Peculiar Histopathological Features of Giardiasis in Distal Duodenal Biopsies

Pages with reference to book, From 206 To 209

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Abstract

Histological changes in 20 Giardia positive duodenal biopsies (Group A) were compared with 50, Giardia negative duodenal biopsies (Group B), taken during the same period. Stool examinations in Group B were negative for Giardia. Surface epithelium, villous and crypt architecture and cellular infiltrates were examined and compared between the groups. Atrophic changes in the villi were more common in Group A as compared to B(P<0.0001). lntraepithelial neutrophil infiltration (P<0.001), infiltration of the lamina propria with plasma cells (P<0.4), and presence of eosinophils in the lamina propria (PcO.001) were significant findings in group A. Some of the changes were related to the density of Giardia colonization e.g., the goblet celldepletion (P<0.05) and the density of plasma cell infiltration in lamina propria (PcO.01). Erosions and ulcerations were less commonly seen in group A. Thus we conclude that giardiasis manifests its peculiar features in the distal duodenal mucosa and a biopsy of this region is an important diagnostic tool for detection of this disease. (JPMA 44:206,1994).

Introduction

Giardiasis is a disease of the small intestine caused by the flagellated protozoan, Giardialamblia. It has a worldwide distribution. There is an extreme variation in the clinical response to Giardia in man[1]. Patients may remain asymptomatic, develop diarrhoea[2,3] and later on malabsorption[4] or present with symptoms of dyspepsia such as bloating belching, nausea or epigastric discomfort. The histological[5-8] and immunological[9-13] responses are also variable. Available methods for diagnosis of giardiasis include stool examination[14-17] the enterotest[18], duodenal aspirate[19-21] endoscopic brush cytology[22], biopsy examination[23-26] and inununodiagnostic techniques[27-32]. In the developing world where Giardiasis still remains one of the important unresolved health problems, selection of a single and reliable diagnostic technique remains elusive[33]. In order to define the histopathological changes associated with giardiasis, we reviewed our cases diagnosed on distal duodenal biopsy alone.

Materials and Methods

Twenty consecutive cases of giardiasis (Group A), diagnosed between 1990 and 1992, on histopathological evaluation of distal duodenal biopsies, were included in this study. These biopsies were taken from the distal most accessible part of the duodenum during upper gastrointestinal endoscopy. Fifty cases were selected from all the distal duodenal biopsies done during the same period using simple random sampling (Group B). These patients had upper gastrointestinal complaints and duodenal biopsies were routinely obtained. Both the biopsies and the stool examinations of these patients were negative for Giardia. The specimens were fixed in 10%bufferedformalinand embedded in paraffin wax. Atleast, seven sections were obtained on the microtome for each specimen, each 3-5 um thick, and stained with haematoxylin and eosin. In doubtful cases, sections were stained with Giemsa\'s. All the slides were reviewed under the light microscope prospectively in accordance with a

designed proforma. Surface epithelium was reviewed for nature of cells, whether columnar or cuboidal, and for erosions orulcerations; focal ordiffuse. Erosions were defined as superficial denuded areas involving the upper third of mucosa while ulcerations were considered as excavating lesions involving more than two thirds of the mucosa. The pattern was defined semi-quantitatively as (a) normal, (b) shortened and widened, (c) partial atrophy and (d) subtotal atrophy. The crypts were examined for distortion, elongation, branching and irregularity and the crypt-villous ratio was recorded, normal being 1:3. Crypt hyperplasia was graded as mild, moderate or severe depending on the number of mitoses, hyperchromasia and cellular stratification. Type of cellular infiltration in the surface epithelium and lamina propria was noted and graded for presence o lymphocytes, plasma cells, eosinophils and neutrophils. Lymphoid follicles were defined as focal aggregates of lymphocytes with or without genninal centres. Two more histopathological features were defined for group A only - Goblet cell depletion in the surface epithelium and density of plasma cell infiltrate in the lainina propria. Goblet cells were graded semi-quantitatively as normal or reduced when viewed under high power and plasma cell infiltrates as normal, Grades I, II and Ill. The relative density of colonization by Giardia was determined as Grade I: <5, Grade II: 5-10, Grade Ill:>l0 organisms seen per high power field. Histopathological findings were analyzed using dBASE lIT PLUS and SPSS computer packages. P value was calculated by applying Chi square with Yate's correction.

