Clin Rheumatol (2008) 27:1045–1048
DOI 10.1007/s10067-008-0904-2

BRIEF REPORT

Occurrence of organ-specific and systemic autoimmune diseases among the first- and second-degree relatives of Caucasian patients with connective tissue diseases: report of data obtained through direct patient interviews

Marta Mosca · Linda Carli · Anna d'Ascanio · Chiara Tani · Rosaria Talarico · Chiara Baldini · Laura Bazzichi · Antonio Tavoni · Paola Migliorini · Stefano Bombardieri

Received: 1 April 2008 / Revised: 7 April 2008 / Accepted: 7 April 2008 / Published online: 29 May 2008

Abstract Studies have demonstrated a familial aggregation of systemic and organ-specific autoimmune diseases. The aim of the present survey was to obtain, by patient interviews, a preliminary estimate of the prevalence of systemic and organ-specific autoimmune diseases among the first- and second-degree relatives of Caucasian patients with connective tissue diseases (CTD) or inflammatory arthritis followed at our unit. Between June 2007 and January 2008, 626 patients and 85 controls (patients with osteoarthritis, osteoporosis, or fibromyalgia) were interviewed. Three hundred ten patients (50%) versus 21 controls (25%) were found to have at least one relative affected with an autoimmune condition ($p<0.0001$). The most common conditions were organ-specific autoimmune diseases: 160 (34%) autoimmune thyroid (AT) disease, 112 (24%) psoriasis, 21 vitiligo, and 19 insulin-dependent diabetes mellitus. Systemic autoimmune diseases were reported in 126 relatives: rheumatoid arthritis (66 cases, 14%), 16 sacroileitis, and CTD (43 cases). A significant difference was observed in the prevalence of AT disease between the relatives of the patients and controls (3% versus 0.5%). In conclusion, these data confirm the high prevalence of autoimmune conditions, particularly of AT disease, among the relatives of patients.

Keywords Autoimmune thyroid disease · Connective tissue diseases · Familial aggregation · Organ-specific autoimmune diseases

M. Mosca (✉) · L. Carli · A. d'Ascanio · C. Tani · R. Talarico · C. Baldini · L. Bazzichi · S. Bombardieri
Rheumatology Unit, Department of Internal Medicine,
University of Pisa,
Via Roma 67,
56126 Pisa, Italy
e-mail: marta.mosca@int.med.unipi.it

A. Tavoni · P. Migliorini
Immuno-allergology Unit, Department of Internal Medicine,
University of Pisa,
Pisa, Italy

Introduction

Many studies have demonstrated the existence of a familial aggregation of different systemic and organ-specific autoimmune diseases [1–15]. Furthermore, an increased prevalence of autoimmune diseases has been described among the relatives of patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), scleroderma (SSc), and other connective tissue diseases (CTDs) [1–10].

The aim of the present survey was to obtain, by means of patient interviews, a preliminary estimate of the prevalence of systemic and organ-specific autoimmune diseases among the first- and second-degree relatives of Caucasian patients with CTDs or inflammatory arthritides being followed at the Rheumatology Unit and the Immuno-allergology Unit of the University of Pisa.

Materials and methods

Patients suffering from RA, spondyloarthropathies, or CTDs were invited to participate in this study during the course of one of their regular checkup visits. Patients with a diagnosis of osteoarthritis, osteoporosis, or fibromyalgia were recruited as controls.

Using a structured questionnaire designed ad hoc for this study, patients and controls were asked about the presence of the following autoimmune conditions among their first- and second-degree relatives: systemic autoimmune diseases (CTD, RA, or spondyloarthropathies), autoimmune thyroid disease (Hashimoto's thyroiditis [HT] or Graves' disease), psoriasis, vitiligo, discoid cutaneous lupus erythematosus, hemolitic anemia, idiopathic thrombocytopenia, insulin-dependent diabetes mellitus (IDDM), autoimmune hepatitis, primary biliary cirrhosis, coeliac disease, demyelinating diseases, myasthenia gravis, and idiopathic uveitis.

All of the variables were analyzed independently using the χ^2 test.

Results

Between June 2007 and January 2008, a total of 711 subjects (626 patients and 85 controls) were interviewed. The diagnoses of the patients are summarized in Table 1.

Three hundred ten patients (50%) versus 21 controls (25%) were found to have at least one first- or second-degree relative affected with an autoimmune condition ($p<0.0001$). No significant differences between the disease subgroups were observed in the frequency of this association, as shown in Table 1.

