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Coexistence of Systemic Lupus Erythematosus and Inflammatory Bowel Disease

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Abstract

The coexistence of systemic lupus erythematosus (SLE) and inflammatory bowel disease (IBD) is rare. This report reviews the English and Japanese literature covering the reported cases of concomitant SLE and IBD. We identified 17 cases of concomitant SLE and Crohn's disease (CD) and 13 cases of concomitant SLE and ulcerative colitis (UC). We observed that many patients (19/28) developed SLE before IBD. Furthermore, SLE was almost never active at presentation of IBD, and flares of SLE were uncommon after IBD development.

Keywords: Systemic lupus erythematosus; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis

Introduction

Systemic lupus erythematosus (SLE) and inflammatory bowel disease (IBD) are systemic diseases caused by abnormal immune responses, which are dependent on the interactions between genetic susceptibility and environmental factors [1]. SLE is a multisystem disease that frequently develops in females of childbearing age, whereas IBD is a chronic recurrent disease characterized by intestinal mucosal inflammation; it includes Crohn's disease (CD) and ulcerative colitis (UC) [2].

Autoimmune diseases often coexist [3], and SLE often exists in combination with other collagen disorders such as rheumatoid arthritis and Sjögren's syndrome [4]; however, cases of concomitant SLE and IBD are rare [3]. As a result, there are few systematic literature reviews of concomitant SLE and IBD [3,5].

Methods

We aimed to review the English and Japanese literature on these conditions and summarize the findings in this report. We searched literature using the following keywords: (1) systemic lupus erythematosus and inflammatory bowel disease; (2) systemic lupus erythematosus and Crohn's disease; (3) systemic lupus erythematosus and ulcerative colitis. English and Japanese literature searches were performed using PubMed and Japana Centra Revuo Medicina (Igaku Chou Zasshi), respectively.

After identifying the appropriate literature, we excluded suspected cases of SLE and cases of drug-induced lupus-like syndrome (i.e., induced by IBD treatments such as tumor necrosis factor alpha (TNF-α) blockers and sulfasalazine). Cases of SLE diagnosed according to the American Rheumatism Association criteria were included. IBD (CD or UC) was diagnosed based on endoscopic, histological, and/or clinical findings.

Concomitant SLE and IBD

SLE and IBD have common genetic susceptibilities [2,6,7], and IBD may occur incidentally in patients with SLE [7-9]. We identified 30 cases of concomitant SLE and IBD in the English and Japanese literature. Cases were diagnosed as outlined in the Methods section. Of these, there were 17 cases of concomitant SLE and CD and 13 cases of concomitant SLE and UC.

In most instances, (19/28) SLE developed before IBD. SLE was almost never active at presentation of IBD [1], and flares of SLE were not common after IBD development.

IBD subgroup: cases of SLE and CD: We identified 17 patients who developed concomitant SLE and CD; 11 in the English-language literature [1,2,6-15] and 6 in the Japanese-language literature [16-21]. The patient characteristics are summarized in Table 1. CD was diagnosed on the basis of endoscopic or histological findings in all reports, 14 cases (82%) were female, and the concomitant diagnoses were made between the ages of 15 and 56 years. In total, 11 patients (65%) developed SLE before CD. Yamashita et al. [9] reported that the mean time between SLE and CD development was 12 years among the 6 patients developing CD after SLE. In the 17 reported cases of concomitant SLE and CD, the time interval between the development of SLE and CD was 2-36 years.

Patients with CD who concomitantly develop SLE usually receive drugs such as corticosteroids or sulfasalazine [9]. More recently, TNF-α blockers have also been introduced [9]. With respect to the prognosis of concomitant SLE and CD, drug-refractory cases have been reported [1]. However, remission was no slower than in patients isolated CD: many cases achieved remission with favorable prognoses following drug therapy [1,7]. In cases of concomitant SLE and CD, SLE generally entered remission following either the development of CD or successful treatment [1, 11].

Other presentations of SLE and CD have also been reported, including familial CD, in which SLE developed after CD [6]; a female with SLE and CD, who developed rheumatoid arthritis and Sjögren's syndrome [16]; and 2 cases associated with lupus nephritis [15,17].

