

Endoscopic features of coeliac disease

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Abstract. Gastrointestinal endoscopy is not the first line diagnostic tool in coeliac disease. However, awareness of its basic endoscopic features may alert endoscopists to the presence of the disease. Endoscopic features of coeliac disease comprise reduction in the number or loss of folds, mosaic appearance, scalloping, fissures or grooves of folds in the jejunum, and visible vascular pattern (in the duodenum) and (micro-) nodularity. Loss of intestinal villi can be set off with the immersion technique. Chromoendoscopy using indigo carmine or methylene blue can enhance the mosaic pattern of intestinal mucosa. Push-enteroscopy and/or capsule endoscopy is important in the follow-up and diagnostics of complications of coeliac disease (refractory sprue, ulcerative jejunoileitis and T-cell lymphoma).

Key words: coeliac disease, small bowel endoscopy, refractory sprue, ulcerative jejunoileitis, T-cell lymphoma

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Souhrn. Digestivní endoskopie není zpravidla u celiakie diagnostickou metodou první řady. Nicméně znalost endoskopických obrazů je velmi důležitá pro správné rozpoznání klinicky němých nebo oligosymptomatických případů celiakální sprue a pro následnou dispenzarizaci nemocných či diagnostiku komplikací celiakie. Endoskopický obraz celiakie zahrnuje redukci počtu (nebo ztrátu) příčných řas sliznice tenkého střeva, mozaikový vzhled, vroubkování či rýhování sliznice. V duodenu může být patrná abnormální cévní kresba a nodulární reliéf. Endoskopické změny jsou nejvíce vyjádřeny v jejunu, méně v ileu. U většiny pacientů je charakteristický endoskopický obraz patrný i v duodenu. V některých případech však je v duodenu nález nespecifický anebo jsou přítomny jen nepřímé známky (abnormální cévní kresba a nodulární reliéf), a teprve po překonání duodenojejunální flexury se objeví charakteristický endoskopický obraz celiakální sprue. V případě nejasného nativního endoskopického obrazu může být prospěšné imersní zobrazení (vynikne chybění klků) a/nebo chromoendoskopie (zvýrazní se mozaikový reliéf atrofické sliznice). Při vyšetřování osob se sideropenickou anémií byla celiakie endoskopicky diagnostikována u 2 – 9 % pacientů. Při rutinní gastroskopii (z jiné indikace) byla celiakální sprue nově diagnostikována u 0,5 – 5 % pacientů. Tyto údaje zdůrazňují význam aktivního pátrání po charakteristických endoskopických znacích celiakie. Enteroskopie, endoskopické vyšetření tenkého střeva, je důležitá zejména při diagnostice komplikací celiakie, především refrakterní sprue, ulcerózní jejunoileitidy a T-buněčného lymfomu. V literatuře byly nedávno uveřejněny také první zprávy o využití kapslové endoskopie v diagnostice celiakie a v rozpoznání komplikací tohoto onemocnění.

Klíčová slova: celiakální sprue, endoskopie tenkého střeva, refrakterní sprue, ulcerózní jejunoileitida, T-buněčný lymfom

Coeliac disease is the most common cause of primary malabsorption in Europe. In the Czech Republic the prevalence rate is estimated to be 1:200 to 1:250 (20,44). Diagnosis is based on serum antiendomysial & anti-tissue transglutaminase antibodies, histological

proof of characteristic villous atrophy of jejunal mucosa, with hypertrophic crypts and increased intraepithelial lymphocytes, and clinical response to gluten-free diet (41,58). Gastrointestinal endoscopy is not the first line diagnostic tool. However, awareness of

basic endoscopic features of coeliac disease is mandatory. This paper is a review of current literature on endoscopy in coeliac disease and also provides some images adopted from our monograph on enteroscopy (6) and from our endoscopy picture archive.



Figure 1 / Obr. 1
Coeliac disease. Proximal jejunum. The most typical and characteristic endoscopic feature of coeliac disease is a mosaic pattern.
Celiakální sprue. Proximální jejunum. Nejvíce typickým a charakteristickým endoskopickým znakem celiakie je mozaikový reliéf.

