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SHORT REPORT

Eosinophilic-Crohn overlap colitis and review of the literature

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Abstract

Eosinophilic colitis is an idiopathic inflammation of the alimentary canal and is characterized by infiltration of the intestinal wall by eosinophils, massive submucosal edema, and peripheral eosinophilia. However, the presence of eosinophils in a colon biopsy requires thorough searching for secondary causes and eosinophilic colitis remains a diagnosis of exclusion.

A 67-year-old male patient underwent a diagnostic ileocolonoscopy because of recurrent episodes of diarrhea for the last six months. Colonoscopy revealed a normal terminal ileum while in the entire colon an erythematous mucosa with very slight edema on a continuous pattern that was more pronounced in the left colon. The laboratory workup demonstrated eosinophils slightly elevated, biochemical tests were unremarkable and further clinical and laboratory workup was unremarkable. Histology showed overlapping findings of eosinophilic colitis and Crohn's colitis. Patient started on mesalazine 2.4 with very good results.

A review of the literature shows that the spectrum of eosinophil involvement in inflammatory bowel disease as well as in eosinophilic colitis is largely varying, including also some exceptional cases that parallel the case described herein.

1. Introduction

The presence of activated tissue[1] and peripheral blood[2] eosinophils in chronic inflammatory bowel disease (IBD) has been reported since many years. Moreover, different regulations of eosinophil activity in Crohn's disease (CD) compared with ulcerative colitis (UC) have been demonstrated.[3] In addition, eosinophilic granulocytes in the rectal mucus[4] and increased fecal[5] or gut lavage fluid[6,7] eosinophil cationic protein have been shown to be present in patients with IBD.

Abbreviations: CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease.

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Of interest, allergic symptoms and respiratory symptoms including cases with eosinophilic pneumonia,[8] bronchial hyperreactivity, abnormal lung function tests and skin prick test positivity were found to be more common among the IBD patients in comparison with the controls.[9]

Of interest, CD patients without any clinical respiratory involvement have airway eosinophilia[10] while the percentage of sputum eosinophils is significantly different between UC patients with proctitis and pancolitis.[11]

Eosinophilic gastroenteritis, an idiopathic inflammation of the alimentary canal, is characterized by infiltration of the intestinal wall by eosinophils, massive submucosal edema, and peripheral eosinophilia.[12] It is generally confined to the gastric antrum and proximal small intestine.[13] The colon is rarely cited as a site for the condition[14] while eosinophilic ileocolitis is extremely rare.[15,16]

Eosinophilic ileitis must be always differentiated from Crohn's disease, infectious diseases, spondyloarthropathies, vasculitides, ischemia, neoplasms, food induced allergy[17]and medication-induced lessions.[18]

Eosinophilic colitis has a broad differential diagnosis because colon tissue eosinophilia often occurs in many other conditions, such as inflammatory bowel disease, neoplasms, parasitic infection (pinworms, roundworms, or whipworms), allergic colitis, drug-induced reactions (clozapine, carbamazepine, rifampicin, non-steroidal anti-inflammatory agents, tacrolimus, and gold), inflammatory bowel disease, and various autoimmune connective tissue diseases (including scleroderma, dermatomyositis and polymyositis), as well as with allogeneic bone marrow transplantation and the rare Tolosa-Hunt syndrome that features inflammatory ophthalmoparesis. Therefore, the presence of eosinophils in a colon biopsy requires thorough searching for secondary causes that may be specifically treated with antibiotics or dietary and drug elimination and EC remains a diagnosis of exclusion.[19–24]

Herein is described a case of a patient with chronic diarrhea who was diagnosed with overlap eosinophilic and Crohn's colitis.

2. Case report

A 67-year-old male patient underwent a diagnostic ileocolonoscopy in our department because of recurrent episodes of diarrhea for the last six months. Colonoscopy revealed a normal terminal ileum while in the entire colon an erythematous mucosa with very slight edema on a continuous pattern that was more pronounced in the left colon; at very careful bowel inspection there were no ulcers, diverticula, focal inflammatory lesions or adenomas. Multiple biopsies were taken and the patient empirically started 2.4 gr of mesalazine.

