ULTRASTRUCTURAL ASPECTS OF THE COLONIC EPITHELIUM IN ULCERATIVE COLITIS

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Received: March 2008; Published: May 2008

ABSTRACT. Introduction: The colonic epithelium is a barrier between the luminal antigens and the immune cells from lamina propria. Previously, the colonic mucus layer has been shown to be thinner in ulcerative colitis (UC) than in normal subjects. Aim: To assess ultra structural changes of the rectal epithelium in patients with active/quiescent UC. Methods: Rectal biopsies were taken during endoscopy from patients with UC (n=8) and from healthy subjects (n=8). Pathological assessment of adjacent biopsies was made to determine if patients were normal or suffered from UC (active/quiescent). The specimens for ultra structural investigation were specifically processed and examined with a JEM-1010 transmission electron microscope (JEOL, Tokyo, Japan). Results: Compared with the normal mucosa, in the active UC we observed severe epithelial changes – rarefaction of the goblet cells, depletion/absence of microvillus, destruction of the tight junctions, vacuolisation and lyses of the cytoplasm, picnosis of the nucleus, alterations of endoplasmic reticulum, mitochondria, Golgi complexes – resulting in a drastic decrease of mucus formation. In the quiescent UC, the thickness of the epithelium and the goblet-cells were more reduced than in normal, modified microvillus, enlarged intercellular spaces and still alterations of the organdies were seen. Conclusions: The colonic epithelium is compromised in active UC and is only partially restored when UC is in remission. Ultrastructural alterations of the epithelium play an important role in the pathophysiology and relapse of the disease.

Keywords: colonic epithelium, ulcerative colitis, electron microscopy, colonic inflammation

INTRODUCTION

There are two major forms of unspecific inflammatory bowel disease (IBD) and these are: Crohns’ Disease – which can affect any part of the gastrointestinal tract and ulcerative colitis (UC) which is localized at the large intestine. Ulcerative colitis is a relatively uncommon, chronic, recurrent inflammatory disease of the colonic or rectal mucosa (Chutkan, 2001). Often a lifelong illness, the condition has profound emotional and social impact on the affected individual. The prevalence of UC varies between 35-120/10^5 people, males being more affected than women (Lapidus, 2001).

The term that we use today – ulcerative colitis – belongs to Samuel Wilks and Moxon from 1875, although there is a very detailed description of the disease made by Wilks in 1859, when he differentiated UC from dysentery.

Because of the fact that we do not known for sure the etiologic agent as well as the pathogenesis of the disease (Scaldaferrri et al., 2007), UC is diagnosed and treated by means of some clinical, endoscopic and morphologic characteristics. The colonic epithelium plays an important role in this illness because it represents the barrier between endoluminal antigens and immune cells from lamina propria (Gibson et al., 1995).

In a patient suspected to have IBD, the colonoscopic examination reveals mucosal injuries and it allows us: to evaluate the activity of the disease, to take tissue samples from the affected areas, to analyze the response to different treatments and in some cases to establish the opportunity of surgical castigation. The endoscopic examination must comprise some essential elements for an accurate diagnosis: the localization and distribution of the injury, the type of the lesion, and it must clearly describe all of the above (Kiesslich et al., 2007).

There are some essential elements for the diagnosis of UC: diffuse, symmetrical mucosal lesions, without spare regions. The lesions appear in the most distal part of the rectum (which is affected in more than 95% of the cases) and there is no lesion-free area. The inflammatory process begins in the rectum and it extends progressively on a variable distance (Odze, 2003). Accordingly, as the disease enters a remission phase, the oedema, the congestion and inflammation diminish, the mucosa gets its normal colour and the tendency to haemorrhage is smaller. The vascular pattern starts to be observed, but it remains erratic. The remission process might not be the same in all the regions and the lesions may become asymmetrical, inhomogeneous, having a false plot aspect.

Therefore the endoscopic examination has a very special meaning for the positive and differential
diagnosis of UC and especially to be able to insulate UC from Crohns’ disease or other types of colitis: ischemic, infectious or drug induced (Ugljesic, 2000).

The inflammation is localized and also limited to the colonic mucosa and submucosa. The pathologic process begins with intense vascular dilatation, oedema and eritrodiapedesis, with the distension of the gland lumen by high amounts of mucus. Epithelial cells become flat and suffer a process of exfoliation (Kucharzik et al., 2001). Progressively, a process of epithelial cells destruction is installed. Their cytoplasm suffers the phenomena of vacuolisation, the cells become scattered and the nucleus is disrupted (Gassler, 2001).

The purpose of our paper was to establish the ultrastructural alterations from the rectal epithelium in patients suffering from UC whether the disease is active or quiescence.