Results

The number of cases in Group A were 20, 14 males and 6 females, a ratio of 2.3:1 and a meanage of 38.6 years (Mean age ± standard deviation = 38.6±16.2), ages ranging between 22 to 66 years. The number of cases in group B were 50, 28 males and 22 females, a ratio of 1.3:1 and a mean age of 35.2 years (Mean age±standard deviation = 35.2±17.7), ages ranging between 17-72 years. The histological changes have been described below as a comparison between the two groups, along with their respective P values. (Table I, Figures 1-3).

Table I. Histopathological changes in giardiasis and controls - a comparison.

Histopathological Characteristics	Giardia Present (Group A) n=20	Giardia Absent (Group B) n=50	P Value (Yates corrected)
Surface epithelium			
Columnar	20(100)	49(98)	
Cuboidal	00(0)	01(2)	
Erosions			
Focal	02(10)	13(26)	
Diffuse	00(0)	03(06)	
Absent	18(90)	34(68)	
Ulcerations			
Focal	01(05)	03(06)	N.S
Diffuse	00(0)	02(04)	(Characteristic
Absent	19(95)	45(90)	# 2 and 3 present vs absent
Nuclear Alignment			
Regular	19(95)	33(66)	0.05*
Irregular	01(05)	17(34)	
Villi			
Normal	06(30)	41(82)	0.001*
Short and wide	12(60)	08(16)	(Normal vs
Partial atrophy	02(10)	01(02)	Abnormal)
Crypt architecture			
Normal	17(85)	27(54)	0.05*
Distorted	03(15)	23(46)	
Crypt-Villous Ratio			
Normal	11(55)	43(86)	0.05*
Altered	09(45)	07(14)	
Crypt Hyperplasia			
Normal	14(70)	16(32)	0.05*
Mild	05(25)	25(50)	(Normal to mild
Moderate	01(05)	06(12)	vs Moderate to
Severe	00(0)	03(06)	Severe)
Surface Epithelium			
Cellular Infiltrate			
Lymphocytes	08(40)	14(28)	N.S
Neutrophils	15(60)	04(08)	0.001*
Density of Infiltrate			
Grade I	15(75)	12(24)	0.001*
Grade II	03(15)	03(06)	(present vs
Grade III	02(10)	35(70)	absent)
Lamina Propria			
Cellular Infiltrate			
Lymphocytes	08(40)	47(94)	0.0001*
Plasma cells	20(100)	37(74)	0.05*
Eosinophils	17(85)	09(98)	0.001*
Neutrophils	00(0)	03(06)	N.S
Density of Infiltrate			
Grade I	01(05)	22(44)	0.001*
Grade II	15(75)	22(44)	(Normal and I vs
Grade III	04(20)	04(08)	II & III)
Normal	00(0)	02(04)	
Lymphoid Aggregates			
Present	04(20)	05(10)	N.S
Absent	16(80)	45(90)	
Muscularis Mucosa			
Normal	07(35)	15(30)	
Thickened	01(05)	20(40)	
Absent in Biopsy	12(60)	15(30)	

