Identification of primary Sjogren’s syndrome family cases

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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-
Examination of patients with ocular and oral sicca symptoms (n = 418)

Diagnosis of primary Sjogren's syndrome (n = 84)

Suspicion of primary Sjogren's syndrome family cases (n = 68 families)

Identification of primary Sjogren's syndrome family cases (n = 11 families)

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).

Modified European classification criteria for Sjogren's syndrome

Identification of Sjogren's syndrome family cases

Table 1. Identification of Sjogren's syndrome family cases

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

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

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

- first patient with primary Sjogren's syndrome
- second patient with primary Sjogren's syndrome

Most of patients in our study were females. Sjogren's syndrome occurs at all ages.
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.

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PIRMINIO SJOGRENO SINDROMO ŠEIMINIO ÅTVEJØ ÐEIMIKINIMAS

Santrauka
Sjogreno sindromo etiologija nėra išaiškinta iki galo; manoma, kad ji yra multifaktorinė ir jos atsiradimà lemia genetiški bei aplinkos veiksniai. Galvoti apie genetiná polinká sirti Sjogreno sindromu skatina šeiminiai šios ligos atvejai, gynimo modeliai bei geno – „kandidato“ ryšas tyrimo rezultatai.

Darbo tikslas. Išaiškinti pirminio Sjogreno sindromo šeiminius atvejus.

Tiriamieji asmenys ir metodai. Dėl akio ir burnos sausumo simptomø konsultavome 418 ligoniø. Ligoniams diagnozuotas pirminis Sjogreno sindromas pagal modifikuotus Europos Sjogreno sindromo klasifikacijos kriterijus. Pagal ðeimos anamnezë ðeimui pirminà Sjogreno sindromà bent vienam ðeimos nariui, giminystës ryðiais susijà ir pirminiai Sjogrenos sindromas ðeimos nariai buvo tirti panaudojus tuos paþius diagnostinius kriterijus siekiant iðaiðkinti, ar jie neserger ir pirminiu Sjogreno sindromu. Pirminio Sjogreno sindromo ðeiminiai atveja tyrimo duomenys analizuoti rekonstruotos kohortos metodu (vieno ðeima – kohorta), lyginant kohortos ligos atvejus su atveju-kontrole.


Raktas: Sjogreno sindromas, modifikuoti Europos Sjogreno sindromo klasifikacijos kriterijai, pirminio Sjogreno sindromo ðeiminiai atvejai