Table 1 The patient cohort ($n=711$), grouped by diagnosis, and the reported occurrence of autoimmune conditions among their first- and second-degree relatives

Disease	Number of patients	Number of patients with affected relatives
RA	216	98 (45%)
SSc	58	27 (47%)
Psoriatic arthritis	62	36 (58%)
UCTD	42	24 (57%)
Spondylitis	62	34 (55%)
SLE	49	23 (47%)
SS	53	31 (58%)
Systemic vasculitides	39	15 (38%)
MCTD	5	3 (60%)
Behcet's disease	10	6 (60%)
Antiphospholipid syndrome	8	4 (50%)
Polydermatomyositis	22	9 (41%)
Controls	85	21 (25%)

UCTD Undifferentiated connective tissue diseases, *MCTD* mixed connective tissue diseases

Table 2 Distribution of autoimmune diseases among the relatives of the patients

	Patients (%)	Controls (%)
Siblings	27	3
Mothers	18	3
Offspring	14	7
Fathers	8	3
Grandparents	5	0
Grandchildren	1	1

Among the 310 patients, 197 (63%) had one relative, 83 (27%) had two relatives, 27 (9%) had three relatives, one (0.3%) had four relatives, and two (0.7%) had five relatives affected with an autoimmune disease. Among the controls, 17 (81%) had one affected relative and four (20%) had two affected relatives.

Therefore, in our patient cohort, a total of 473 affected relatives were reported. The most common conditions were organ-specific autoimmune diseases (in 358 subjects), beginning with 160 relatives (34%) suffering from autoimmune thyroid (AT) disease and followed by 112 relatives (24%) with psoriasis, 21 relatives with vitiligo, and 19 relatives with IDDM.

Systemic autoimmune diseases were reported in 126 relatives and were distributed as follows: 66 RA (14%), 16 sacroileitis, ten undifferentiated CTDs (UCTDs), eight SLE, seven SSc, eight psoriatic arthritis, six Sjögren's syndrome (SS), three systemic vasculitis, one antiphospholipid syndrome, and one overlap syndrome.

Among the controls, organ-specific autoimmune diseases were observed in 19 relatives (thyroiditis, four; psoriasis, seven; vitiligo, two; IDDM, one) and systemic autoimmune diseases in seven relatives (three RA, one diabetes mellitus, one UCTD, one spondylitis, one overlap syndrome).

Among the patients, first-degree relatives were more frequently affected (13%) than second-degree relatives (6%), in the following order: siblings (27%), mothers (18%), offspring (14%), fathers (8%), grandparents (5%), and grandchildren (1%) (Table 2).

A significant difference was observed in the prevalence of AT disease between the relatives of the patients and controls (3% versus 0.5%).

Discussion

In the present study, we evaluated by means of patient interviews the prevalence of organ-specific and systemic

autoimmune diseases among the first- and second-degree relatives of patients with CTDs, RA, and spondyloarthropathies being followed at our hospital units.

We found a higher prevalence of autoimmune conditions among the relatives and in particular among the mothers and siblings of patients compared with controls. The most frequently reported condition was AT disease, which was observed in 34% of the affected relatives, followed by psoriasis (24%) and RA (14%).

On average, systemic and organ-specific autoimmune diseases occur in 5–8% of the general population. A familial aggregation for autoimmune conditions has been described in patients with CTDs, as well as AT disease and celiac disease [1–15].

To evaluate the familial aggregation of systemic autoimmune diseases, it is necessary to determine the prevalence of these conditions among individuals with different degrees of kinship. The majority of published studies have examined homozygous twins or individuals who share 50% of their genetic background (parents, brothers, dyzygous twins) compared with individuals who are not genetically related. For the CTDs, the data suggest a concordance rate of about 30% among homozygous twins and 2–5% among dyzygous twins and brothers, while in the general population the prevalence of these conditions varies between 0.1% and 1%.

In patients with CTDs, a familial aggregation for systemic and organ-specific conditions has been reported. In the majority of studies, first-degree relatives appear to be more frequently affected [1–10].

In the Grupo Latinoamericano de Estudio del Lupus Eritematoso cohort, a familial aggregation of autoimmune conditions among SLE patients was observed. It is interesting that, as in our study, an increased prevalence of AT disease was observed [2].

Similar results have been reported for SS, where relatives of SS patients were found to be primarily affected by AT disease, vitiligo, and IDDM [3, 4].

