CASE 5

DRUG INDUCED ULCERATION AND PERFORATION OF THE SMALL INTESTINE

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This case is the strangest drug induced ulcer with perforation of the small intestinal wall that I have ever seen! The patient had taken his drug (Motilium) just like the nurse had told him to do, but as he was confused he did not remove the package and swallowed it with the known results of clinical perforating terminal ileal tumour and the histology of ileal perforation as illustrated on the slides.

The majority of changes amongst drug induced pathology consist of ulcerations, stricture formation, inflammatory processes and ischaemia which are really non-specific signs. Clues indicating drug-induced aetiology may be apoptotic epithelial cells, increased intra-epithelial lymphocytes and the presence of eosinophils.

The drug-induced pathology has been claimed to be responsible for a large proportion of the pathological conditions affecting the small intestine (present in up to 70% of chronic non-steroidal anti-inflammatory drugs -NSAID- users!). The morphological features as seen in drug induced small intestinal the various conditions which may lead to a diagnosis and to consider mechanisms in important for the pathogenesis of the small intestinal damage.

Drug-induced pathology

The presence of focal active inflammation can indicate acute infectious ileitis, resolving infectious enteritis and early chronic inflammatory bowel disease - especially when eosinophilic cryptitis and crypt abscesses occur but it can also be related to the use of drugs like NSAID and is then called NSAID enteropathy. Although the gastric and duodenal
Ulcerations are known since many years, the small intestinal drug-induced alterations are less
recognized and this because the ileum is less frequently reached at endoscopy. The exact
pathogenesis of NSAID enteropathy is not fully understood but increased mucosal
permeability, loss of tight junction function, intracellular organelle damage are implicated and
factors that contribute further to the mucosal lesions are vascular. They include a decrease in
blood flow, impaired neutrophil function, defects in mucosal defence and inhibition of
prostaglandins. Access of luminal content and bacteria to the mucosa will induce an
inflammatory infiltration and ulceration, responsible for the clinical symptoms of protein loss
and unexplained anaemia. In ileal biopsies the lesions are mostly mild and present as
superficial erosions, increased apoptotic figures as well as eosinophilic infiltrates causing
cryptitis and crypt abscesses. Non-specific ileal ulcers may be induced by NSAID.

One condition which is very rare is distinctive and is claimed to be typical of NSAID
enteropathy, namely diaphragm disease. This typically presents with single (rarely) or many
diaphragms that are web-like mucosal septa causing luminal narrowing and obstruction. They
are in general perpendicular fibrotic bands covered by a reactive mucosa that can be ulcerated
or eroded at the surface.

Drugs which can cause intestinal damage include potassium chloride, administered orally in
the treatment of hypokalemia. It may cause ulcers and strictures throughout the
gastrointestinal tract by irritation of localized high salt concentrations or localized ischaemia.
Kayexalate, sodium polystyrene sulphonate in sorbitol, that is administered orally, via a
nasogastric tube or by enema in patients with hyperkalemia can induce ulceration, necrosis,
perforation. It is well distinguishable in slides as polygonal basophilic crystals, staining
maroon with Ziehl–Neelsen.

Selective Internal Radiation Therapy (SIRT), radioembolization of primary or metastatic liver
tumours by injection of biocompatible microspheres carrying radioisotopes into hepatic artery
or its branches can induce gastrooduodenal injury due to misplacement of radioactive
microspheres in the gastrointestinal tract.

References

Cuvelier C, Demetter P, Mielants H, Veys EM, De Vos M.
The interpretation of ileal biopsies: morphological features in normal and diseased mucosa.
Histopathology 2001, 38: 1-12
Evans SM, Whittle BJR.

Hotz-Behofsits CM, Walley MJ, Simpson R, Bjarnason IT.
COX-1, COX-2 and the topical effect in NSAID-induced enteropathy. Inflammopharmacol 2003, 11: 363-370

Lee F D.

Leite AZA, Sipahi AM, Damião et al.


Schneider A R, Benz C, Riemannn J F.
Adverse effects of nonsteroidal anti-inflammatory drugs on the small and large bowel. Endoscopy 1999, 31: 761-767

Smale S, Tibble J, Sigthorsson G, Bjarnason I.

Tanaka A, Hase S, Miyazawa T, Takeuchi K.