Rev Esp Patol 1999; Vol. 32, N0 3: 397-408

Short Course 4

Short Course in honor of Christoph E. Hedinger: Progress in pathology of diseases of the extrahepatic biliary tract and the duodenum

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Lessons from duodenal biopsies

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Clinicopathological correlation is crucial in reporting duodenal pathology. In patients with proven endoscopic duodenal ulcer or duodenitis most clinicians will only biopsy the gastric antrum to determine *Hellcobacter pylon* status. However, in investigation of other gastroduodenal disease, *e.g.,* polyps, HIV, malabsorption, celiac disease, dermatitis herpetiformis, Crohn's disease, indeterminate colitis, nonsteroidal antlinflammatory drug (NSAID) damage, investigation of unexplained diarrhea and upper gastrointestinal pathogens, biopsy is useful (1-5) and examination of the postbulbar duodenum can be considered an elective part of routine endoscopy (6).

Normal duodenal anatomy and histology

The gastroduodenal junction may be crenated with finger-like processes of gastric epithelium extending up to 6 mm into the duodenum (7). At endoscopy the duodenum is divided into the duodenal bulb (first part), which is 4-6 cm long and 2-3 m wide, which curves posteriorly at the genou (superior duodenal angle) into the descending duodenum, which is 10 cm long, 3-5 cm wide and marked by prominent transverse folds (folds of Kerckring). The ampulla of Vater is situated on the medial wall 8-10 cm from the pylorus, although this is rarely viewed with the forward viewing endoscope employed at gastroduodenoscopy. The descending duodenum curves to the horizontal (third part) and, at the inferior duodenal angle, becomes the ascending or fourth part, the total length being 25 cm.

Normal mucosa is understated in reports (8) and defined as a normal duodenal architecture (a villus:crypt ratio of >2:1 in most areas) with or without Brunners glands above the muscularis mucosae and no increase in lamina propia cellularity or evidence of epithelial damage (8, 9).

Duodenal biopsy specimen handling

Is biopsy size and type important? Use of normal endoscopy biopsy forceps gives an adequate sized biopsy (10) and four biopsies should preferably be taken for an adequate sample. However, it is important that the biopsies are taken from the correct site in given clinical circumstances and thus the optimal biopsy site in the duodenum depends on the clinical presentation. Without question, obvious tumors should be biopsied. Peptic duodenitis and gastric metaplasia occur in the bulb and are rare in the second part (11, 12). To assess partial villus atrophy in coeliac disease or dermatitis herpetiformis, this is patchy and is only present in the second and third parts. Duodenitis is reported in inflammatory bowel disease, particularly Crohns disease (5) and can be present throughout the duodenum. Pathogens may occur in the first, second and third parts of the duodenum, although *H. pylon* only occur on gastric metaplasia.

The duodenum should be sampled in quadrants *i.e.,* the anterior, posterior walls, roof and floor. The optimum number of biopsies again depends on the pathological situation. Duodenitis is a stage of duodenal disease which may be focal (12) and which can be missed on one biopsy only, two being a minimal requirement, in the anterior wall and roof, which will also detect gastric metaplasia in 95% of cases and must be biopsied more than 10 mm distally from the pylorus to avoid sampling errors. In suspected celiac disease, four biopsies should be taken from the second and third parts (13). Regarding the orientation of biopsies the question of whether we need low power microscopy should be asked. With the demise of the capsule biopsy most endoscopic biopsies are too small for accurate visualization of villi so this is not necessary. The biopsy should be embedded on edge and it should be accepted that some villus distortion is going to occur. Routine staining of the duodenal biopsy should be with hematoxylin and eosin and periodic acid-Schiff (for detection of gastric metaplasia). In addition, a Giemsa stain can be used for pathogens although other pathogens may require electron microscopy or immunostaining if the clinical information suggests that immunodeficiency such as HIV and cytomegalovirus is suspected.

