



SHORT REPORT

# Sjogren's syndrome in a patient with ulcerative colitis and primary sclerosing cholangitis: Case report and review of the literature

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Received 12 February 2009; received in revised form 23 March 2009; accepted 23 March 2009

## KEYWORDS

Inflammatory bowel disease;  
Crohn's disease;  
Ulcerative colitis;  
Sicca syndrome;  
Sjogren's syndrome;  
Sclerosing cholangitis

## Abstract

Inflammatory bowel disease has been reported to co-exist with other autoimmune diseases. Sjogren's syndrome is an autoimmune disorder characterized by xerostomy and/or xerophthalmia. Sjogren's syndrome occurring in IBD has been very rarely reported.

A 45-year old woman diagnosed ten years ago with ulcerative pancolitis and primary sclerosing cholangitis was referred to our outpatient IBD clinic because of xerostomy but not for xerophthalmia for the previous three months. The patient had been under azathioprine maintenance treatment (2 mg/kg) and achieved long-term disease remission for the past 4 years. Patient clinical examination and laboratory tests were unremarkable. Salivary gland biopsy and complete ophthalmologic investigation were performed and the patient was diagnosed with Sjogren's syndrome.

Understanding sicca manifestations in IBD is difficult since the pathogenesis of this intestinal disorder is not yet clear. Of these complex autoimmune phenomena which occur along with IBD it is quite difficult to categorize concomitant Sjogren's syndrome as primary or secondary and literature is conflicting. The possibility of Sjogren's syndrome should always be considered and properly investigated in patients diagnosed with inflammatory bowel disease who develop a constellation of constitutional sicca symptoms. © 2009 Published by Elsevier B.V. on behalf of European Crohn's and Colitis Organisation.

*Abbreviations:* SS, Sjogren's syndrome; CD, Crohn's disease; IBD, Inflammatory bowel disease; UC, Ulcerative colitis.

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## 1. Introduction

Inflammatory bowel disease (IBD) is a disease of unknown origin which affects both sexes<sup>1–3</sup> and for which many factors (genetic,

autoimmune, allergic, microbiological, psychological) have been suggested. IBD is a chronic systemic disorder often accompanied by extraintestinal manifestations –almost from all systems– mainly from the skin, joints, liver and the eyes.<sup>1–5</sup>

Inflammatory bowel disease (IBD) has been reported to co-exist with other autoimmune diseases. The relationship of IBD in the form of Crohn's disease (CD) or ulcerative colitis (UC) with other extraintestinal autoimmune phenomena has been frequently reported; however, data is still scarce as the exact mechanism(s) linking all these disorders under an umbrella of common pathogenetic mechanisms have not been clearly established. Sjogren's syndrome (SS) is an autoimmune disorder characterized by xerostomy or xerophthalmia. It may also be manifested as a generalized sicca syndrome with both xerostomy and xerophthalmia (dry eye) in patients with or without other concomitant disorders, such as primary sclerosing cholangitis.<sup>6</sup> Sjogren's syndrome has been associated with many of the disorders in which autoimmunity is considered likely to play a major role in pathogenesis and can be primary or secondary.<sup>7</sup> Criteria for secondary SS include subjective dry eye and/or dry mouth symptoms; also the presence of either one of the following: objective evidence of reduced tear formation or salivary flow rate and a positive labial gland biopsy. Sjogren's syndrome concurrently with IBD has very rarely been reported and seems to follow IBD diagnosis.<sup>8</sup> Herein is a report of a patient with ulcerative colitis and primary sclerosing cholangitis who was diagnosed with concomitant secondary Sjogren's syndrome.

## 2. Case report

A 45-year old woman diagnosed ten years ago with ulcerative pancolitis and primary sclerosing cholangitis was referred to the outpatient IBD clinic presenting with xerostomy though without symptoms of xerophthalmia for the three previous months. Patient was under azathioprine maintenance treatment (2 mg/kg) and had achieved long-term disease remission for the past 4 years.

Patient clinical examination and laboratory tests were unremarkable. Immunological tests showed rheumatoid factor positivity but in low titers (1/80).

Due to the severity of symptoms it was decided to further investigate the clinically suspected sicca syndrome.

Salivary gland biopsy and complete ophthalmologic investigation were performed as described previously.<sup>3</sup>

Ophthalmological examination was negative for dry eye or any other ocular abnormality in the patient but the salivary gland biopsy was compatible with Sjogren's syndrome.

Histology of the salivary gland specimen showed diffuse lymphocyte infiltrations strongly supporting the diagnosis of Sjogren's syndrome for this patient.

## 3. Discussion

We reported herein a rare case of a patient with UC and PSC diagnosed with secondary Sjogren's syndrome, which was manifested with xerostomia but not with xerophthalmia. It is noteworthy that very few cases of IBD patients diagnosed with SS have so far been reported [Table 1]. In Crohn's disease, concomitant diagnosis of SS has been reported in five

**Table 1** Overview of inflammatory bowel disease patients diagnosed with Sjogren's syndrome and other concomitant manifestations.

