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Human intestinal spirochetosis: right-side preference in the large intestine☆

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ABSTRACT

Human intestinal spirochetosis (HIS) is a colorectal bacterial infection, and its clinicopathologic features remain unclear. The aim of this study was to examine its characteristics. We histologically reviewed paraffin-embedded section slides made in 2001, 2006, and 2011 at a single institution in Japan. Cases histologically exhibiting a distinct fringe formation were considered to have HIS. Information was obtained from pathology request forms. We identified 85 HIS cases among 4930 patients (7 cases [0.5%] in 2001, 29 [1.7%] in 2006, and 49 [2.8%] in 2011]. Gastrointestinal symptoms were observed in 7.1% of HIS cases. Human intestinal spirochetosis was more frequent in the right-side large intestine than in the left side. Among 224 samples from HIS cases, conventional (tubular, tubulovillous, and villous) adenomas were found in 148 samples. These adenomas were more frequent in the right side than in the left side, although neither their size nor morphology differed between the sides. Histopathologic evaluation suggested a year-upon-year increasing prevalence of HIS in Japan. A small number exhibited gastrointestinal symptoms. Both histologic sign of HIS and conventional adenomas were more frequent in the right-side large intestine. Therefore, a right-side preference may be a characteristic of HIS.

1. Introduction

Human intestinal spirochetosis (HIS), one of the zoonoses, is caused by colonization by *Brachyspira* species bacteria within human large intestines [1,2]. Since the establishment of the entity of HIS, as long ago as 1967 [3], HIS has been reported from both developing and developed countries, including Japan [4–6]. In developing countries, HIS may be transmitted from infected animals or from contaminated water [1,2,7], whereas in developed countries, there seems to be an association with homosexual behavior in some HIS patients [8]. Most cases are asymptomatic, and some authors have considered HIS to be harmless in humans [1,2]. However, a detailed analysis of HIS cases has not previously been performed, and its clinicopathologic features remain unclear.

To examine the characteristics of HIS, we histologically reviewed samples made at a single institution located in central Japan and performed a clinicopathologic analysis on them.

2. Materials and methods

We histologically reviewed paraffin-embedded section slides that had been made at the JCHO Saitama Medical Center (in Saitama, which is close to Tokyo, Japan). Samples were also provided by endoscopic sections of other hospitals within the same prefecture. The study samples were taken under colonoscopy in 2001, 2006, and 2011. The total numbers of cases reviewed those 3 years were 1459 in 2001 (male-female = 875:584; 13 to 90 years old; median age, 60), 1702 in 2006 (1072:630; 15 to 96 years old; median age, 61), and 1769 in 2011 (1094:675; 13 to 98 years old; median age, 62). Most of the patients were considered immunocompetent. Histologically, the existence of HIS was considered to be indicated by the presence of a distinct, hematoxylinophil fringe formation (ie, a parallel arrangement of spirochetes) on the luminal surface of the colorectal surface epithelium in hematoxylin-eosin–stained glass slides. In some cases, Giemsa-stained glass slides were added for the confirmation of fringe formation. Equivocal cases were excluded from the HIS cases reported in this study. Cases were considered to have HIS when one and over sample histologically exhibited a distinct fringe formation.

Information about clinical manifestations, endoscopic findings, and the colorectal regions providing samples was obtained from pathology request forms. In the statistical analysis, a χ^2 test and unpaired t test were performed. This study was approved by the local ethics committee of the JCHO Saitama Medical Center (approval no. 14-15 [April 28, 2014]).

☆ Conflict of interest: none.

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3. Results

The prevalence of HIS was found to be 0.5% (7 of 1459 cases) in 2001, 1.7% (29 of 1702) in 2006, and 2.8% (49 of 1769) in 2011, and thus it apparently increased progressively over that period. Its prevalence in males averaged 2.4% in those 3 years (0.8% in 2001, 2.3% in 2006, 3.7% in 2011), whereas in females, it was only 0.6% (0% in 2001, 0.6% in 2006, and 1.2% in 2011). Human intestinal spirochetosis was found significantly more frequently in males than in females ($P < .05$). The HIS cases were distributed between 28 and 77 years of age, with median age seeming quite similar between HIS and non-HIS cases. Moreover, the monthly prevalence data did not reveal any obvious seasonality for HIS (Table 1).

To judge from the clinical and endoscopic findings reported on by the pathology request forms (Table 2), most of the HIS cases seemed to have a relation to polyps. Gastrointestinal symptoms (eg, diarrhea, soft stool, and abdominal pain) were exhibited by 6 HIS cases (7.1%). Inflammation was also found endoscopically in 10 HIS cases (11.8%).

Examination of the positive rate for HIS among 229 samples from 85 HIS cases—in which the median number of samples taken from the large intestine was 2—revealed that a distinct fringe formation was observed in 70.7% of such samples (Table 3). When we analyzed the relationship between the colorectal regions providing the samples and fringe formation among the 84 HIS cases for which sample-site information was available (Table 4), fringe formation was present in 63.6% of 11 cecum samples, 82.2% of 45 ascending colon samples, 69.4% of 49 transverse colon samples, 58.8% of 17 descending colon samples, 75.9% of 54 sigmoid colon samples, and 54.9% of 51 rectum samples. When the large intestines were divided for the analysis into 2 regions (right side: from cecum to transverse; left side: from the splenic flexure to rectum), HIS was found significantly more frequently in the right side than in the left (74.3% vs 64.8%; $P < .05$).