IBD subgroup: cases of SLE and UC: In a controlled study, 6.6% patients with UC had at least one additional autoimmune disorder. Conversely, only 2% healthy controls and 1.9% CD patients had at least one autoimmune disorder [4,22,23]. The rate of concurrent SLE and UC has been reported to be 0%-0.5% [22], whereas the incidence of UC in SLE patients is approximately 0.4% (2/520) [2,3,12,23].

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Case	Sex	Age at diagnosis of SLE(years)	Age at diagnosis of CD(years)	SLE prior to CD	Remarks	References
1	F	18	21	+		[1]
2	F	29 or 30	25	–	Familial CD case	[6]
3	F	37?	40	+		[7]
4	F	44?	49	+		[8]
5	F	19	55	+		[9]
6	F	42	55	+		[10]
7	F	41?	39?	–		[11]
8	F	15 or 16	24	+		[12]
9	F	12	15	+		[13]
10	F	21?	28	+		[14]
11	M	14	22	+	Lupus nephritis	[15]
12	F	53	56	+	RA, Sjögren's syndrome	[16]
13	M	34	24	–	Lupus nephritis	[17]
14	F	27	20 or 21	–		[18]
15	F	27 or 28	21 or 22	–		[19]
16	F	38?	30?	–		[20]
17	M	37	46	+		[21]

SLE: systemic lupus erythematosus; CD: Crohn's disease; F: female; M: male; RA: rheumatoid arthritis

Table 1: Characteristics of 17 Patients with Comorbid Systemic Lupus Erythematosus and Crohn's Disease.

Case	Sex	Age at diagnosis of SLE(years)	Age at diagnosis of UC(years)	SLE prior to UC	Remarks	References
1	F	28	42	+	Lupus nephritis	[3]
2	M	43	51	+	Lupus nephritis	[3]
3	F	19	25	+		[3]
4	F	46	41	–		[3]
5	M	24	10	–	Primary sclerosing cholangitis	[4]
6	F	16	16	Sim		[5]
7	F	36	36	Sim		[22]
8	F	42	53	+		[22]
9	F	12	15	+		[23]
10	F	18	21	+	Primary sclerosing cholangitis	[24]
11	M	46	46	+		[25]
12	F	44	54	+	Non-Hodgkin lymphoma	[26]
13	M	31	19	–	Lupus nephritis	[27]

SLE: systemic lupus erythematosus; UC: ulcerative colitis; F: female; M: male; Sim: simultaneous

Table 2: Characteristics of 13 Patients with Comorbid Systemic Lupus Erythematosus and Ulcerative Colitus.

We identified 13 reports of concurrent SLE and UC; 12 English-language literature [3-5,7,22-26] and 1 Japanese-language literature [27]. The case characteristics are summarized in Table 2. UC was diagnosed by either endoscopy or histology in all reports, 9 cases (69%) were females, and the concomitant diagnoses were made between the 15-54 years of age. This was consistent with the findings for concurrent SLE and CD cases. Moreover, 2 patients received diagnoses of SLE and UC at the same time, and 8 of the remaining cases (73%) developed SLE before UC. In the 13 reported cases of concomitant SLE and UC, the time interval between the development of SLE and CD was 0-14 years. In addition, there was no subsequent relapse of SLE when UC developed after SLE [3]. Serious organ involvement was rarely seen [3].

It is noteworthy that 2 of the 13 cases of concomitant SLE and UC also developed primary sclerosing cholangitis [4,24]. Other presentations of SLE and UC were also reported. Bourikas et al. [26] reported a case with SLE and left-sided UC complicated by non-Hodgkin lymphoma. Furthermore, there were 3 reported cases were associated with lupus nephritis [3,27].

Differentiation of gastrointestinal complications of SLE from those of IBD

Gastrointestinal symptoms are common in SLE [2], being present in approximately 50% patients [1]. Occasionally, the gastrointestinal complications of SLE can be difficult to differentiate from those of IBD [6-12] because these conditions present with similar clinical symptoms; furthermore, there are no clear differentiating criteria. Moreover, some CD patients also meet the criteria for SLE, which further complicates the diagnosis. SLE can present with potentially dangerous gastrointestinal complications such as small-vessel vasculitis [2,7]. Although only a few cases of clinically obvious bowel vasculitis associated with SLE have been reported (approximately 2%), the presence or absence of histological vasculitis is useful for differentiating between the gastrointestinal complications of SLE and concurrent IBD [9,10,13]. Despite difficulties in differentiation, endoscopic and histological findings remain beneficial in their diagnosis [1].

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