* = Statistically significant value. Percentages are given in Parentheses

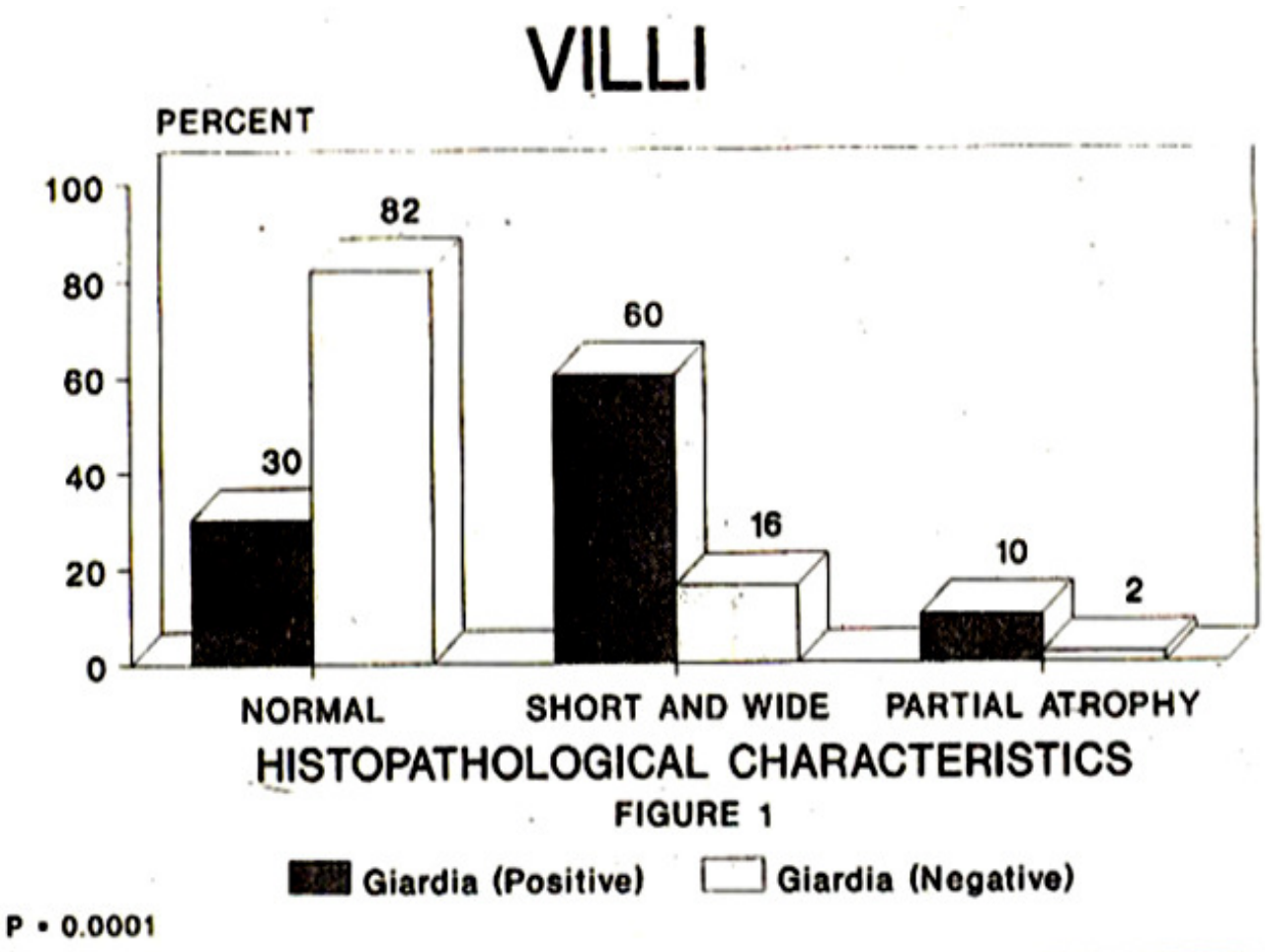
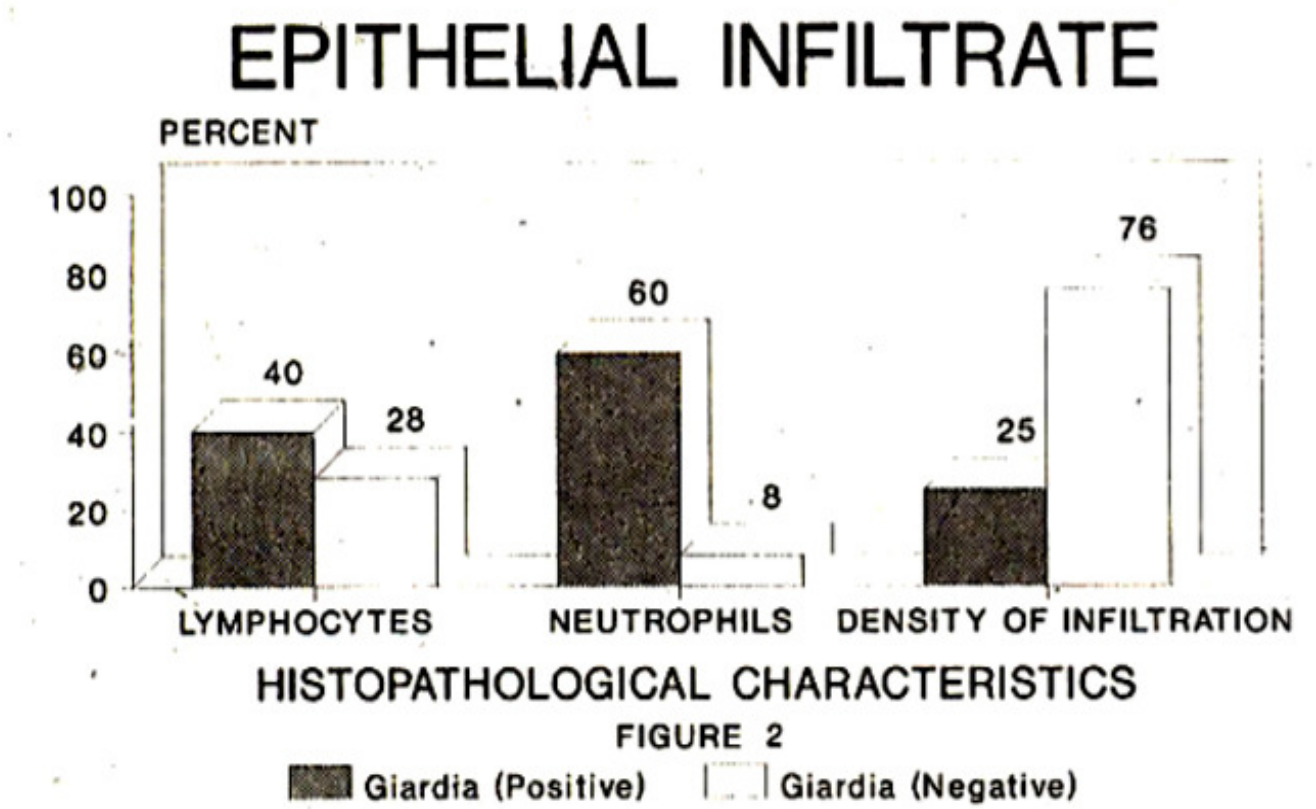