The otherwise not smoker healthy patient denied any history abdominal pain, bloody stool, and a family history of inflammatory bowel disease, pulmonary and allergic symptoms.

The patient did not take any medication on a long-term basis prior to colonoscopy including heavy metals and NSAIDs. There was no history of recent radiation therapy for a contiguous cancer. The patient originated from our area and he did not make any trip abroad or change his food habits recently. No other patients presented with similar complaints so far.

The laboratory workup demonstrated eosinophils slightly elevated (6400 cells per mm^3, 6.4%), erythrocyte sedimentation rate at 22 mm/h and negative C-reactive protein. Biochemical tests were unremarkable and chest and abdominal computed tomography did not reveal any other metastatic lesions. There was no evidence for collagen vascular diseases.

Histology showed overlapping findings of eosinophilic colitis and Crohn's colitis (Figs. 1–4). There were no other features of chronicity such as Paneth cell metaplasia and basal plasmocytosis present in the colonic biopsies. The distribution of the histological abnormalities was rather symmetrical over the colon. Biopsies from the terminal ileum did not reveal something remarkable.

Subsequent full work up for allergy of any type or parasites proved negative and the patient was given the diagnosis of colitis with overlapping characteristics of that of eosinophilic and of Crohn's colitis.

Patient was advised to continue mesalazine and was advised to undergo a follow up endoscopy after six months in the hope that in that time we will be able to provide a conclusive diagnosis.

3. Discussion

A review of the literature shows that the spectrum of eosinophil involvement in IBD and eosinophilic gastroenteritis is largely varying, including also some exceptional cases that parallel the case described herein.

In the upper gastrointestinal tract an interesting case of a patient who presented with multiple small submucosal nodules with granulomatous inflammation in the minor salivary glands of the oral cavity is described.[25] Sarcoidosis, Crohn's disease, tuberculosis and atypical mycobacterial infection were not identified by medical examination and authors suggested the term 'allergic granulomatous sialadenitis'. Another interesting case of eosinophilic esophagitis with Crohn's disease has been described as a new association or an overlapping immune-mediated enteropathy.[26]

In the lower gastrointestinal tract a case of an inflammatory fibroid polyp characterized as eosinophilic granuloma and Crohn's disease located in the ileum has been reported.[27] Another case of a child with Crohn's disease who developed a eosinophilic gastroenteritis has been reported.[28] Although symptoms of eosinophilic gastroenteritis at this child could mimic those of Crohn's disease, laboratory, radiographic and histologically studies were clearly different with peripheral blood eosinophilia, high serum IgE level and normal C-reactive protein and erythrocyte sedimentation rate. Eosinophilic gastroenteritis was due to bovine serum albumin (BSA) hypersensitivity, confirmed with skin tests, serum levels to specific IgE and IgE-immunoblotting and a strict meat-free diet was started, with progressive relief of symptoms and decrease of eosinophil count twelve months later.

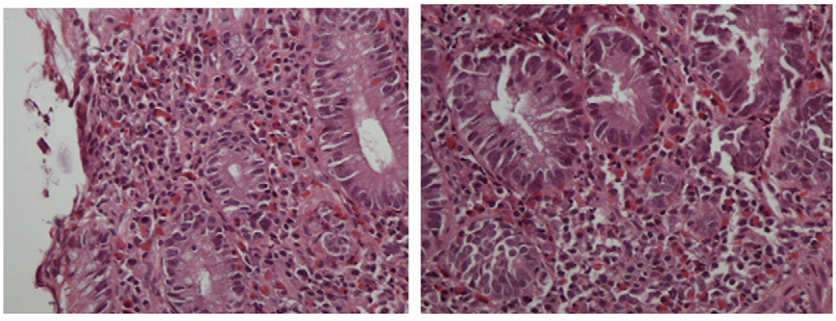

Figure 1 Eosinophilic infiltration of lamina suggesting eosinophilic colitis.