Endoscopic appearance of the duodenum and/or jejunum

Endoscopic features of coeliac disease comprise reduction in the number or loss of folds, mosaic appearance, scalloping, fissures or grooves of folds in

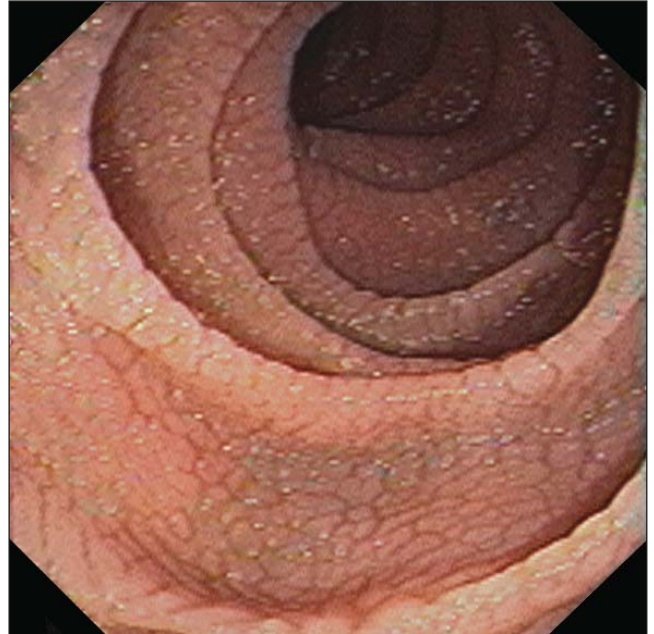


Figure 2 / Obr. 2
Dilatation of jejunal lumen in coeliac disease. Mucosa is atrophic, the characteristic mosaic pattern is finer in this case.
Dilatace lumen jejuna u celiakie. Sliznice je atrofická, charakteristický mozaikový reliéf je v tomto případě jemnější.



Figure 3 / Obr. 3
Dilated duodenum with large volume of stagnating fluid is another characteristic sign of coeliac disease. Vascular pattern shows through atrophic mucosa.
Dilatované duodenum s velkým objemem stagnující tekutiny je dalším charakteristickým znakem celiakální sprue. Atrofickou sliznicí prosvítá cévní kresba.

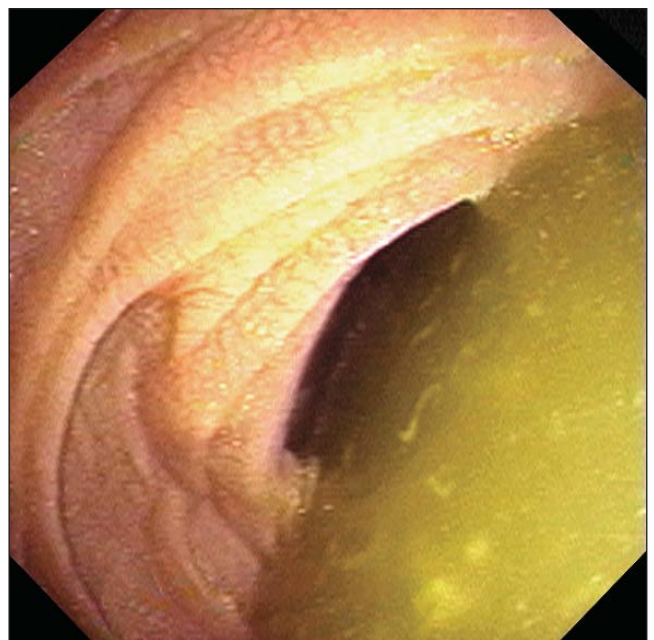


Figure 4 / Obr. 4
Coeliac disease. Large volume of stagnating fluid in dilated jejunal loops and tiny mosaic pattern are seen.
Celiakální sprue. Velký objem stagnující tekutiny v dilatovaných kličkách jejuna. Jemný mozaikový reliéf.