Figure 1. Histopathological characteristics - Villi.



P=0.489 (LYMPHOCYTES)
P=0.0000001 (NEUTROPHILS)
P=0.00002 (DENSITY)

Figure 2. Histopathological characteristics - Epithelial Infiltrate.

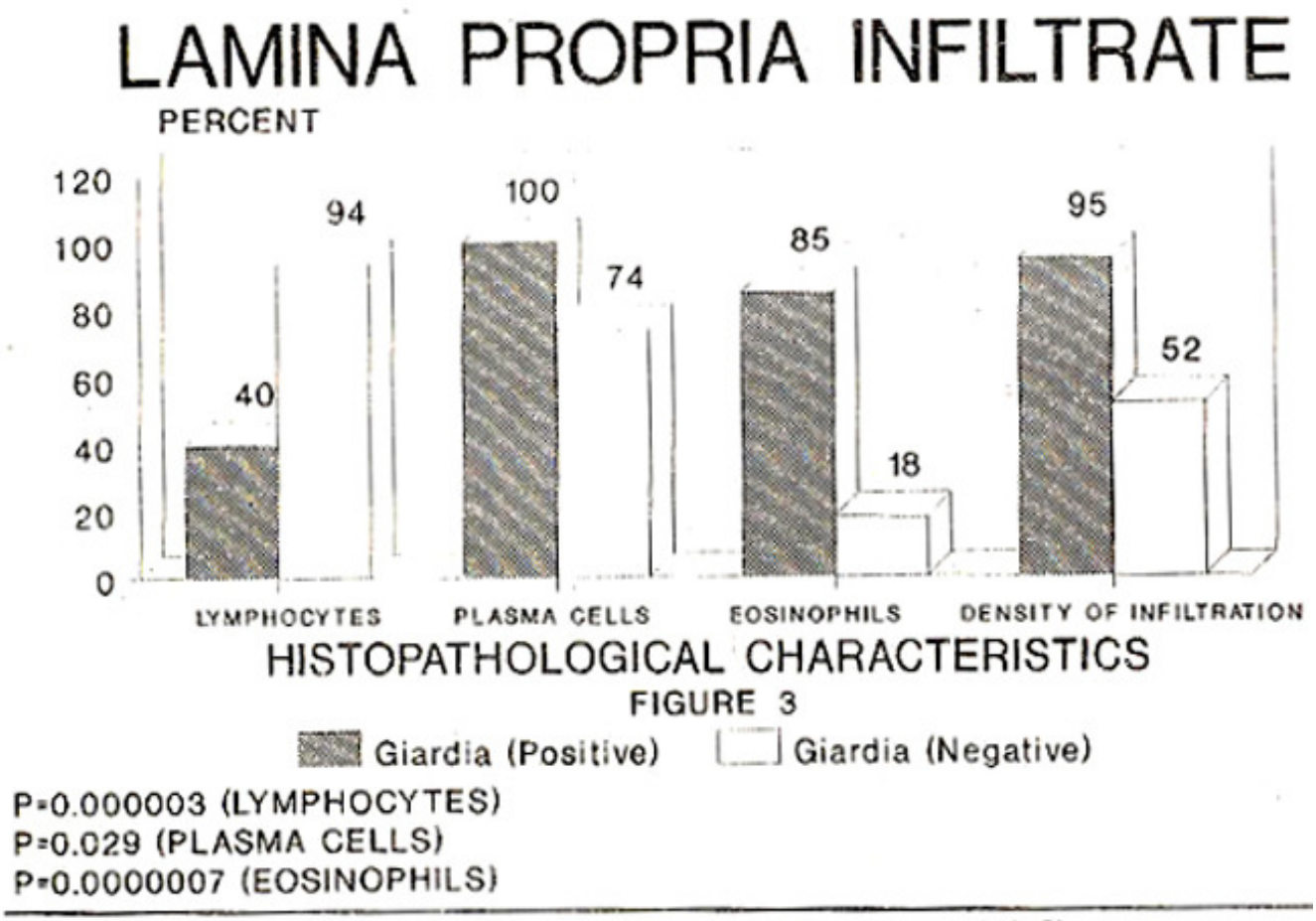


Figure 3. Histopathological characteristics - Lamina propria infiltrate.

Atrophic changes in the viIIi, crypt hyperplasia, intnepithelial neutrophil infiltration, plasma cell predominance in the lanilna propria along with lymphocytes and eosinophil presence were the significant features of group A (Figure 4).