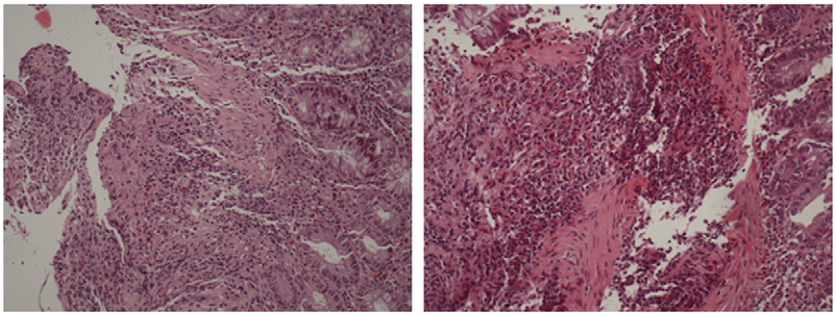

Figure 2 The inflammatory infiltrate crosses the muscularis mucosae, suggesting Crohn's disease.

A case of a patient undergoing hemicolectomy due to eosinophilic gastroenteritis involving the ileocecal area[29] and who on follow up had not shown evidence of recurrence or extension of the disease to the stomach or proximal small intestine clearly implies a parallelism to that of Crohn's disease potential for post-surgery recurrence.

Atypical syndromes implicating similar phenotypes or overlap of Crohn's disease and eosinophilic gastroenteritis are cases of primary sclerosing cholangitis associated with eosinophilic[30] colitis or colonic Crohn's disease and marked eosinophilia[31] or of diffuse eosinophilic fasciitis, atypical rash, and chronic inflammatory disease of the colon[32] or of eosinophilic colitis with perianal disease.[33] Finally an interesting couple case of eosinophilic enteritis in the husband and Crohn's disease in the wife has been reported.[34]

In this case there are several histological characteristics favoring either the eosinophilic or the Crohn's disease diagnosis and supporting this overlap. However, studies on the frequency and role of intestinal eosinophils in patients with inflammatory bowel disease have yielded conflicting results. Histopathology studies have contributed to a better understanding on the role of eosinophils and activated eosinophils in IBD.

Eosinophils are normal constituents of the mucosa of the gastrointestinal tract and there has been no definitive determination of the number of eosinophils that can be defined as normal. They are not distributed uniformly along the length of the bowel, and in the large intestine, it is well recognized that they are usually more numerous in the cecum and ascending colon than elsewhere. Normal values for tissue eosinophils vary widely between different segments of the colon, ranging from <10 eosinophils per high-power field in the rectum to >30 in the cecum, thus location of the biopsy is critically important for interpretation of findings.[35]

A diagnosis of EC is made if the eosinophils infiltrate the crypts or there are focal collections of 10 or more eosinophils per high power field, in the absence of other identifiable abnormalities. EC is characterized by a florid tissue and peripheral blood eosinophilia with some histopathological similarities to chronic inflammatory bowel disease. Unlike CD, granulomas, pseudopyloric metaplasia, architectural distortion, and fibrosis are usually not features of EC. Futhermore, inflammatory infiltrate of CD is usually mixed and not exclusively eosinophils. The crypt architectural distortion of ulcerative colitis is not also present in EC. In some cases, the patients will eventually be diagnosed with CD. However, in other patients the cause of changes is never determined.[36]

In our case, histopathological examination showed focal distortion of the architecture without mucin depleted or even reduced. On the lamina

