ACTA MEDICA LITUANICA. 2004. VOLUME 11 No. 4. P. 55–58

Identification of primary Sjogren's syndrome family cases

Diana Mieliauskaitë,
Algirdas Venalis,
Elvyra Redaitienë,
Jolanta Dadonienë,
Vida Graþienë,
Gailutë Kirdaitë

Institute of Experimental and Clinical Medicine at Vilnius University, Vilnius, Lithuania

Author for correspondence: Diana Mieliauskaitë, Þygimantø 9, Vilnius, Lithuania. E-mail: diana.mieliauskaite@ekmi.vu.lt

The aetiology behind Sjogren's syndrome is probably multifactorial and influenced by the genetic and environmental factors that are as yet unknown. A genetic predisposition to Sjogren's syndrome has been suggested on the basis of familial aggregation, animal models and candidate gene association studies.

The aim of the study was identification of primary Sjogren's syndrome family cases.

Patients and methods. 418 patients with sicca ocular and oral symptoms referred by general practitioners and specialists were examined. For primary Sjogren's syndrome diagnosis, modified European classification criteria for Sjogren's syndrome were used. For identification on family cases of primary Sjogren's syndrome we examined family members under suspicion of Sjogren's syndrome by family history. Data on family cases were analyzed using the method of familial analysis of reconstructed cohorts (one family – one cohort) in a case-control study.

Results. There were identified 11 family primary Sjogren's syndrome cases using the modified European classification criteria for Sjogren's syndrome. We identified two primary Sjogren's syndrome cases in each family. The most frequent connection of consanguinity (sisters) was found. The first symptom at the onset of primary Sjogren's syndrome was identical for nine families.

Key words: Sjogren's syndrome, modified European classification criteria for Sjogren's syndrome, primary Sjogren's syndrome family cases

INTRODUCTION

Sjogren's syndrome is a multisystem inflammatory rheumatic disease with cardinal features in the eye and mouth. The aetiology behind this autoimmune exocrinopathy is probably multifactorial and influenced by the genetic as well as by environmental factors that are as yet unknown. A genetic predisposition to Sjogren's syndrome has been suggested on the basis of familial aggregation, animal models and candidate gene association studies (1). Recent advances in molecular and genetic methodologies should further our understanding of this complex disease.

The aim of the present study was identification of primary Sjogren's syndrome family cases.

PATIENTS AND METHODS

418 patients with sicca ocular and oral symptoms referred by general practitioners and specialists (rheumatologists, oculists, dentists, endocrinologists. etc.) were examined at our institution.

For primary Sjogren's syndrome diagnosis, the most functional modified European classification criteria for Sjogren's syndrome, which include a list of exclusions (2–4), were used.

For identification of family cases of primary Sjogren's syndrome we examined family members under suspicion for Sjogren's syndrome by family history, using modified European classification criteria for Sjogren's syndrome. Data of family cases were analyzed using the method of familial analysis of reconstructed cohorts (one family – one cohort) in a case-control study (5).

RESULTS

418 patients with sicca ocular and oral symptoms were examined, and 84 patients with primary Sjogren's syndrome were identified using modified European classification criteria for Sjogren's syndrome. Family history of primary Sjogren's syndrome patients determined suspicion for 68 family cases. We examined members of 68 mentioned families according to mo-

dified European classification criteria for Sjogren's syndrome. There were identified 11 family primary Sjogren's syndrome cases (Table and Fig. 1).

Table 1. **Identification of Sjogren's syndrome family cases**

Family	Number of family members	Number of primary Sjogren's syndrome cases	Gender of primary Sjogren's cases	Relation
I	4	2	Female	Mother + daughter
II	3	2	Female	Sisters
III	4	2	Female	Sisters
IV	3	2	Female	Sisters
V	3	2	Female	Sisters
VI	3	2	Female	Mother + daughter
VII	3	2	Female	Mother + daughter
VIII	3	2	Female	Sisters
IX	3	2	Male + female	Brother + sister
X	3	2	Male + female	Son + mother
XI	3	2	Male + female	Son + mother