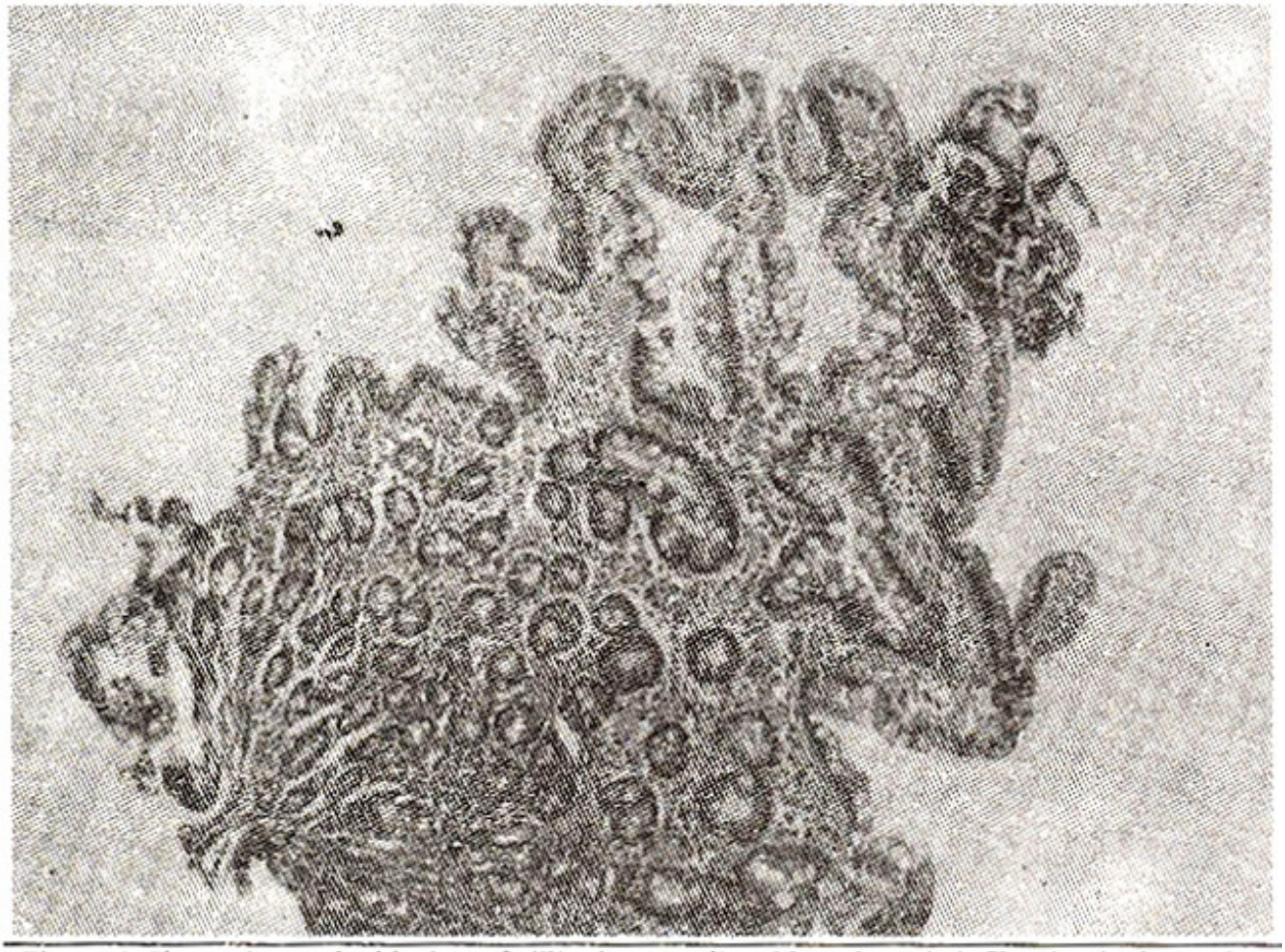


Figure 4. Shortening and widening of villi, plasma cell and lymphocytic infiltration in the lamina propria (H&Ex100).

Erosions were seen more commonly in group B. Group B had two cases of ciyptosporidiosis where some of the changes were similar to those of group A. Though lymphoid aggregates were present in some cases of Giardiasis, there was no significant difference between the gmups. Mild to moderate goblet cell depletion was observed while reviewing the slides of Group A (Figure 5).