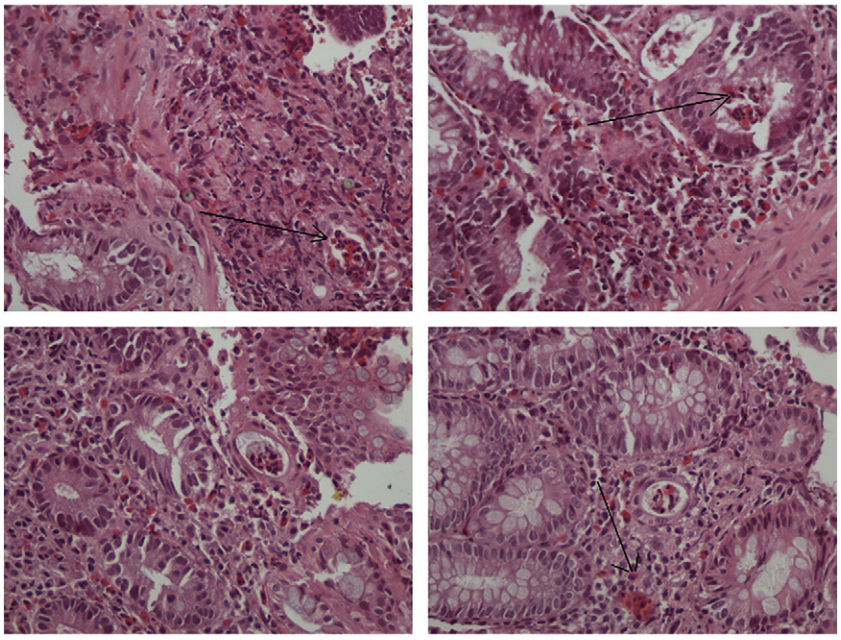

Figure 3 The arrows in the panel show crypt abscesses that consists almost entirely of eosinophils. There is also an increased number of eosinophils in the lamina propria.

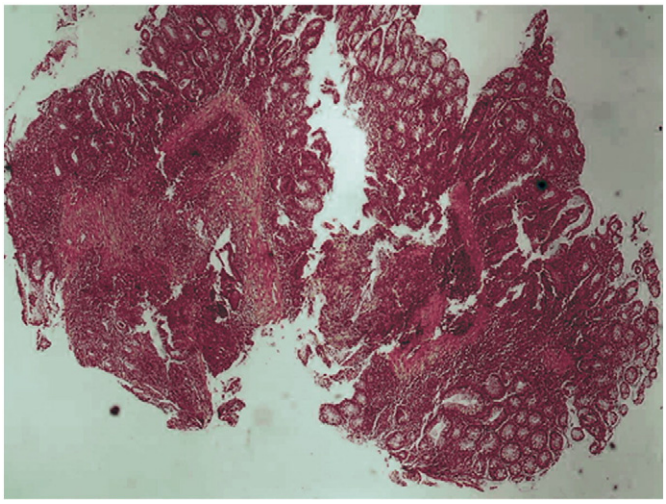

Figure 4 Mucosal biopsy with mild glandular irregularity. There is an intense inflammatory infiltrate in the submucosa, which crosses the muscularis mucosae, suggesting Crohn's disease.

propria, there is a medium inflammatory infiltrate consisted of lymphocytes, plasma cells and many eosinophils. The mean eosinophil count was 50 per high-power field. In normal conditions gastrointestinal eosinophils do not infiltrate the epithelial layer, as they do under some pathological situations. Moreover, the eosinophils formed aggregates, while they infiltrate the crypts as well. The inflammatory infiltrate had also a few neutrophils, which together with the eosinophils infiltrated some crypts. It was also giving the impression that the inflammatory infiltrate crossed the muscularis mucosae. There were no granulomas.

Eosinophils have been also implicated in the pathogenesis of IBD.[37] According to one of these studies it has been demonstrated that the number of intestinal mast cells and eosinophils is altered in patients with inflammatory bowel diseases as compared to controls and was dependent on disease activity and drug treatment, suggesting that both cell types are involved in the pathogenesis of chronic intestinal inflammation.[38] Another study showed that focal eosinophilic mucosal infiltration in CD is more common than epithelioid cell granulomas, and emerges as an important parameter in the histologic differential diagnosis between colonic CD and UC with CD presenting significantly higher mean percentage of eosinophils in areas with focal inflammation.[39]