Duodenal bioPsy patholopy

Duodenitis

In assessing duodenitis the biopsy must be systematically examined for surface erosions, regeneration, intraepithelial lymphocytes (IELs), neutrophils (IENs) and pathogens. Gastric metaplasia is restricted to the surface epithelium. In the lamina propria chronic inflammation is seen as a definitive increase in lymphocytes and any neutrophils are abnormal (9). The presence of granulomas or macrophages must be assessed. Gastric heterotopia may be seen as small sessile nodules on endoscopy, the incidence varies from 0.9-1.4%. On histology, these are seen as aggregates of body type glands in by gastric epithelium (14).

Partial villus atroohl

Partial villus atrophy can be seen on endoscopy as scalloping with a smooth shiny mucosa but may be quite normal in appearance

(15). Biopsy of established villus atrophy is easily recognized but more subtle early changes can be difficult to diagnose with confidence. There is a wide variation in villus height and age has no effect on morphometry (16). The normal villus height:crypt depth ratio is 3:5 and the surface enterocyte height is normally 29-34 pm. Crypt hyperplasia is a pointer and counting of intraepithelial lymphocytes is paramount. The normal range is 10-30/1 00 enterocytes (13).

Differential diagnoses of celiac disease include infective enteropathy, tropical sprue, graft *versus* host and transient food sensitivities (eggs, fish, Soya, etc.), immunoproliferative disease and drug damage. Duodenal pathology in partial villus atrophy associated with dermatitis herpetiformis is identical to celiac disease. Celiac disease is a clinicopathological diagnosis with a characteristic lesion of the small intestine, malabsorption and prompt improvement on a gluten-free diet. Symptoms are related to the extent of mucosa involved. Antigliadin antibody screening tests are useful in at risk groups but biopsy is the gold standard for diagnosis (17).

Pathogens

Numerous microorganisms infect duodenal mucosa, particularly in immunosuppressed patients and may be either asymptomatic or symptomatic, leading to endoscopy and biopsy. Principal pathogens are cytomegalovirus, microsporidiosis, cryptosporidiosis in immunosuppression, in which a high index of suspicion is needed for diagnosis, as the changes are subtle. *Giardia lamb/ia* infection also shows nonspecific pathological changes (18). Whipples disease is a rare multisystem bacterial infection with characteristic duodenal pathology. The organism is *Tropheryma whippelli.* The diagnosis is usually established by duodenal biopsy but the gut is not inevitably involved (19).

SugQested reporting orotocol for duodenum

Systematically note:
Site (*+1*– Brunners glands)? DI, D2
Villus architecture – normal/distorted
Surface – erosion, IELs, lENs, gastric metaplasia – *±1*—extent?
Inflammation, active and/or chronic, grade mild, moderate, severe-epithelium/lamina propria
Pathogens
Other pathologies *(e.g.,* granulomas, macrophages)?

This gives the algorithm

Depending on biopsy site:
DI – Active duodenitis, lENs + gastric metaplasia + antral *H. pylon* = DU risk
D2 – Definite villus distortion, no neutrophils, $IELs = partial villus atrophy
D1/2 – Chronic duodenitis – think of other pathology *e.g.,* pathogens, IBD, etc.

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Tumors of the amputla: Pathogenesis and prognostic factors

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Ampullary epithelial neoplasms include benign (5%) and malignant tumors (95%), which represent 5% of all gastrointestinal tumors but which account for up to 36% of the surgically operable pancreaticoduodenal tumors (1). Ampullary carcinoma is a tumor topographically centered in the region of the ampulla of Vater, which is formed by three anatomical components: the ampulla (common channel), the intraduodenal portion of the bile duct and the intraduodenal portion of the pancreatic duct. Thus, it may show infestinal or pancreatobiliary morphology. The unequivocal establishment of ampullary origin is possible in small lesions by applying strict topographical criteria obtained at gross and histological examination. The presence of 'preinvasive" (adenomas or areas of dysplasia) modification in the anatomical structures of the ampulla (2) and the intestinal type of the carcinoma can help in the distinction (3). Periampullary carcinoma, is a widely used term to define a heterogeneous group of neoplasms arising from the head of the pancreas, the terminal common bile duct and the duodenum. The din-