Figure 5 / Obr. 5

Coeliac disease. Severe mucosal atrophy of the postbulbar duodenum (D1), uneven irregular nodular pattern is caused by hypertrophy of Brunner's glands.
Celiakální sprue. Těžká atrofie sliznice postbulbárního duodena (D1). Hrbolatý nepravidelný nodulární reliéf je podmíněn hypertrofií Brunnerových žlázek.

the jejunum, and visible vascular pattern (in the duodenum) and (micro-) nodularity (5,6,25,29,41,45), see Figs. 1 – 6. This appearance is expressed mostly in the jejunum, less pronounced in the duodenum and ileum. Among those endoscopic features, mosaic pattern has sensitivity 89 % and specificity 100 % for coeliac disease, scalloped folds 86 and 100 %, reduction in number or loss of folds 44 % and 99 %, visible underlying blood vessels 5 % and 100 %, and one or more markers have sensitivity 94 % and specificity 99 % for coeliac disease (40). According to another study, mosaic appearance and scalloped fold have a sensitivity of 94 % and specificity of 92 % for the diagnosis of coeliac disease (35). Tursi et al. (53) described positive association of endoscopic features with histological grading according to the Marsh classification (34). It is important to remark that taking biopsy specimens of atrophic mucosa can cause a bleeding lesion.

In most patients diagnosis of coeliac disease can be made by means of duodenoscopy using conventional gastroscope carefully assessing the second part of the duodenum and taking biopsy specimens for histology (5,10,38). However, in some cases duodenal appearance could be abnormal but non-specific. Thus push-enteroscopy is a substantial tool for proper recognition, and the typical mosaic pattern is uncovered in the jejunum after getting over duodeno-



Figure 6 / Obr. 6

Coeliac disease. Jejunal folds are reduced in number, low and smooth. Small intestinal mucosa has tiny granular pattern with small reddish areas.
Celiakální sprue. Příčné řasy jejunu jsou řídké, nízké a vyhlazené. Sliznice tenkého střeva má jemný mozaikový reliéf s malými ploškami zarudnutí.

jejunal junction at the ligament of Treitz. Diagnostic yield of enteroscopy varies in specific studies. In a French study, push-enteroscopy with jejunal biopsies had diagnostic value in only 2/16 (12 %) patients with malabsorption of unclear origin with normal duodenal biopsy and in 2/9 (22 %) patients with abnormal but inconclusive findings of duodenal biopsy (11). In some patients, normal endoscopic appearance of the second part of the duodenum can be found, with biopsies showing non-specific mucosal inflammation but no villous atrophy (54). In specific studies, the endoscopic appearance of the duodenum was indicative of coeliac disease in 16/22 (73 %), 70/88 (79.5 %) (55), 99/129 (77 %) (13), and in 73/78 (94 %) adult patients (2). Among children, endoscopic markers of coeliac disease in the duodenum have even much lower sensitivity: loss of folds only 47 %, mosaic pattern 12 % and scalloping only 6 % (42). In case of suspected coeliac disease with normal or non-specific both endoscopic and histological duodenal findings, we recommend performance of enteroscopy to assess jejunal appearance and that several biopsy specimens of jejunal mucosa are taken. According to another study, duodenal biopsies are sufficient to diagnose coeliac disease of Marsh III grade, but Marsh I-II lesions may be missed in some cases (51).