In this patient food-induced allergy cannot definitely be excluded although no positive history or allergy test was supportive of this probability. The most typical presentation of eosinophilic colitis is allergic eosinophilic proctocolitis, which affect babies under 3 months and responds to an immune reaction triggered by the intake of foreign proteins, especially cows' milk proteins, even if they are consumed by the mother and excreted with breast milk. Analytical alterations are not usually found and allergic skin tests and specific IgE are negative reinforcing the idea that food allergy is not usually mediated by type-1 immune reactions.[40–42]

Furthermore the answer to the enigma whether Crohn's disease is a food-induced disease still cannot be answered. In fact, food-induced immune responses cause or influence a number of intestinal diseases. There are diseases where food is the primary factor in the pathogenesis, such as food allergy and gluten-sensitive enteropathy. Furthermore, allergic reactions may play a role in eosinophilic esophagitis and eosinophilic gastroenteritis. In IBD food influences the disease by the modulation of various factors such as intestinal bacterial flora or the inflammatory cascade and this may have some significance in the perpetuation of intestinal inflammatory processes in patients with Crohn's disease.[43]

Eosinophil accumulation and activation[44] are also characteristic features of inflammation in host defense against parasites such as ascariasis where an IgE-mediated response is characterized by a dramatic increase in mucosal-type cells and eosinophils in both the mucosa and the deeper layers of the intestinal wall.[45] By contrast, in a study with immunnohistological assessment of intestinal eosinophil activation in patients with eosinophilic gastroenteritis and IBD it has shown that in IBD patients eosinophils seem to be activated but their number is not or only slightly elevated compared to controls.[46]

Interesting data has been also accumulated supporting that eosinophils are functionally involved in the pathophysiology of IBD. Eotaxin is a chemokine with potent and selective chemotactic activity for eosinophils and two serum studies[47,48] and one in full thickness bowel wall specimens[49] showed elevated serum eotaxin levels in IBD patients. Another two studies have suggested an important role for eosinophil protein X[50] in feces and for tissue content[51] of eosinophilic cationic protein in IBD. In fact, mucosal infiltration by eosinophils may represent a pivotal phenomenon in early IBD or in acute forms of the disease the so-called "acute self-limited colitis".[52]

A study to in patients presenting with symptoms of inflammatory bowel disease showed that eosinophils together with granulomas, solitary giant cells, pseudopyloric gland metaplasia, and a disturbed villous architecture were the most important lesions observed in early Crohn's disease and were contributive for this diagnosis.[53] In two other cases dense eosinophilic infiltration mimicking eosinophilic colitis preceded ulcerative colitis.[54]

Finally there is a potential role for eosinophils in CD recurrence. In fact, it has been demonstrated that there is an increased response of blood eosinophils to various chemotactic agents, including eotaxin, in clinically quiescent Crohn disease[55] and activated eosinophil and interleukin 5 expression has been demonstrated in early recurrence of CD.[56]

The overlapping of those idiopathic diseases of the colon that was described herein may reflect their overlapping etiology. In fact, the gastrointestinal tract is continuously in contact with a multitude of antigens and therefore contains a well-developed defense mechanism.[57] From initial inflammatory reaction until disease manifestation a large individuality seems to be present regarding the perpetuation as well as the end-point of inflammation.

References

1. Choy MY, Walker-Smith JA, Williams CB, MacDonald TT. Activated eosinophils in chronic inflammatory bowel disease. *Lancet* 1990;**14**(336):126–7.
2. Coppi LC, Thomazzi SM, de Ayrizono ML, Coy CS, Fagundes WJ, Goes JR, et al. Comparative study of eosinophil chemotaxis,