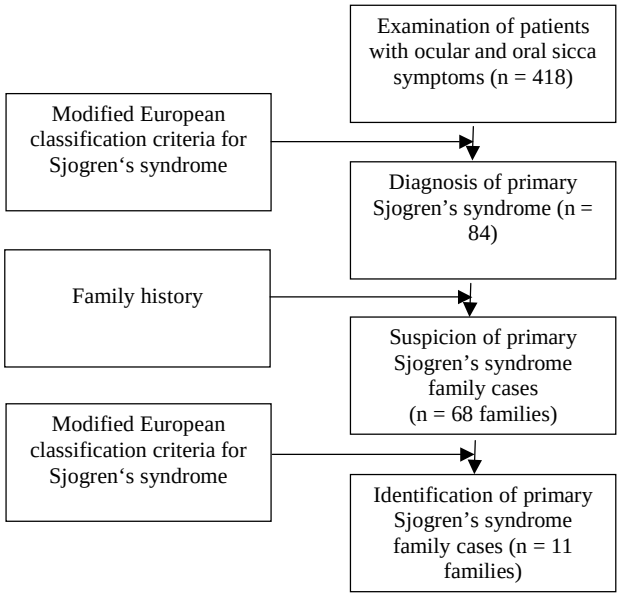

Fig. 1. Identification of primary Sjogren's syndrome family cases

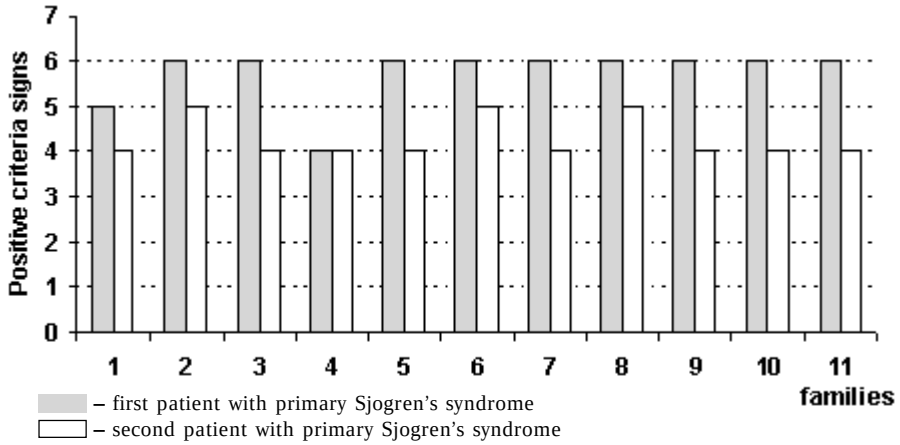

Fig. 2. Positive signs of modified European classification criteria for Sjogren's syndrome

Three or four members of each family were examined. We identified two primary Sjogren's syndrome cases in each family. The most frequent connection of consanguinity – sisters – was found.

Primary Sjogren's syndrome was diagnosed by four to six positive signs of modified European classification criteria for Sjogren's syndrome in all family cases (Fig. 2). Only members of family IV showed the same positive signs.

An interval of one to eight years between the first sicca symptom and primary Sjogren's syndrome diagnosis was found in members of all families (Fig. 3).

Members of families VII and VIII had the same first symptoms – sicca ocular symptoms and members of families I, II, III, IV, VI, X, XI had sicca oral symptoms. The different first sicca symptoms were found in families V and IX (Fig. 4).

DISCUSSION

Sjogren's syndrome is an autoimmune exocrinopathy of unknown aetiology. The aetiology behind this autoimmune exocrinopathy is probably multifactorial and influenced by both genetic and environmental factors that are as yet unknown. Genetic predisposition to Sjogren's syndrome has been suggested on the basis of familial aggregation, animal models and candidate gene association studies.

There are no common disease-specific diagnostic criteria for Sjogren's syndrome. For the diagnosis, most functional are modified European classification criteria, which include a list of exclusions (1).

For identification of eleven primary Sjogren's syndrome family cases we used modified European classification criteria for Sjogren's syndrome.

Genetic predisposition to Sjogren's syndrome does appear to exist, and several families involving two or more cases of Sjogren's syndrome have been described. Most of patients in our study were females. Sjogren's syndrome occurs at all ages.