We analyzed the relationship between the histologic types of lesions and the HIS-positive rate among the HIS cases. We focused our attention on 5 lesions (viz, inflammation, hyperplastic nodule [mucosal thickening that is histologically similar to hyperplastic polyp but without epithelial serration], serrated polyp, conventional [tubular, tubulovillous, and villous] adenoma, and adenocarcinoma) while excluding diagnostic categories (scar [2 samples], lymphangioma [2 samples], and colonic mucosubmucosal elongated polyp [1 sample]) other than the above 5. Although a distinct fringe formation was frequently detected in normal regions around the neoplastic lesions, we recognized such lesions as HIS positive. Positive rates for HIS among these diagnostic categories were between 40% and 80%. Among 224 samples from 84 HIS cases, a fringe formation was found in 59.3% of 27 inflammation samples, in 80.0% of 20 hyperplastic nodule samples, in 63.2% of 19 serrated polyp samples, in 72.3% of 148 conventional adenoma samples, and in 40.0% of 10 adenocarcinoma samples (Table 5). However, no characteristic relation between histologic diagnosis and the examined year was found. Next, when we analyzed the relationship between histologic types of lesions and colorectal regions in 222 HIS samples from the 83 HIS cases for which sample-site information was available, conventional adenomas were observed more frequently in the right side than in the left side (80 samples in the right vs 66 in the left; Table 6), whereas inflammation, hyperplastic nodules, and serrated polyps were each less frequent in the right side than in the left. Furthermore, we analyzed the relationship among size, morphology, and HIS-positive rate for each of the 89 conventional adenomas for which information about site, size, and morphology was available (Table 7). Concerning morphology, conventional adenomas were more frequently of the sessile type than of the pedunculated type, whereas size was smaller for the sessile type than for the pedunculated type. Positive rates of HIS in conventional adenomas did not differ between these 2 groups. No difference in either the size or morphology of conventional adenomas could be detected between the 2 sides.

Table 1
Relationship between examination month and HIS-positive rate in 3-year cumulative data.

	Jan	Feb	Mar	Apr	May	Jun	
Total cases (n)	355	402	401	387	406	420	
HIS cases (n)	5	6	13	8	3	8	
(%)	1.4	1.5	3.2	2.1	0.7	1.9	
	Jul	Aug	Sep	Oct	Nov	Dec	Overall
Total cases (n)	462	422	368	462	413	430	4928
HIS cases (n)	7	12	6	4	5	8	85
(%)	1.5	2.8	1.6	0.9	1.2	1.9	1.7

Table 2
Clinical and endoscopic findings in HIS cases.

	2001	2006	2011	Overall cases (%)
HIS cases (n)	7	29	49	85 (100)
Clinical findings				
Extensive testing for polyps	7	10	16	33 (38.8)
Positive for occult fecal blood	0	8	11	19 (22.4)
Gastrointestinal symptoms	0	1	5	6 (7.1)
Endoscopic findings				
Polyps	7	28	45	80 (94.1)
Diverticula	2	6	9	17 (20.0)
Inflammation	2	2	6	10 (11.8)

4. Discussion

From our detailed clinicopathologic analyses of HIS cases in a regional medical center located in central Japan, we identified 4 important characteristics of HIS as follows: (1) HIS was encountered rarely, but increased year upon year, in Japan; (2) most of the HIS cases seemed to have a clinical relation to polyps, but a small number of cases exhibited gastrointestinal symptoms and endoscopic inflammation; (3) HIS was found more frequently in the right-side large intestine than in the left side; and (4) in HIS cases, conventional adenomas were observed more frequently in the right-side large intestine than in the left side, although generally they are relatively more frequent in the left side [9]. On the basis of these results, we propose that HIS may be related to the development of neoplastic lesions.

In the previous literature on HIS in Japan, its prevalence was reported to be less than 1% [5]. In the present study, however, its prevalence increased progressively year upon year, reaching 2.8% in 2011. Our medical center is a general hospital located in central Japan, and participants ranged from apparently healthy persons who had an annual health checkup to patients exposed to extensive testing. Hence, the present study may have provided an insight into the representative features of HIS in Japan. On the other hand, there was a male predominance among the total cases examined, and a significant male predominance was also confirmed among HIS cases in the present study, although the reason is not yet known.

The transmission routes for HIS in Japan remain unclear. If HIS depends upon transmission from infected wild animals or contaminated water, a seasonality of infection might be expected. However, we could find no obvious seasonality among our HIS cases, although it is possible that an indolent infection with mild clinical symptoms might mask such seasonality. Few immunocompromised patients were included in

Table 3
Number of samples per case and HIS-positive rate among 229 samples from 85 HIS cases.

	2001	2006	2011	Overall
Cases (n)	7	29	49	85
Median no. of samples per case	5	2	2	2
Min-max	2-8	1-14	1-6	1-14
HIS-positive rate (% of samples)	60.0	73.7	71.7	70.7