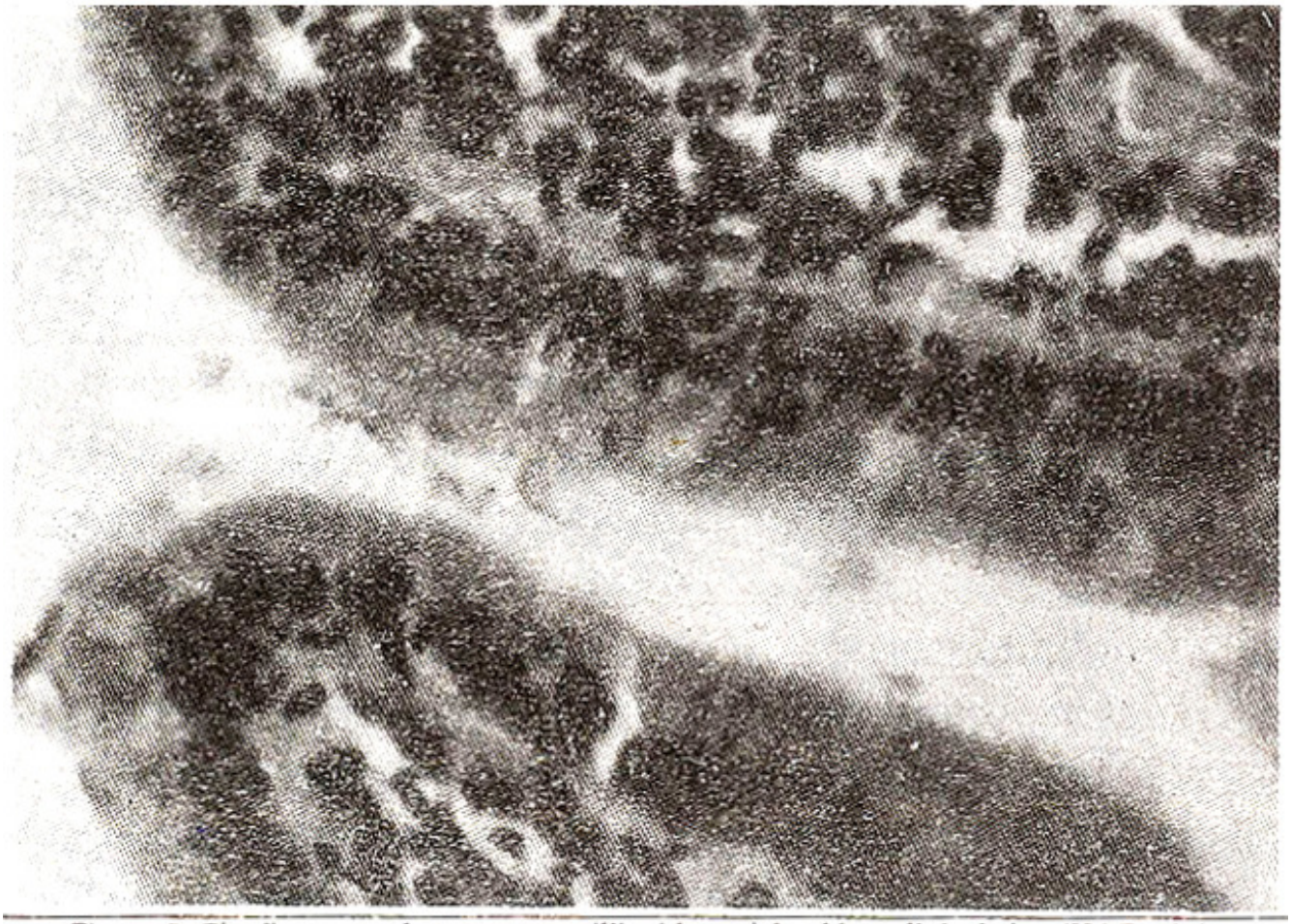


Figure 5. Giardia present between two villi with partial goblet cell depletion (H&Ex400).