adhesion, and degranulation in vitro in ulcerative colitis and Crohn's disease. *Inflamm Bowel Dis* 2007;**13**:211–8.
3. Lampinen M, Backman M, Winqvist O, Rorsman F, Rönnblom A, Sangfelt P, et al. Different regulation of eosinophil activity in Crohn's disease compared with ulcerative colitis. *J Leukoc Biol* 2008;**84**:1392–9.
4. Anthonisen P, Riis P. Eosinophilic granulocytes in the rectal mucus of patients with ulcerative colitis and Crohn's disease of the ileum and colon. *Scand J Gastroenterol* 1971;**6**:731–4.
5. Berstad A, Børkje B, Riedel B, Elsayed S, Berstad A. Increased fecal eosinophil cationic protein in inflammatory bowel disease. *Hepatogastroenterology* 1993;**40**:276–8.
6. Levy AM, Gleich GJ, Sandborn WJ, Tremaine WJ, Steiner BL, Phillips SF. Increased eosinophil granule proteins in gut lavage fluid from patients with inflammatory bowel disease. *Mayo Clin Proc* 1997;**72**:117–23.
7. Troncone R, Caputo N, Esposito V, Campanozzi A, Campanozzi F, Auricchio R, et al. Increased concentrations of eosinophilic cationic protein in whole-gut lavage fluid from children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 1999;**28**:164–8.
8. Basseri B, Enayati P, Marchevsky A, Papadakis KA. Pulmonary manifestations of inflammatory bowel disease: case presentations and review. *J Crohns Colitis* 2010;**4**:390–7.
9. Ceyhan BB, Karakurt S, Cevik H, Sungur M. Bronchial hyperreactivity and allergic status in inflammatory bowel disease. *Respiration* 2003;**70**:60–6.
10. Louis E, Louis R, Shute J, Lau L, Franchimont D, Lamproye A, et al. Bronchial eosinophilic infiltration in Crohn's disease in the absence of pulmonary disease. *Clin Exp Allergy* 1999;**29**:660–6.
11. Fireman E, Masarwy F, Groisman G, Shtark M, Kopelman Y, Kivity S, et al. Induced sputum eosinophilia in ulcerative colitis patients: the lung as a mirror image of intestine? *Respir Med* 2009;**103**:1025–32.
12. Kerr PJ. Eosinophilic gastroenteritis: clinical experience with 15 patients. *World J Gastroenterol* 2004;**10**:2923.
13. Naylor AR, Pollet JE. Eosinophilic colitis. *Dis Colon Rectum* 1985;**28**: 615–8.
14. Verger P, Blais J, Hamon JF, Senghor C, Haffaf Y. Eosinophilic ileocolitis: two case reports. *Rev Méd Interne* 1998;**19**:841–2.
15. Tedesco FJ, Huckaby CB, Hamby-Allen M, Ewing GC. Eosinophilic ileocolitis: expanding spectrum of eosinophilic gastroenteritis. *Dig Dis Sci* 1981;**26**:943–8.
16. Haberkern CM, Christie DL, Haas JE. Eosinophilic gastroenteritis presenting as ileocolitis. *Gastroenterology* 1978;**74**:896–9.
17. Paillas J, Viellefond A, Sinico M. Eosinophilic segmentary enteritis. Allergenic role of chocolate. *Nouv Presse Méd* 1982;**11**:943.
18. Quallich LG, Greenson J, Haftel HM, Fontana RJ. Is it Crohn's disease? A severe systemic granulomatous reaction to sulfasalazine in a patient with rheumatoid arthritis. *BMC Gastroenterol* 2001;**1**:8.
19. Cao J, Liu WJ, Xu XY, Zou XP. Endoscopic findings and clinicopathologic characteristics of colonic schistosomiasis: a report of 46 cases. *World J Gastroenterol* 2010;**16**:723–7.
20. Montalto M, Miele L, Marcheggiano A, Santoro L, Curigliano V, Vastola M, et al. Anisakis infestation: a case of acute abdomen mimicking Crohn's disease and eosinophilic gastroenteritis. *Dig Liver Dis* 2005;**37**:62–4.
21. Dilauro S, Crum-Cianflone NF. Ileitis: when it is not Crohn's disease. *Curr Gastroenterol Rep* 2010;**12**:249–58.
22. Gutierrez Y, Bhatia P, Garbadawala ST, Dobson JR, Wallace TM, Carey TE. Strongyloides stercoralis eosinophilic granulomatous enterocolitis. *Am J Surg Pathol* 1996;**20**:603–12.
23. Müller S, Schwab D, Aigner T, Kirchner T. Allergy-associated colitis. Characterization of an entity and its differential diagnoses. *Pathologe* 2003;**24**:28–35.
24. Bischoff SC, Mayer JH, Manns MP. Allergy and the gut. *Int Arch Allergy Immunol* 2000;**121**:270–83.
