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LETTERS TO THE EDITOR

Why is damage limited to the mucosa in ulcerative colitis but transmural in Crohn's disease?

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Abstract

It has been a big puzzle as why the inflammation of ulcerative colitis (UC) is limited to the mucosa, while in Crohn's disease (CD) the inflammation is transmural and can be seen in all layers of the gut. Here, I give a tentative explanation extended from the unified hypothesis I proposed on the etiology of inflammatory bowel disease. This hypothesis suggested that both UC and CD are caused by weakening of the gut barrier due to damage of the protective mucus layer and the underlying tissue by the poorly inactivated digestive proteases resulting from a reduction of gut bacteria by dietary chemicals like saccharin and sucralose. However, the large amounts of bacteria in the colon make the recruitment of neutrophils and formation of crypt abscess the main manifestation of UC, while the infiltration of antigens and dietary particles in the small and large intestine mainly cause the recruitment of macrophages and formation of granulomas as the main manifestations in CD. The fast reacting and short life span of neutrophils make the fight and damage limited to the surface of the mucosa. In contrast, the long life span and constant movement of macrophages may bring the harmful agents deep into the tissue. Therefore, the pathogenesis of UC may be more like bacterial pneumonia, while CD may be more like pneumoconiosis or tuberculosis of the lung.

Key words: Inflammatory bowel disease; Ulcerative colitis; Crohn's disease; Pathogenesis; Neutrophils; Macrophages

Core tip: In my opinion, ulcerative colitis is more like bacterial pneumonia with the involvement of mainly neutrophils, capacious exudates into the cavity but limited damage of the tissue, while Crohn's disease is more like pneumoconiosis, such as silicosis or berylliosis, or tuberculosis of the lung with the involvement of mainly macrophages and manifested as granulomatous inflammation in the interstices, destruction of the tissue, extensive proliferation of fibroblasts and formation of fibrosis.

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TO THE EDITOR

As we know, the inflammation of ulcerative colitis (UC) is limited to the mucosa, while in Crohn's disease (CD) the inflammation is transmural and can be seen in all layers of the gut[1,2]. These key features reflect the root mechanism of pathogenesis of the disease but a coherent explanation remains lacking. Here, I give a tentative explanation extended from a unified hypothesis I proposed on the etiology of inflammatory bowel disease (IBD), including the cause and mechanism of IBD, as well as the relationship between UC and CD[3]. This hypothesis suggested that both UC and CD are caused by weakening of the gut barrier due to damage of the

protective mucus layer and the underlying tissue by the poorly inactivated digestive proteases resulting from a reduction of gut bacteria by dietary chemicals like saccharin and sucralose. However, the large amounts of bacteria in the colon make the recruitment of neutrophils and formation of crypt abscess the main manifestation of UC, while the infiltration of antigens and dietary particles in the small and large intestine mainly causes the recruitment of macrophages and formation of granulomas as the main manifestations in CD. With a life span of just a couple of days, neutrophils are the fast reaction army of the body and will be dispatched to the very front and fight vigorously there until they die. However, macrophages are the cleaner and order keeper inside the body, with a primary duty of clearing up debris like the dead cells. They have a life span of months and can fulfill their job by eating the debris, digesting them, moving around and picking up again for quite a while and distance. However, things like dietary particles and multiple species of bacteria, such as *Mycobacterium*, *Salmonella*, *Listeria*, *Shigella* and adherent-invasive *Escherichia coli*, are beyond the ability of macrophages to digest. Hence, the macrophages may have carried and moved them quite far inside before they die. Then, the particles or bacteria will be released and picked up by other macrophages and moved further inside. The persistent existence of these foreign bodies results in the recruitment of more macrophages and other immune cells, eventually leading to the initiation of the quarantine process and formation of granulomas[4,5]. In my opinion, UC is more like bacterial pneumonia (but long lasting due to the continuous existence of large amounts of bacteria in the colon) with the involvement of mainly neutrophils, capacious exudates into the cavity (crypts and lumen in the gut and alveoli in the lung) but limited damage of the tissue[6], while CD is more like pneumoconiosis, such as silicosis or berylliosis[7], or tuberculosis of the lung with the involvement of mainly macrophages and manifested as granulomatous inflammation in the interstices, destruction of the tissue, extensive proliferation of fibroblasts and formation of fibrosis.

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