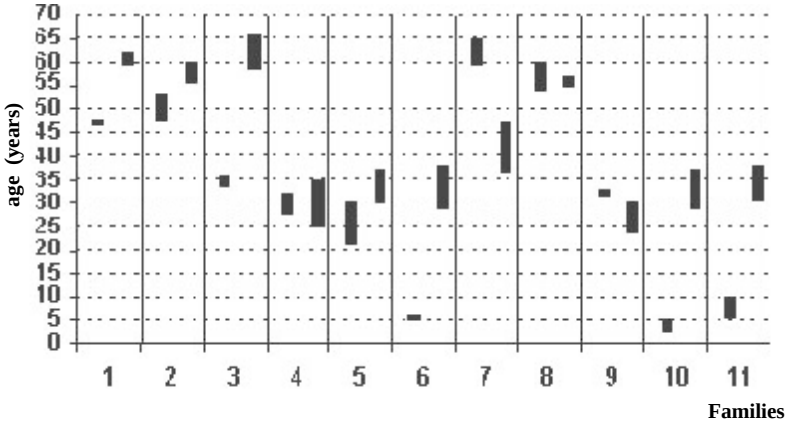

Fig. 3. Interval between first sicca symptom and diagnosis of primary Sjogren's syndrome

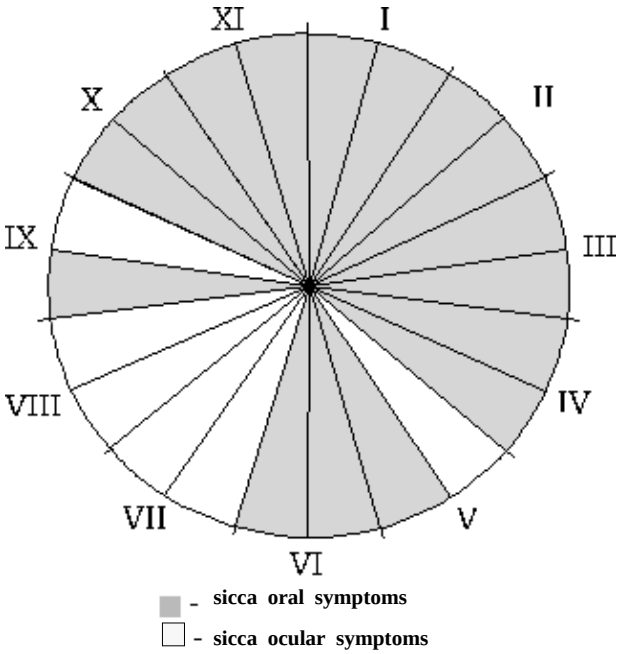

Fig. 4. First sicca symptoms of primary Sjogren's syndrome family cases

The female male ratio of incidence is 9:1 (1). The most frequent connection of consanguinity (sisters) was found in our study.

The level of genetic contribution in Sjogren's syndrome is not known. Since large twin studies in Sjogren's syndrome are lacking, the twin concordance rate cannot be estimated. Only a few case reports describing twins with primary Sjogren's syndrome are available (1, 6, 7). Twins exhibited a very similar phenotype with an almost identical clinical presentation, including sicca ocular and oral symptoms, similar serological data and identical labial salivary gland focus scores.

Primary Sjogren's syndrome was diagnosed by 4 to 6 positive signs of modified European classification criteria for Sjogren's syndrome in all family cases. Members of only one family showed the same positive signs.

An interval of one to eight years between the first sicca symptom and primary Sjogren's syndrome diagnosis was found in members of all families.

Members of families VII and VIII had the same first symptoms – sicca ocular symptoms and members of families I, II, III, IV, VI, X, XI had sicca oral symptoms.

The different first sicca symptoms were found in V and IX families.

Human linkage studies of Sjogren's syndrome families, in addition to analyses of gene expression signatures on microarrays, will probably be an important source of information in the future. Identification of new genetic markers may lead to development of better diagnostic and prognostic tests in Sjogren's syndrome, including its systemic complications. However, as with the other rheumatic diseases, it is anticipated that both overlap and discrepancies will be detected during genome screens. Given the likely heterogeneity of Sjogren's syndrome, advances will probably not be made without future global collaboration.