Loss of intestinal villi can be set off with the immer-

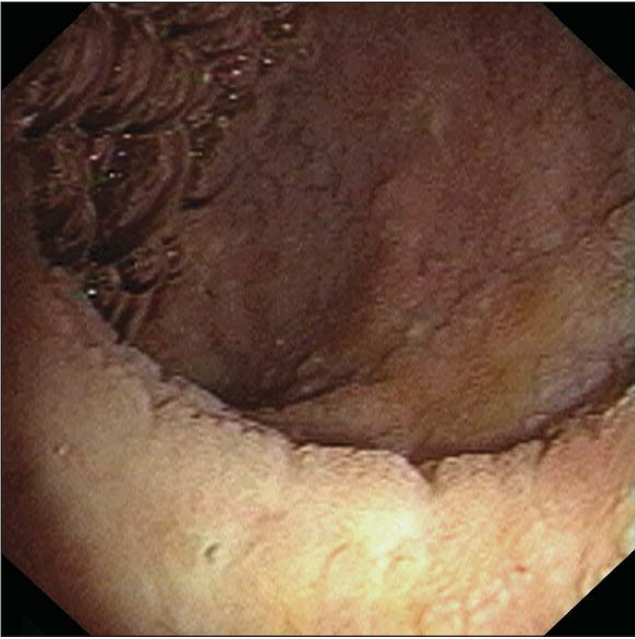


Figure 7 / Obr. 7

Immersion picture of severely atrophic jejunum. Tangential view nicely shows grooves of folds, another typical character of coeliac disease.

Imerzní obraz těžce atrofického jejunum. Tangenciální pohled zřetelně ukazuje rýhování slizničních řas, další typický znak celiakie.

sion technique that may further increase the diagnostic accuracy of endoscopy for coeliac disease (21,28) (Fig. 7). Chromoendoscopy can further improve the diagnostic yield of enteroscopy (Figs. 8 and 9). Indigo carmine or methylene blue chromoendoscopy enhances the mosaic pattern and thus prevents false negative reading of partial villous atrophy (40). The combination of magnifying endoscopy and dye scattering method could be useful for closer observation of intestinal mucosa in coeliac disease (37).

Unexplained iron-deficiency anaemia

Push-enteroscopy along with standard upper gastrointestinal endoscopy increases the diagnostic yield when evaluating asymptomatic patients (8,23). However, other authors stated that coeliac disease can be distinguished by standard duodenoscopy in most cases, taking a sufficient number of biopsies (3,54). Prevalence of occult coeliac disease was 2.8 % (30), 4.7 % (15), 8.7 % (26) and 1.8 % (33) in patients presented with iron-deficiency anaemia.

Unsuspected coeliac disease

Unsuspected coeliac disease can be diagnosed during routine endoscopy by recognition of changes in the duodenum. Nine patients with newly diagnosed coeliac disease were recognized among 1,749 routine



Figure 8 / Obr. 8

Chromo-endoscopy. Abnormal but non-specific native enteroscopy appearance of the jejunum in a patient investigated because of malabsorption.

Chromoendoskopie. Abnormální avšak nespecifický nativní enteroskopický obraz jejunum nemocného vyšetřovaného pro malabsorpční syndrom.



Figure 9 / Obr. 9

Chromo-endoscopy. Indigo carmine sprayed into the jejunum revealed the characteristic mosaic pattern of coeliac disease. The same patient as seen in Fig. 8.

Chromoendoskopie. Po aplikaci indigokarmínu do jejunum se zobrazuje charakteristický mozaikový reliéf celiakie. Stejný nemocný jako na obr. 8.

upper gastrointestinal endoscopies (0.5 %), with findings of reduced or absent folds (6 patients), scalloped folds (5 subjects), mosaic pattern (3 persons), and mucosal fissures (2 subjects). These patients were



Figure 10 / Obr. 10

Coeliac disease. A giant ulcer in the duodenal bulb in a patient with refractory sprue. Helicobacter pylori was negative by means of ^{13}C -urea breath test and by histology.

Celiakie. Velký vřed v bulbu duodena u nemocného s refrakterní sprue. Vyšetření na přítomnost infekce Helicobacter pylori bylo negativní dechovým testem s ^{13}C -ureou a histologickým vyšetřením.

referred for endoscopy because of iron deficiency (5 persons), folate deficiency (1 subject) and metabolic bone disease (6 patients) (25). Unsuspected coeliac disease was diagnosed at endoscopy by recognition of changes in the duodenum 1.6 % (open access endoscopy) (16), 4.7 % (referred for iron-deficiency anaemia) (15), 1.8 % (iron-deficiency anaemia) (33). These figures suggest that coeliac disease may be under-diagnosed in this country, too. Further education and awareness of typical endoscopic features may improve proper recognition of asymptomatic coeliac disease in patients referred for "standard" upper gastrointestinal endoscopy for reasons other than malabsorption. Routine biopsies of distal duodenum should become standard at upper gastrointestinal endoscopy (4,24). Six cases of coeliac disease were described histologically from 4,199 biopsies (0.14 %) from the endoscopic normal distal duodenum (57).

