44
Permanent visual loss	13 (13.4)	14 (12.4)	0.83
Cerebrovascular accidents	3 (3.1)	1 (0.9)	0.25
Limb claudication of recent onset	4 (4.1)	2 (1.8)	0.27
ESR, mean ± SD, mm/h	91.0 ± 22.1	94.6 ± 22.7	0.50***
Hemoglobin, mean ± SD, g/dl	12.2 ± 1.8	11.4 ± 1.4	0.0002††
Platelet count, mean ± SD, mm^3	407,000 ± 143,000	412,000 ± 126,000	0.39
Raised ALP†	25 (25.8)	31 (27.7)	0.76

* Number in parentheses indicates the total proportion of patients with a particular variable. ** From onset of symptoms until time of diagnosis. # Asthenia, anorexia, and weight loss ≥ 4 kg. † If values at diagnosis were > 2 times above the upper normal range. *** Adjusted by age and hemoglobin. †† Adjusted by age.

Table 2. Comparison of clinical and laboratory features of biopsy-proven GCAaccording to place of residence (rural or urban).

Variable	Rural, n = 132 (62.9%)*	Urban, n = 78 (37.1%)*	p
Men, n	71 (53.8)	26 (33.3)	0.004
Age at diagnosis, yrs± SD	74.0 ± 6.7	75.6 ± 7.3	0.06
Delay to diagnosis, weeks**	9.9 ± 11.7	11.1 ± 10.9	0.23
Headache	114 (86.4)	69 (88.5)	0.66
Scalp tenderness	42 (31.8)	30 (38.5)	0.33
Constitutional syndrome#	89 (67.4)	46 (59.0)	0.22
Abnormal temporal arteries on examination	98 (74.3)	60 (76.9)	0.66
Jaw claudication	53 (40.2)	33 (42.3)	0.76
Dysphagia	9 (6.8)	2 (2.6)	0.16
Polymyalgia rheumatica	58 (43.9)	29 (37.2)	0.34
Fever (temperature ≥ 38˚C)	13 (9.9)	8 (10.3)	0.92
Visual manifestations	27 (20.5)	22 (28.2)	0.20
Permanent visual loss	17 (12.9)	10 (12.8)	0.99
Cerebrovascular accidents	2 (1.5)	2 (2.6)	0.59
Limb claudication of recent onset	3 (2.3)	3 (3.9)	0.40
ESR, mean ± SD, mm/h	92.3 ± 22.6	94.2 ± 22.3	0.80***
Hemoglobin, mean ± SD, g/dl	11.9 ± 1.7	11.6 ± 1.5	0.56††
Platelet count, mean ± SD, mm^3	408,000 ± 120,000	410,000 ± 144, 000	0.45
Raised ALP†	36 (27.3)	20 (26.0)	0.84

* Number in parentheses indicates the total proportion of patients with a particular variable. ** From onset of symptoms until time of diagnosis. # Asthenia, anorexia, and weight loss ≥ 4 kg. † If values at diagnosis were > 2 times above the upper normal range. *** Adjusted by age, sex, and hemoglobin. †† Adjusted by age and sex.

Table 3. Comparison of clinical and laboratory features and site of residence in biopsy-proven GCAaccording to age of disease onset.

Variable	Onset < 70 Years, n = 42 (20%)*	Onset ≥ 70 Years, n = 168 (80%)*	p
Men, n	20 (47.6)	77 (45.8)	0.84
Patients living in urban areas	13 (31.0)	65 (38.7)	0.35
Delay to diagnosis, weeks**	12.4 ± 12.4	9.9 ± 11.2	0.10
Headache	37 (88.1)	146 (86.9)	0.84
Scalp tenderness	11 (26.2)	61 (36.3)	0.22
Constitutional syndrome#	32 (76.2)	103 (61.3)	0.07
Abnormal temporal arteries on examination	28 (66.7)	130 (77.4)	0.15
Jaw claudication	12 (28.6)	74 (44.1)	0.07
Dysphagia	0 (0.0)	11 (6.6)	0.08
Polymyalgia rheumatica	22 (52.4)	65 (38.7)	0.11
Fever (temperature ≥ 38˚C)	5 (11.9)	16 (9.5)	0.65
Visual manifestations	9 (21.4)	40 (23.8)	0.74
Permanent visual loss	5 (11.9)	22 (13.1)	0.84
Cerebrovascular accidents	2 (4.8)	2 (1.2)	0.13
Limb claudication of recent onset	3 (7.1)	3 (1.8)	0.10
ESR, mean ± SD, mm/h	99.7 ± 22.0	91.3 ± 22.3	0.22***
Hemoglobin, mean ± SD, g/dl	11.3 ± 1.6	11.9 ± 1.6	0.017††
Platelet count, mean ± SD, mm^3	437,000 ± 152,000	402,000 ± 131,000	0.07
Raised ALP†	20 (47.6)	36 (21.6)	0.001

* Number in parentheses indicates the total proportion of patients with a particular variable. ** From onset of symptoms until time of diagnosis. # Asthenia, anorexia, and weight loss ≥ 4 kg. † If values at diagnosis were > 2 times above the upper normal range. *** Adjusted by sex and hemoglobin. †† Adjusted by sex.

explained, at least in part, by the inclusion of patients with a negative temporal artery biopsy. However, in both Rochester and Lugo the frequency of visual ischemic manifestations was similar in both sexes. Visual manifestations but no jaw claudication were more common in men from Jerusalem[6]. The importance of this finding might be limited by the small number of men with biopsy-proven GCA (n = 17) assessed in this Israeli series. However, in agreement

with our findings, PMR manifestations were also more common in women with GCAfrom Israel[6].

Reinhold-Keller, *et al* suggested that regional differences in the medical care structure were a contributing factor to the differences in the prevalence of GCAbetween rural and urban areas in Germany[7]. This factor seems to be negligible in Lugo, as patients with clinical manifestations of GCA or PMR from both rural and urban areas are sent to the same hospital.

The higher inflammatory response and the longer delay to diagnosis in our younger age group of patients from Northwest Spain indicate a need for higher physician awareness of this vasculitis among individuals younger than 70 years.

Our findings confirm some clinical and laboratory differences in GCA according to patients' sex and age at disease onset.

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