Author (year)	Number of cases	Diagnosis	Other manifestations
Gainey R <sup>7</sup> (1985)	1	Crohn	
Fujimori J <sup>12</sup> (1987)	1	Crohn	Rheumatoid arthritis Lupus erythematosus
Johnson CD <sup>13</sup> (1989)	1	Ulcerative colitis	Sarcoidosis
Triantafillidis J <sup>15</sup> (1994)	2	Ulcerative colitis	
Steuer A <sup>16</sup> (1996)	1	Ulcerative colitis	Selective IgA deficiency
Cox NH <sup>14</sup> (1996)	1	Ulcerative colitis	Sarcoidosis Gastric autoantibodies
Carneros JA <sup>11</sup> (2002)	1	Crohn	Hashimoto thyroiditis
Rhew EY <sup>10</sup> (2003)	1	Crohn	
Foster EN <sup>9</sup> (2005)	1	Crohn	Sweet's syndrome

patients<sup>7,9–12</sup> some of whom also manifest other concomitant disorders, such as Sweet's syndrome,<sup>9</sup> Hashimoto thyroiditis<sup>11</sup> and rheumatoid arthritis with systemic lupus erythematosus.<sup>12</sup>

Ulcerative colitis concurrently with SS has been reported in five cases<sup>13–16</sup>; some of them also manifest other concomitant disorders such as gastric autoantibodies,<sup>14</sup> sarcoidosis<sup>13,14</sup> and selective IgA deficiency.<sup>16</sup>

Understanding sicca manifestations in IBD is difficult, since the pathogenesis of this intestinal disorder is not yet clear. On the other hand, the spectrum of disorders associated with SS is wide and the acronym TOASSUC (thyroiditis, other autoimmunity, Sjogren's syndrome, sarcoidosis, ulcerative colitis) has been suggested some years ago.<sup>14</sup>

Of these complex autoimmune phenomena occurring along with IBD it is quite difficult to categorize concomitant SS as primary or secondary.<sup>7</sup> It seems that in the absence of other known primary causes of SS, the features of some cases with IBD and SS co-existence are suggestive of a direct relationship between these disorders.

Of note, secondary SS in IBD patients may also be related to treatment with sulphasalazine; immunosuppression and withdrawal from sulphasalazine may result in rapid resolution and disappearance of autoantibodies.<sup>16</sup>

According to a six-year post-diagnostic prevalence study of SS, sicca symptoms, tear and saliva production were not decreased in IBD patients as compared to controls, indicating a lack of association between SS and inflammatory bowel disease.<sup>17</sup> By contrast, a recent prospective study demonstrated higher frequency of dry eye in IBD patients, as compared to the background population.<sup>18</sup>

The above patient did not have any symptoms or findings suggestive of dry eye. The prevalence of dry eye in IBD is currently unknown but in the control population of our area the overall prevalence of dry eye is 11%, which is remarkably lower compared to that found in our cohort of IBD patients

**Table 2** Clinical data of IBD patients from the northwest Greece IBD cohort diagnosed with dry eye (n=13).

Patient/ gender	Age	IBD	IBD location	Hospitalized/ outpatient	Maintenance therapy	Other extraintestinal manifestations	Ophthalmologic manifestation	Duration of disease (years)
1/F	29	U.C.	P	O	Mesalazine	No	Dry eye	4 (2003)
2/M	50	U.C.	L	O	AZA	No	Dry eye	20 (1987)
3/F	67	Crohn	S	O	MTX, mesalazine	No	Dry eye, cataract	17 (1990)
4/F	89	U.C.	P	H	Mesalazine	Arthritis, nephrolithiasis	Dry eye	29 (1978)
5/M	52	Crohn	C	H	Mesalazine	Alopecia	Dry eye, conjunctivitis	4 (2003)
6/F	34	U.C.	P	H	AZA, mesalazine	No	Dry eye	1 (2006)
7/F	50	U.C.	P	H	Mesalazine	PSC	Dry eye	14 (1993)
8/M	37	Crohn	S	H	MTX, AZA	Ankylosing spondylitis	Dry eye, cataract, optical neuritis	9 (1998)
9/M	29	Crohn	S+L	H	AZA, mesalazine	No	Dry eye	6 (2001)
10/M	57	U.C.	Pr	O	Mesalazine	No	Dry eye, vasculitis	15 (1992)
11/M	39	Crohn	C	O	AZA	Erythema nodosum	Dry eye	8 (1999)
12/M	48	U.C.	L	O	Mesalazine	No	Dry eye	12 (1995)
13/M	53	U.C.	P	H	AZA, mesalazine	Arthritis	Dry eye	23 (1984)

Abbreviations used in the table: AZA=azathioprine, CD=Crohn's disease (S=small bowel, C=colon), F=female, H=hospitalized, M=male, MTX= methotrexate, O=outpatient, PSC=Primary sclerosing cholangitis, UC=ulcerative colitis (P=pancolitis, L=left-sided, Pr=proctitis).

(22%).<sup>18</sup> Of interest, in our cohort of IBD patients diagnosed with 'dry eyes' [Table 2] was also identified, not however with Sjogren's syndrome, another female patient with ulcerative colitis, PSC and 'dry eye'.

Therapeutic options in patients with IBD and SS syndrome in terms of immunosuppression include standard immunosuppressives such as azathioprine and methotrexate and biological therapies. Azathioprine in standard doses is the basis and seems to be efficient in this group of patients; however, in Crohn's disease patients with concomitant rheumatologic comorbidity, treatment with methotrexate is also a logical approach. Infliximab was successfully used in a patient with Crohn's disease together with Sweet's and SS.<sup>9</sup> However, large clinical experience is lacking.

The clinical course of SS in IBD patients seems not to substantially differ from that of patients without IBD. In the great majority of cases reported so far, SS is manifested many years after the initial IBD diagnosis and its course is rather mild. Moreover, none of the reported SS-IBD patients presented any evidence of gland disease deterioration or even lymphoma diagnosis. According to our experience with 'dry eye' IBD patients,<sup>18</sup> the severity of 'dry eye' symptoms is independent of the IBD course and does not parallel disease exacerbations and bowel symptoms.

To conclude, we believe that the possibility of Sjogren's syndrome should always be considered and properly investigated in patients diagnosed with inflammatory bowel disease who develop a constellation of constitutional sicca symptoms.

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