A higher occurrence of autoimmune disorders among the relatives of juvenile RA (JRA) patients has also been reported. In a recent study, a prevalence of 12.6% was observed among relatives versus 4% among controls. The only disorder that showed a statistically different rate of occurrence between JRA families and control families was HT, with the authors reporting a frequency of 6.1% and 5.1%, respectively, in the first- and second-degree relatives of JRA patients versus 2.1% and 1.3% in the relatives of controls [9].

Similarly, in our cohort, we found a high prevalence of AT disease among the first- and second-degree relatives of patients: 34% of the first-degree relatives and 3% of the second-degree relatives. It must be taken into account, in addition, that subclinical hypothyroidism has been associated with a number of conditions (including obstetric pathology, dementia, and cardiac complications) and AT disease may be difficult to diagnose [16].

One major limitation of the present study is the fact that the data were gathered indirectly, through interviews with patients and not with the relatives themselves. Nonetheless, we believe that our data are reliable since our evaluation was restricted to close relatives, regarding whom it can be supposed that the patients had a good knowledge of any eventual autoimmune conditions.

Disclosures None

References

1. Steinsson K, Alarçòn-Riquelme ME (2005) Genetic aspects of rheumatic diseases. Scand J Rheumatol 34:167–177
2. Alarçòn-Segovia D, Alarçòn-Riquelme ME, Cardiel MH, Caeiro F, Massardo L, Villa AR et al (2005) Familial aggregation of systemic lupus erythematosus, rheumatoid arthritis, and other autoimmune diseases in 1,177 lupus patients from the GLADEL cohort. Arthritis Rheum 52:1138–1147
3. Anaya J-M, Tobon GJ, Vega P, Castiblanco J (2006) Autoimmune disease aggregation in families with primary Sjögren's syndrome. J Rheumatol 33:2227–2234
4. Scofield HR, Bruner GR, Harley JB, Namjou B (2007) Autoimmune thyroid disease is associated with a diagnosis of secondary Sjögren's syndrome in familial systemic lupus. Ann Rheum Dis 66:410–413
5. Fietta P (2004) Systemic vasculitides: immunogenetics and familial clustering. Clin Exp Rheumatol 22:238–251
6. Prokunina L, Alarçòn-Riquelme M (2004) The genetic basis of systemic lupus erythematosus—knowledge of today and thoughts for tomorrow. Hum Mol Genet 13:R143–R148
7. Alarçòn-Riquelme ME (2006) The genetics of systemic lupus erythematosus: understanding how SNPs confer disease susceptibility. Springer Semin Immunopathol 28:109–117
8. Klareskog L, Padyukov L, Ronnelid J, Alfredsson L (2006) Genes, environment and immunity in the development of rheumatoid arthritis. Curr Opin Immunol 18:650–655
9. Prahalad S, Shear ES, Thompson SD, Giannini EH, Glass DN (2002) Increased prevalence of familial autoimmunity in simplex and multiplex families with juvenile rheumatoid arthritis. Arthritis Rheum 46:1851–1856
10. Plamondon S, Dent PB, Reed AM (1999) Familial dermatomyositis. J Rheumatol 26:2691–2692
11. Marwahah RK, Sen S, Tandon N, Sahoo M, Walia RP, Singh S et al (2003) Familial aggregation of autoimmune thyroiditis in first-degree relatives of patients with juvenile autoimmune thyroid disease. Thyroid 13:297–300
12. Biro E, Szekanecz Z, Czirjak L, Danko K, Kiss E, Szabo NA et al (2006) Association of systemic and thyroid autoimmune diseases. Clin Rheumatol 25:240–245
13. Strieder TGA, Prummel MF, Tijssent JGP, Endert E, Wiersinga WM (2003) Risk factors for and prevalence of thyroid disorders

in a cross-sectional study among healthy female relatives of patients with autoimmune thyroid disease. Clin Endocrinol 59:396–401
14. Cataldo F, Marino V (2003) Increased prevalence of autoimmune diseases in first-degree relatives of patients with celiac disease. J Pediatric Gastroenterol Nutrition 36:470–473
15. Petaros P, Martellossi S, Tommasini A, Torre G, Caradonnan M, Ventura A (2002) Prevalence of autoimmune disorders in relatives of patients with celiac disease. Dig Dis Sci 47:1427–1431
16. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC (2000) The Colorado thyroid disease prevalence study. Arch Intern Med 160:526–534