Differential diagnosis

Mosaic pattern is a typical sign of coeliac disease but not fully pathognomonic. Mosaic pattern, mucosal grooves and/or scalloping of folds are found in tropical sprue but also in some cases of infectious jejunitis in HIV-positive patients (Cryptosporidium, Isospor-

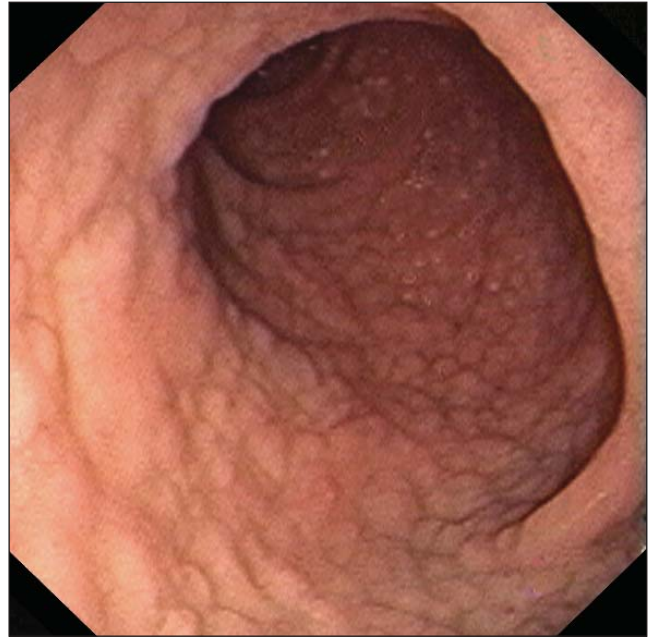


Figure 11 / Obr. 11

Coeliac disease. Severe involvement of the proximal jejunum in refractory sprue. Swelling in atrophic mucosa creates irregular nodular pattern of the jejunum. Transverse folds are absent, mucosa is reddish in colour.

Celiakie. Těžké postižení proximálního jejunum u refrakterní sprue. Otok atrofické sliznice vytváří nepravidelný nodulární reliéf jejunum. Příčné řasy jsou vymizené, sliznice je zarudlá.

ra, cytomegalovirus, Microsporidia), HIV-enteropathy or eosinophilic enteritis (48). Some authors emphasize that it is also important to exclude giardiasis (27,48). According to our experience (6) small bowel involvement in Giardia lamblia infection is different in most cases, with jejunal grape-like nodular pattern due to lymphoid hyperplasia, some nodules look like small sessile polyps. In case of uncertainty, it is necessary to search for parasites. Scalloping of the duodenal mucosal folds is generally due to villous atrophy most commonly associated with coeliac disease. Individual patients with scalloping of duodenal folds and histological confirmation of villous atrophy due to Crohn's disease were also published (12).

Follow-up and complications

Push-enteroscopy is an important tool in follow-up of patients with coeliac disease, especially of those in higher risk. Coeliac disease can be associated with refractory or recurrent Helicobacter pylori negative ulcers of the duodenal bulb (50) (Fig. 10). There were also ulcers of the postbulbar duodenum and jejunum (18,46). Erosions confined to the second part of duodenum are specific for villous atrophy although the sensitivity is low (14). Gastric metaplasia to the distal duodenum is frequently found in untreated coeliac