25. Irié T, Maeda Y, Aida T, Sumitani K, Nagumo M, Tachikawa T. Multiple granulomatous inflammation in the minor salivary glands: a proposed new entity, allergic granulomatous sialadenitis. *Pathol Int* 2004;**54**:850–3.
26. Suttor VP, Chow C, Turner I. Eosinophilic esophagitis with Crohn's disease: a new association or overlapping immune-mediated enteropathy? *Am J Gastroenterol* 2009;**104**:794–5.
27. Catalá M, Sánchez A, Hinojosa J, Primo J, Flors C, Calvete J, et al. An inflammatory fibroid polyp (eosinophilic granuloma) and Crohn's disease located in the ileum. *Rev Esp Enferm Dig* 1992;**82**:193–5.
28. Tella R, Gaig P, Lombardero M, García-Ortega P, Bartra J, Papo M, et al. Allergic eosinophilic gastroenteritis in a child with Crohn's disease. *J Investig Allergol Clin Immunol* 2004;**14**: 159–61.
29. Schulze K, Mitros FA. Eosinophilic gastroenteritis involving the ileocecal area. *Dis Colon Rectum* 1979;**22**:47–50.
30. Gaia E, Cavalot F, De Giuli P, Emanuelli G. Primary sclerosing cholangitis associated with colonic Crohn disease and marked eosinophilia. Description of a case. *Minerva Gastroenterol Dietol* 1991;**37**:59–63.
31. Uchida N, Ezaki T, Fukuma H, Tsutsui K, Kobara H, Matsuoka M, et al. Concomitant colitis associated with primary sclerosing cholangitis. *J Gastroenterol* 2003;**38**:482–7.
32. Martin JR, Williams JP, Barrowman JA. Diffuse eosinophilic fasciitis, atypical rash, and chronic inflammatory disease of the colon; Crohn's disease? *J Rheumatol* 1980;**7**:928–9.
33. Lee FI, Costello FT, Cowley DJ, Murray SM, Srimankar J. Eosinophilic colitis with perianal disease. *Am J Gastroenterol* 1983;**78**:164–6.
34. Gilinsky NH. Eosinophilic enteritis in the husband, Crohn's disease in the wife. *Lancet* 1981;**1**:1425–6.
35. Okpara Nnenna, Aswad Bassam, Baffy Gyorgy. Eosinophilic colitis. *World J Gastroenterol* 2009;**15**:2975–9.
36. Fenoglio-Preiser Cecilia M. Gastrointestinal Pathology: an Atlas and a TextThird Edition. . Lippincott Williams & Wilkins Eds; 2008.
37. Wedemeyer J, Vosskuhl K. Role of gastrointestinal eosinophils in inflammatory bowel disease and intestinal tumours. *Best Pract Res Clin Gastroenterol* 2008;**22**:537–49.
38. Bischoff SC, Mayer J, Nguyen QT, Stolte M, Manns MP. Immunnohistological assessment of intestinal eosinophil activation in patients with eosinophilic gastroenteritis and inflammatory bowel disease. *Am J Gastroenterol* 1999;**94**:3521–9.
39. Rubio CA. A method for the detection of eosinophilic granulocytes in colonoscopic biopsies from IBD patients. *Pathol Res Pract* 2003;**199**: 145–50.
40. Mozer-Glassberg Y, Zevit N, Rosenbach Y, Hartman C, Morgenstern S, Shamir R. Follow-up of children with celiac disease — lost in translation? *Digestion* 2011 Feb 1;**83**(4):283–7.
41. Dehlink E, Gruber S, Eiwegger T, Gruber D, Mueller T, Huber WD, et al. Immunosuppressive therapy does not prevent the occurrence of immunoglobulin E-mediated allergies in children and adolescents with organ transplants. *Pediatrics* 2006 Sep;**118**(3): e764–70.
42. Shah U, Walker WA. Pathophysiology of intestinal food allergy. *Adv Pediatr* 2002;**49**:299–316.
43. Seibold F. Food-induced immune responses as origin of bowel disease? *Digestion* 2005;**71**:251–60.
44. Carvalho AT, Elia CC, de Souza HS, Elias PR, Pontes EL, Lukashok HP, et al. Immunohistochemical study of intestinal eosinophils in inflammatory bowel disease. *J Clin Gastroenterol* 2003;**36**: 120–5.
45. Beil WJ, McEuen AR, Schulz M, Wefelmeyer U, Kraml G, Walls AF, et al. Selective alterations in mast cell subsets and eosinophil infiltration in two complementary types of intestinal inflammation: ascariasis and Crohn's disease. *Pathobiology* 2002–2003;**70**:303–13.
46. Bischoff SC, Wedemeyer J, Herrmann A, Meier PN, Trautwein C, Cetin Y, et al. Quantitative assessment of intestinal eosinophils and mast cells in inflammatory bowel disease. *Histopathology* 1996;**28**: 1–13.