The goblet cell depletion and the density of plasma cell infiltration in the lanîina propria had a statistically significant correlation with density of giardial colonization (Table II).

Table II. Histopathological Characteristics of Giardiasis in relation to density of organisms seen per high power field.

Histopathological Characteristic	Giardia Lamblia ≤5/HPF, n=7	Giardia Lamblia >5/HPF,n=13	P Value (Yates Corrected)
Surface Epithelium			
Goblet Cells			
Normal	05	02	0.05*
Reduced	02	11	
Lamina Propria			
Plasma cells			
Normal	00	00	
Grade I	04	00	0.05*
Grade II	03	06	(normal and I vs
Grade III	00	07	Normal and I vs II and III)

Such a relation could not be obtained for the other histophathological characteristics.

Discussion

Giardia lamblia adheres to the upper small intestinal epithelial cells and induces variable degrees of enteropathy[4]. It may also invade the mucosa[34]. Therefore, the biopsy of this region would not only demonstrate the organism but also the histological changes induced by this protozoan. If these changes were peculiar to giardiasis, then the presumptive diagnosis of giardiasis could be suggested even in the absence of Giardia in the biopsy specimen. Unfortunately, many such changes described in the literature are non-specific. The surface epithelium in our cases was columnar with regular nuclear alignment in 95%, which was significantly different from Group B where 66% specimens had a regular nuclear alignment The surface epithelium was intact in most cases of giardiasis. The presence of erosions and ulcerations was more common in the control Group B. ViIIi were shortened, widened or partially atrophic in 70% with an altered crypt-villous ratio in up to 45% of cases. Both these features were statistically significant when compared with Group B. The disease process is not fully understood35 but it appears that Giardia is not directly cytopathic to the intestinal cells as can be seen by the lack of erosions. It is probably more of an immunologically mediated process and some of its features resemble those of coeliac disease[26,36]. The changes in the viIIi point towards an insidious onset and slow disease process, again signifying an immunological pathogenesis. The presence of intraepithelial lymphocyte infiltration has been described in the literature[5,6,37]. In our study, the most frequent cellular infiltrate was of neutrophils, probably suggesting an acute inflammatory response to the organisms. This can also be explained by the fact that in our hospital, biopsies are taken earlier in the disease process, when the patient initially presents with gastrointestinal complaints. In a study of

the time course of infection with Giardia muris, intraepithelial lymphocytes increased only after villous shortening. By this time decrease in brush border disaccharidase had already taken place[38]. Neutrophil infiltration could also be a response to the other organisms including bacteria which produce infection simultaneously[39]. A striking increase of plasma cell infiltrates was observed in the laminaptopria. It should be noted that all of our cases, except one case of IPSID, were apparently immunecompetent. This is then in contrast to IgA deficiency states where plasma cells may be reduced or absent, and if normal, produce IgM antibodies. Predominance of IgM containing cells in the intestinal mucosa has been described before with Giardia infection[23,40,41]. The statistically significant presence of eosinophils in the lamina propria may suggest a hypersensitivity response and degranulation of these cells may be responsible for some of the histological changes described. We were not able to demonstrate organisms in the mucosa or lamina propria but invasion by giardia has been demonstrated before[34]. Lymphoid follicles were present in few cases of both groups and their frequency did not differ significantly between the groups. There were some common features of giardiasis in the distal duodenal biopsies like intact surface epithelium with decreased goblet cells, a vaiying degree of villous atrophy, intraepitbelial neutrophils, dense plasma cell infiltration and presence of eosinophils in the lamina propria. A decrease in goblet cells and an increase in plasma cells in the lamina propria are directly related to the density of giardial colonization. Therefore, in the presence of constellation of these peculiar hi histopathological features, a careful search should be made for Giardia lamblia in the biopsy specimens.

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