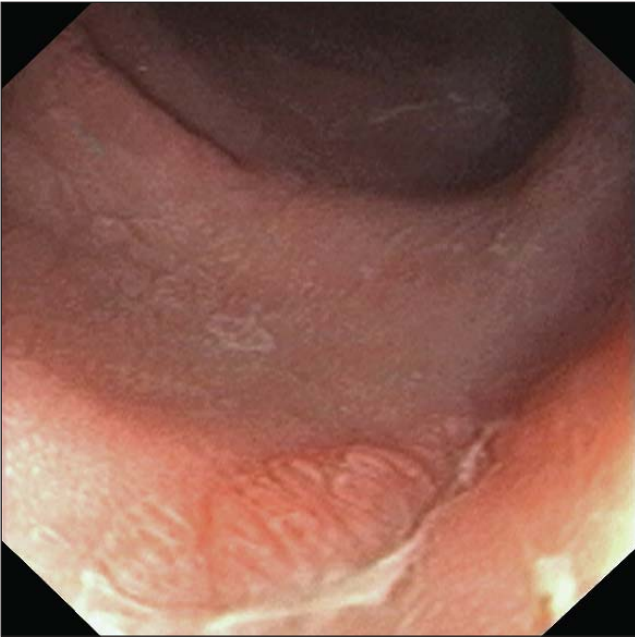


Figure 12 / Obr. 12

Coeliac disease. A linear ulcer of the proximal jejunum (20 mm long and 2 mm wide) in refractory sprue.

Celiakie. Lineární ulcerace proximálního jejunu (20 mm dlouhá a 2 mm široká) u nemocného s refrakterní sprue.



Figure 13 / Obr. 13

Coeliac disease. An ovoid ulcer (of size 5 to 10 mm) at the distal duodenum in refractory sprue.

Celiakie. Ovoidní ulcerace (o rozměru 5 * 10 mm) v distálním duodenu u refrakterní sprue.

disease (up to 70 % of biopsy specimens) if they are searched for (49).

Push-enteroscopy improves diagnostic yield in refractory sprue and enables one to take several jejunal biopsies for intraepithelial lymphocytes phenotyping (7). Endoscopic findings in refractory sprue are solitary jejunal ulcers and strictures (Figs. 11 – 14). Surprisingly extensive gastric heterotopia of the jejunum was found in 70 % of 21 jejunal biopsies of refractory sprue (52).

Refractory sprue is a window between coeliac disease and enteropathy associated T-cell lymphoma (39). In particular, finding of jejunal stricture is very suspicious in this respect. Enteroscopic appearance of early T-cell lymphoma may be discreet (Fig. 15), the affected part of the small bowel is rigid, no peristalsis is apparent, folds are absent and infiltrated mucosa is fragile and reveals granular pattern. It is mandatory to take several biopsies from any flat lesion visible within the small bowel. (19). Advanced small intestinal lymphoma usually form evident tumorous mass, often with ulcerations (6,36) and can be easily recognized.

Ulcerative jejunoileitis is a redoubtable complication of coeliac disease. It is associated with a significant risk of perforation and/or life threatening bleeding. That is why small bowel endoscopy must be considered very cautiously and performed very carefully by a skilled endoscopist. Enteroscopic pattern of

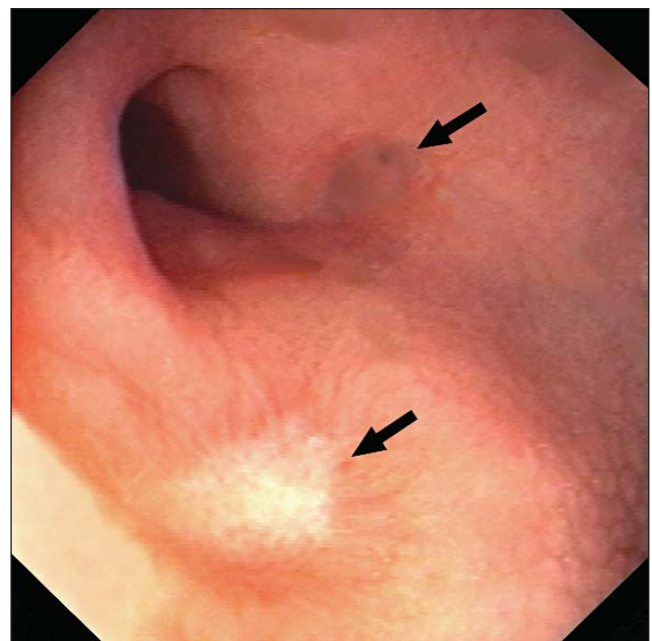


Figure 14 / Obr. 14

Refractory sprue. Stenosis of the D3 duodenum and two ulcers (arrows) in front of stenosis are seen.