CONCLUSIONS

1. There were identified 11 familial primary Sjogren's syndrome cases by using modified European classification criteria for Sjogren's syndrome.

2. We identified two primary Sjogren's syndrome cases in each family.

3. The most frequent connection of consanguinity (sisters) was found.

4. The first sicca symptom of primary Sjogren's syndrome was identical for nine families.

Received 11 May 2004
Accepted 15 October 2004

References

1. Bolstad AI, Jonsson R. Genetic aspects of Sjogren's syndrome. Arthritis Res 2002; 4: 353–9.
2. Vitali C, Bombardieri S, Moutsopoulos HM, Balestrieri G, Bencivelii W. Bernstein RM, Bjerrum KB, Braga S, Coli J, de Vita S et al. Preliminary criteria for the classification of Sjogren's syndrome. Results of prospective concerted action supported by European Community. A proposal for modification of the European classification criteria for Sjogren's syndrome. Arthritis Rheum 1993, 36: 340–7.
3. Vitali C, Bombardieri S, Moutsopoulos HM, and European Study Group for the Classification Criteria for Sjogren's syndrome. Clin Exp Rheum 2000; 18: 118.
4. Manthrope R. Sjogren's syndrome criteria. Ann Rheum Dis 2002; 61: 482–4.
5. Rothman KJ, Greenland S. Modern Epidemiology (USA) 1998; 609–21.

6. Sabio JM, Milla E, Jimenez-Alonso J. A multicase family with primary Sjogren's syndrome. J Rheumatol 2001; 28: 1932–4.
7. Bolstad AI, Haga HJ, Wasmuth R, Jonsson R. Monozygotic twins with primary Sjogren's syndrome. J Rheumatol 2000; 27: 2264–6.

D. Mieliauskaitë, A. Venalis, E. Redaitienë, J. Dadonienë, V. Graþienë, G. Kirdaitë

PIRMINIO SJOGRENO SINDROMO ÐEIMINIØ ATVEJØ IÐAIÐKINIMAS

S a n t r a u k a

Sjogreno sindromo etiologija nëra iðaiðkinta iki galo; manoma, kad ji yra multifaktorinë ir jos atsiradimà lemia genetiniai bei aplinkos veiksniai. Galvoti apie genetiná polinká sirgti Sjogreno sindromu skatina ðeiminiai ðios ligos atvejai, gyvûnø modeliø bei genø – „kandidatø" ryðiø tyrimø rezultatai.

Darbo tikslas. Išaiškinti pirminio Sjogreno sindromo šeiminius atvejus.

Tiriamieji asmenys ir metodai. Dël akiø ir burnos sausumo simptomø konsultavome 418 ligoniø. Ligoniams diagnozuotas pirminis Sjogreno sindromas pagal modifikuotus Europos Sjogreno sindromo klasifikacijos kriterijus. Pagal ðeimos anamnezæ átarus pirminá Sjogreno sindromà bent vienam ðeimos nariui, giminystës ryðiais susijæ serganèiøjø pirminiu Sjogreno sindromu ðeimos nariai buvo tirti panaudojus tuos paèius diagnostinius kriterijus siekiant iðaiðkinti, ar jie neserga pirminiu Sjogreno sindromu. Pirminio Sjogreno sindromo ðeiminiø atvejø tyrimo duomenys analizuoti rekonstruotos kohortos metodu (viena ðeima – kohorta), lyginant kohortos ligos atvejus su atveju-kontrole.

Rezultatai. Pagal modifikuotus Europos Sjogreno sindromo klasifikacijos kriterijus iðaiðkinta 11 ðeiminiø pirminio Sjogreno sindromo atvejø. Pirminio Sjogreno sindromo ðeiminiø atvejø grupëje iðaiðkinta po du pirminio Sjogreno sindromo atvejus. Dauguma serganèiøjø – moterys; daþniausiai pasitaikantis giminystës ryðys – seserys. Pirminio Sjogreno sindromo ðeiminiø atvejø grupëje pirmieji sindromo simptomai sutapo abiem ðeimos nariams devyniose ðeimose.

Raktaþodþiai: Sjogreno sindromas, modifikuoti Europos Sjogreno sindromo klasifikacijos kriterijai, pirminio Sjogreno sindromo šeiminiai atvejai