Concordance of ulcerative colitis in monozygotic twin sisters

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Abstract

The etiology of inflammatory bowel disease is multifactorial and appears to combine both genetic and environmental factors. We experienced here a rare occurrence of woman monozygotic twins with ulcerative colitis (UC). A 45-year-old woman (the elder monozygotic twin) was admitted to our hospital because of bloody diarrhea occurring over 10 times per day, abdominal pain and fever. She was diagnosed as UC at the age of 22, and repeated the relapse and remission. She was diagnosed as relapse of UC and total colitis type. Her younger monozygotic twin sister also suffered from UC at the age of 22. Human leukocyte antigen was examined serologically with DNA type in both patients. DRB1*1502, which was previously shown to be dominant in Japanese patients with UC, was not observed in this case. Although the concordance of monozygotic twin in UC is reported to be 6.3-18.8%, the concordant case like this is relatively rare. We report this rare case of UC and the previously reported cases are also discussed.

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Key words: Ulcerative colitis; Inflammatory bowel disease; Monozygotic twin; Human leukocyte antigen

INTRODUCTION

Ulcerative colitis (UC) is an idiopathic inflammatory bowel disease, which is thought to be multifactorial and appears to combine both genetic and environmental factors. A number of studies have demonstrated aggregation of cases of UC in families, suggesting that patients share a genetic background. The concordance in monozygotic twin in UC is reported to be 6.3-18.8%[1-4]. Although the concordance rate is not so low, patients with twin pairs suffering from UC are relatively rare[5-9] and few observations of the twin pairs with UC have been reported[10-14]. In addition, although previous studies on the associations of UC and human leukocyte antigen (HLA) genes suggest that HLA play a role in this disease, the associations of various HLA loci with UC have yet to be fully elucidated. We experienced here a rare monozygotic twin with UC and determined their HLA serological and DNA type.
revealed that the prevalence of UC is 18.12/100 000 and in European countries, hospital-based investigation in 1991 inflammatory bowel diseases are increasing also in Japan as Japan than in Europe and North America. The prevalence and incidence of UC are much lower in disease in monozygotic twins than in dizygotic twins indicate a higher with that 15.8% monozygotic twins with UC are concordant

Association for Colitis bowel disease from 16 000 members of the National et al. from 6.3% to 18.8% in a Swedish study. The pair concordance rate in monozygotic twins increases with the disease and the proband concordance rate among the UC group, 1 of 16 monozygotic pairs was concordant suffering from inflammatory bowel disease were found. In different places since the younger sister was married and left home. For the purpose of genetic search, HLA was 

Table 1 HLA alleles in the case

| Serological typing | DNA Locus | DR Locus | B Locus | A Locus |
|-------------------|-----------|----------|---------|---------|
| A2                | 0602      | 1302     | 1501    | 0604    |
| A33               | 0602      | 1302     | 1501    | 0604    |
| B44               | 0602      | 1302     | 1501    | 0604    |
| B75               | 0602      | 1302     | 1501    | 0604    |
| DR13              | 0602      | 1302     | 1501    | 0604    |
| DR15              | 0602      | 1302     | 1501    | 0604    |
| DQ1               | 0602      | 1302     | 1501    | 0604    |

DISCUSSION

The pathogenesis of UC and Crohn’s disease is still unknown, but the importance of genetic susceptibility has been clearly shown by epidemiological data from family and twin studies. Several twin studies reported that the concordance rate in monozygotic twin with UC is 6.3-18.8%[1-4]. Tysk et al.[1], used the Swedish twin registry and inpatient hospital records to identify twins affected by inflammatory bowel disease. Among 25 000 pairs of twins identified from the Swedish twin registry, 80 twin pairs suffering from inflammatory bowel disease were found. In the UC group, 1 of 16 monozygotic pairs was concordant with the disease and the proband concordance rate among monozygotic twins was 6.3% for UC. It was reported that the pair concordance rate in monozygotic twins increases from 6.3% to 18.8% in a Swedish study.[10] Thompson et al.[15], also traced 144 twin pairs with inflammatory bowel disease from 16 000 members of the National Association for Colitis and Crohn’s Disease, and found that 15.8% monozygotic twins with UC are concordant with the disease. These studies and case reports all indicate a higher concordance with inflammatory bowel disease in monozygotic twins than in dizygotic twins[1-4]. The prevalence and incidence of UC are much lower in Japan than in Europe and North America[18]. Although inflammatory bowel diseases are increasing also in Japan as in European countries, hospital-based investigation in 1991 revealed that the prevalence of UC is 18.12/100 000 and the incidence is 1.95/100 000 in Japan[13]. Delivery with monozygotic twins is reported to be about 4/1 000. The twin study with UC reported that the concordance rate in monozygotic twins with UC is 6.3-18.8%[1-4]. If prevalence of UC is estimated to be 18.12/100 000, concordance rate to be 18.8% and twin delivery rate to be 4/1 000, concordance twins with UC like this case is estimated to be about 13.6/100 000 000. Thus, concordance twins with UC like this case are about only 13.6 cases in Japan. We searched concordant twins with UC using PubMed by key words ulcerative colitis and twin, and found only 22 cases (Table 2) including our case which was reported.