Refrakterní sprue. Stenóza D3 duodena a dva vředy (šipky) před stenózou.

ulcerative jejunoileitis (Fig. 16) is different from solitary ulcers in untreated coeliac disease or refractory sprue. There are multiple pale star-shaped ulcers surrounded with atrophic jejunal mucosa.

Small intestinal mucosal recovery

In patients on a strict gluten-free diet, the endosco-

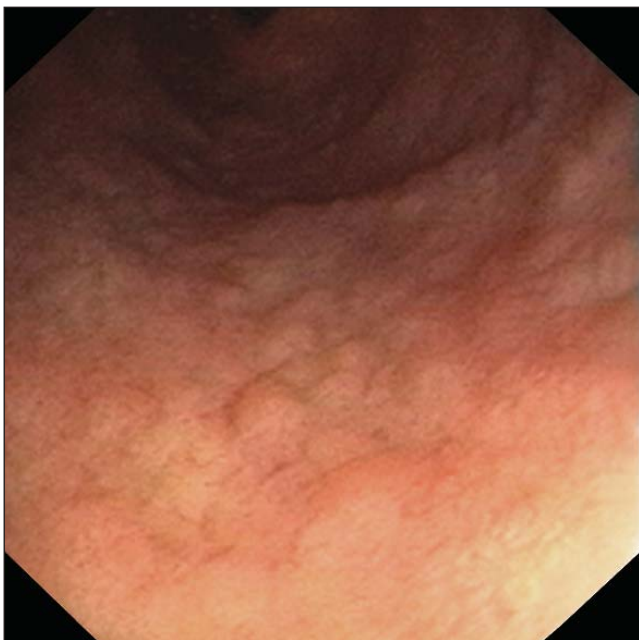


Figure 15 / Obr. 15

T-cell lymphoma complicating coeliac disease. Affected part of distal duodenum is rigid, infiltrated mucosa is fragile and reveals granular pattern.

T-buněčný lymfom komplikující celiakální sprue. Postižená část distálního duodena je rigidní, infiltrovaná sliznice je křehká a má granulární reliéf.



Figure 16 / Obr. 16

Ulcerative jejuno-ileitis complicating coeliac disease. There are multiple stellate ulcers with characteristic pale greyish base, surrounded with atrophic jejunal mucosa.

Ulcerózní jejunoileitida komplikující celiakální sprue. Mnohočetné hvězdicovité vředy s charakteristickou bledou šedavou spodinou, obklopené atrofickou sliznicí jejunu.



Figure 17 / Obr. 17

Coeliac disease in capsule endoscopy. Characteristic mosaic appearance and grooves of folds in the middle jejunum.

Celiakální sprue na kapslové endoskopii. Charakteristický mozaikový reliéf a rýhování řas střední části jejunu.



Figure 18 / Obr. 18

Coeliac disease in capsule endoscopy. Typical scalloping of folds in the distal jejunum.

Celiakální sprue na kapslové endoskopii. Typické vroubkování příčných řas distálního jejunu.

pic pattern of the small bowel normalizes within a few years (6). However, there are controversial data to be found in literature on the persistence of mucosal damage in patients with coeliac disease who maintained a gluten-free diet, reporting both complete recovery (9) and persisting mucosal damage (32,47,56). Brocchi et

al. (1) have emphasized that there could be some potential bias, like lack of proper orientation of biopsy specimens or assessment of strict adherence to gluten-free diet. The true clinical impact of possible persisting minimal mucosal changes in cases of good clinical response must be further clarified (1).