47. Chen W, Paulus B, Shu D, Wilson, Chadwick V. Increased serum levels of eotaxin in patients with inflammatory bowel disease. *Scand J Gastroenterol* 2001;**36**:515–20.
48. Mir A, Minguez M, Tatay J, Pascual I, Peña A, Sanchiz V, et al. Elevated serum eotaxin levels in patients with inflammatory bowel disease. *Am J Gastroenterol* 2002;**97**:1452–7.
49. Jeziorska M, Haboubi N, Schofield P, Woolley DE. Distribution and activation of eosinophils in inflammatory bowel disease using an improved immunohistochemical technique. *J Pathol* 2001;**194**:484–92.
50. Peterson CG, Eklund E, Taha Y, Raab Y, Carlson M. A new method for the quantification of neutrophil and eosinophil cationic proteins in feces: establishment of normal levels and clinical application in patients with inflammatory bowel disease. *Am J Gastroenterol* 2002;**97**:1755–62.
51. Winterkamp S, Raithel M, Hahn EG. Secretion and tissue content of eosinophil cationic protein in Crohn's disease. *J Clin Gastroenterol* 2000;**30**:170–5.
52. Caprilli R, Viscido A. Evolving concepts on inflammatory bowel disease. Are we happy with the present nosology? *Ital J Gastroenterol Hepatol* 1999;**31**:893–7.
53. Geboes K, Ectors N, D'Haens G, Rutgeerts P. Is ileoscopy with biopsy worthwhile in patients presenting with symptoms of inflammatory bowel disease? *Am J Gastroenterol* 1998;**93**:201–6.
54. Uzunismail Hülya, Hatemi İbrahim, Dogusoy Gülen, Akin Onat. Dense eosinophilic infiltration of the mucosa preceding ulcerative colitis and mimicking eosinophilic colitis: report of two cases. *Turk J Gastroenterol* 2006;**17**:53–7.
55. Denis MA, Louis R, Malaise M, Belaiche J, Louis E. Increased response of blood eosinophils to various chemotactic agents in quiescent Crohn disease. *Scand J Gastroenterol* 2001;**36**:190–5.
56. Dubucquoi S, Janin A, Klein O, Desreumaux P, Quandalle P, Cortot A, et al. Activated eosinophils and interleukin 5 expression in early recurrence of Crohn's disease. *Gut* 1995;**37**:242–6.
57. Geboes K. From inflammation to lesion. *Acta Gastroenterol Belg* 1994;**57**:273–84.