The apparently conflicting data on the HLA system in different studies from around the world may be explained by differences in ethnics, cases and genetic heterogeneity[16]. Replicated class II HLA includes HLA DRB1*0103 and DR2 (DRB1*1502) involved in UC susceptibility, and HLA DRB1*03 and DR4 as resistant alleles for Crohn’s disease and UC respectively[16]. The strong association between HLA DR2 and UC has been reported in Japan[17], India[18], and Israel[19]. However, these alleles were not observed in our case. HLA could not explain the occurrence of UC in our case.

The role of environmental factors in the pathogenesis of inflammatory bowel disease is still controversial. The lack of complete concordance in monozygotic twin studies underlines the crucial role played by external factors in the determination of disease expression in patients with genetic susceptibility to inflammatory bowel disease. Non-smoking or a cessation of smoking is a proven risk factor for developing UC[20]. Neither of the twins in our case has ever smoked. Inversely, it has been suggested that appendectomy offers protection against the development of UC[21]. Neither of the twins in our case has received appendectomy.
In summary, we have explained here a rare monozygotic twin with UC. HLA serological and DNA typing were performed. Similar twins are reported to be concordant with inflammatory bowel disease; however the concordant rate is only 6.3–18.8% and the accurate number of these cases is rare. Further accumulations of these cases are needed to clarify the contribution of genetic factors to the development of UC.

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Table 2 Previously reported cases and prevalence of concordant twins with UC

| Author (country) | Total number of twin | IBD1 | Ulcerative colitis2 | Number of concordant cases | Concordance (%) | Reference |
|-----------------|----------------------|------|---------------------|-----------------------------|-----------------|----------|
| Tysk,Halvarson (Sweden) | 25 000 | 80 | 16 (Monozygotic) | 1 (3) | 6.3 (18.8) | Gut 1988;29:990-996 |
| Thompson (UK) | 128 | 38 | Monozygotic | 6 | 15.8 | BMJ 1996;312:95-96 |
| Orholm (Denmark) | 29 421 | 103 | Monozygotic | 3 | 14.3 | Scand J Gastroenterol. 2000;35:1075-81 |
| Lyons (USA) | Case report | 1 | | | | Gastroenterol. 1948;10:545 |
| Webb (USA) | Case report | 1 | | | | Gastroenterol. 1950;15:523-4 |
| Bacon | Case report | 1 | Monozygotic | | | Ulcerative colitis. 1958, pp3 J.B.Lippincott Co. |
| Sleight | Case report | 1 | | | | Gastroenterol. 1971;61:507-12 |
| Sanford | Case report | 1 | | | | Am Surg. 1971;37:512-7 |
| Fausa | Case report | 1 | | | | Scand J Gastroenterol. 1972;16 (Suppl):38 |
| Quigley (USA) | Case report | 1 | | | | Postgrad Med J. 1982;58:112-4 |
| Mayberry (UK) | Case report | 1 | | | | Gastroenterol. 1983;85:1160-5 |
| Musiuchi (Japan) | Case report | 1 | | | | Nippon Shokakibyo Gakkai Zasshi. 1995;92:1966-70 |
| Iwaizumi (Japan) | Case report | 1 | | | | Intern Med. 2002;41:629-32 |
| Our case (Japan) | Case report | 1 | | | | |

Total number of concordant cases of ulcerative colitis in monozygotic twins. IBD1: number of twins, one or both pair suffered from inflammatory bowel disease Ulcerative colitis2: number of twins, one or both pair suffered from ulcerative colitis. UK: United Kingdom, USA: United States of America.