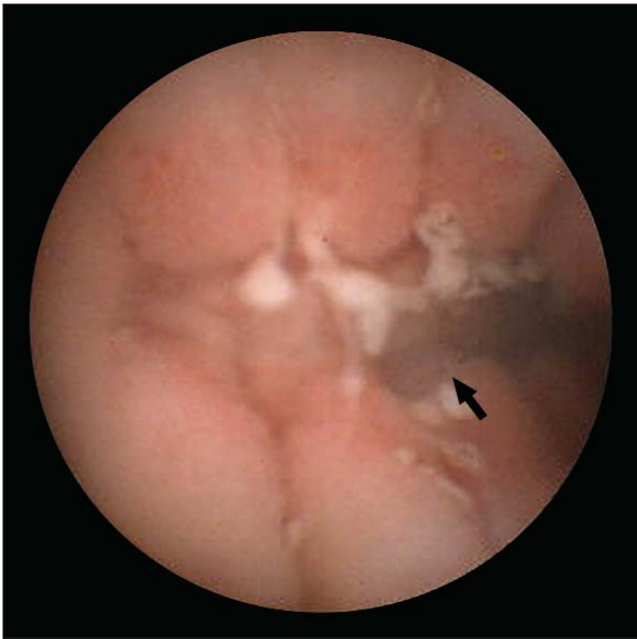


Figure 19 / Obr. 19

T-cell lymphoma in coeliac disease. An ulcer in the middle part of the ileum (3 to 8 mm in size, marked by an arrow) surrounded by mucosal grooves. Capsule endoscopy.
T-buněčný lymfom u celiakální sprue. Ulcerace ve střední části ilea (o rozměru 3 * 8 mm, označena šipkou). Okolní sliznice je vroubkovaná. Kapslová endoskopie.

Capsule endoscopy in coeliac disease

Wireless capsule endoscopy is a promising non-invasive method to investigate the entire small intestine. Its role in coeliac disease is still to be defined (17,22,31,43). It can be useful in diagnostics of coeliac disease as a cause of unclear malabsorption and/or iron deficiency anaemia (Figs. 17 and 18). Capsule endoscopy will hopefully be utilized in long-term follow-up of coeliac disease and will be helpful in early recognition of complications, especially T-cell lymphoma (Figs. 19 and 20) or adenocarcinoma.

Conclusions

In summary, it is important to stress that awareness

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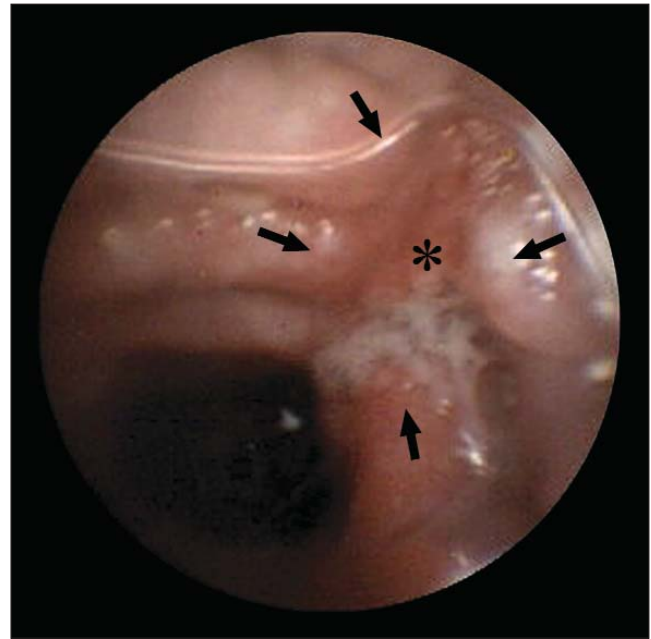


Figure 20 / Obr. 20

T-cell lymphoma in coeliac disease. Infiltration of ileal folds (arrows) with a central ulcer (asterisk). Involved mucosa is reddish, fragile with granular pattern. The same patient as seen in Fig. 19. Capsule endoscopy.
T-buněčný lymfom u celiakální sprue. Infiltrace řas ilea (šipky) s centrální ulcerací (hvězdička). Postižená sliznice je zarudlá, fragilní, s granulárním reliéfem. Stejný nemocný jako na obr. 19. Kapslová endoskopie.

of endoscopic features of coeliac disease may alert endoscopists to the presence of the disease and the need for duodenal biopsies. Push-enteroscopy and/or capsule endoscopy may be useful in recognition of cases with normal or non-specific abnormal duodenal findings. Push-enteroscopy and/or capsule endoscopy are important in the follow-up and diagnostics of complications of coeliac disease.

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