Fig. 1 UC- active phase: the epithelial cell adhesion is profoundly altered and the tight junctions are destroyed (x 7,000)

Fig. 2 UC- active phase: the vacuolization and lyses of the cytoplasm, endoplasmic reticulum dilatation (x 12,000)

MATERIALS AND METHODS

We studied a total number of 16 patients, 8 of them having clinical manifestations of UC or being diagnosed with the disease (active or quiescence) by means of endoscopy and 8 of them were healthy subjects.

The patients were investigated in ambulatory or they were hospitalized for further investigation and treatment in Clinical County Hospital Oradea- 3rd Medical Clinic and Gastroenterology Department. The examination was performed using an Olympus Exera CLE 145 videendoscope. Rectal biopsies were taken during endoscopy from patients with UC and from healthy subjects. Some of the samples were studied with optical microscopy to determine whether the patient was healthy or suffering from UC.

The specimens from 16 patients were fixed in 2.5 % phosphate buffered 0.1M glutaraldehide sol. (pH 7.4) and then post fixed with 1% osmic acid in phosphate buffer (pH 7.4). After rinsing in distilled water the pieces were dehydrated with acetone, embedded in Vestopal W and then thin sections were cut (70nm), stained with uranyl acetate and lead citrate. Afterwards they were studied with a JEM-1010 transmission electron microscope (JEOL, Tokyo, Japan).

Fig. 3 UC- active phase: the microvillus border is destroyed, the rectal mucosal cells have pycnotic nucleus with irregular contour (x 7,000)

Fig. 4 UC-active phase: the thickness of the mucosa is reduced, in mucosal cells the Golgi complex is flattened and the mitochondria has a rarefied matrix (x 8,000)

RESULTS AND DISCUSSION

From the histological point of view we observed that the active forms were characterized by the existence of a severe inflammatory infiltrate in the lamina propria with the predominance of neutrophils. The quiescence periods had a less intense chronic inflammatory infiltrate with lymphocytes and plasma cells and also abnormal epithelial pattern (the glandular crypts were shortened, with branched appearance and reduced number).

Compared to the normal rectal mucosa – which has overloaded goblet cells, and where the release of the
mucus is made according to the necessities into the lumen and the absorbent cells from around have a normal, thick microvilli – the affected mucosa from UC is displaying severe epithelial alterations.

Thus, we observed the rarefaction or even the absence of the microvilli, the reduction of goblet cells, the shatter of the epithelial junctions (Figure 1), cytoplasmic vacuolisation, dilatation of the endoplasmic reticulum (Figure 2), pycnotic nuclei, the destruction of the mitochondria and Golgi complexes which conducts in the end to the drastic reduction of the mucus production (Figure 3 and 4).

Fig. 5 UC - quiescence phase: rarefaction of the goblet cells which have a disturbed pattern, reduced mucus secretion (x 6,800)

Fig. 6 UC - quiescence phase: rarefaction, shortened or even absent microvilli in some areas (x 6,800)

Fig. 7 UC - quiescence phase: altered Golgi complex which produces inadequate mucus granules (x 12,000)

Fig. 8 UC - quiescence phase: enlarged intercellular spaces, vacuolization of the cytoplasm, inflated mitochondria (x 16,000)

In UC, the inflammation appears as a result of a trigger from the natural environment, but which is not yet fully understood. The inflammatory process is limited to the colonic mucosa and submucosa and it begins in the rectum. From there, it extends proximally on a variable distance (Gheorghe et al., 2003).

The characteristic macroscopic lesions of UC depend on the severity and duration of the illness. The precocious lesions observed during the endoscopic examination were: granular aspect of the mucosa, the disappearing of the lustre, congestion and friability of the mucosa. The ulcerations are superficial, irregular and allomorphic. First the ulcerations are small, but in time they enlarge as the disease progresses and by merging together they can affect large areas of colonic mucosa.

From the pathological point of view, we observed that the characteristic lesion in UC was represented by the existence of neutrophils in the glandular crypts (cryptitis and cryptic abscess) (Utsumi et al., 1999).

The mucus depletion, oedema and focal haemorrhage were alterations met during the active phases of the disease, things that were also remarked in other studies, like those made by Kruschewski et al. (1995) or McLaren et al. (2002). Ultrastructurally, there are important alterations of the cell structures, both in the active phase and in the quiescent phase. It is important to underline that in the affected area tissue necrosis might appear and it represents a precursory
process of ulceration. Along with the destructive phenomenon, there is a cicatrisation and regeneration process (Nagy, 2007).

CONCLUSIONS

In order to draw a conclusion, we can say that on the histological and ultrastructural sections made from tissue samples one can observe the presence and the intensity of the vascular reactions from the mucosa and also appreciate the impact between the aggressive factors and the host organism.

The colonic epithelium is profoundly altered in active UC and only partially recovered in quiescence forms. These ultrastructural alterations play an important role in the physiopathology and recurrent evolution of UC.

REFERENCES