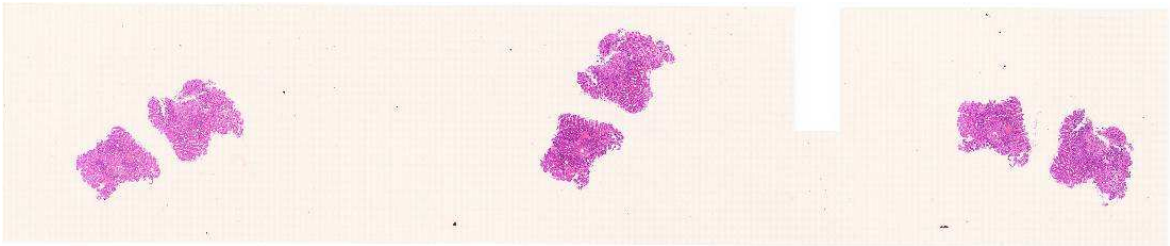
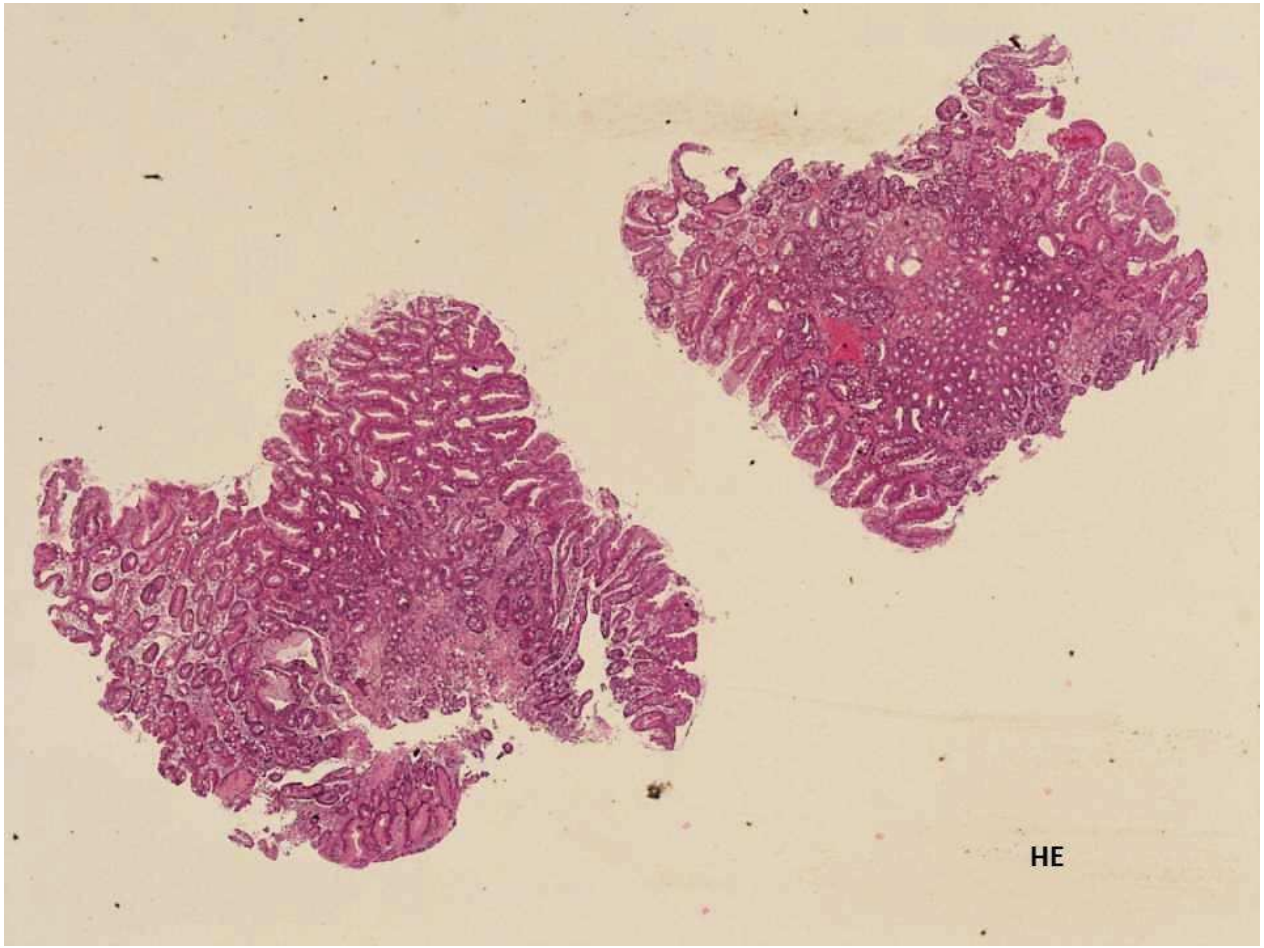
Este caso nos foi gentilmente cedido pela Dra. Miriam Cuatrecasas Freixas de Barcelona

HISTÓRIA CLÍNICA

A 68-year-old male with a history of metastatic androgen-independent prostatic cancer presented with non-specific abdominal pain and dyspepsia. He underwent upper gastrointestinal endoscopy that showed no abonormal signs or lesions on the esophagic, gastric or duodenal mucosa on macroscopic inspection. Gastric biopsy specimens were taken to rule out Helicobacter pylori gastritis; no tissue from the oesophagus or duodenum was obtained.

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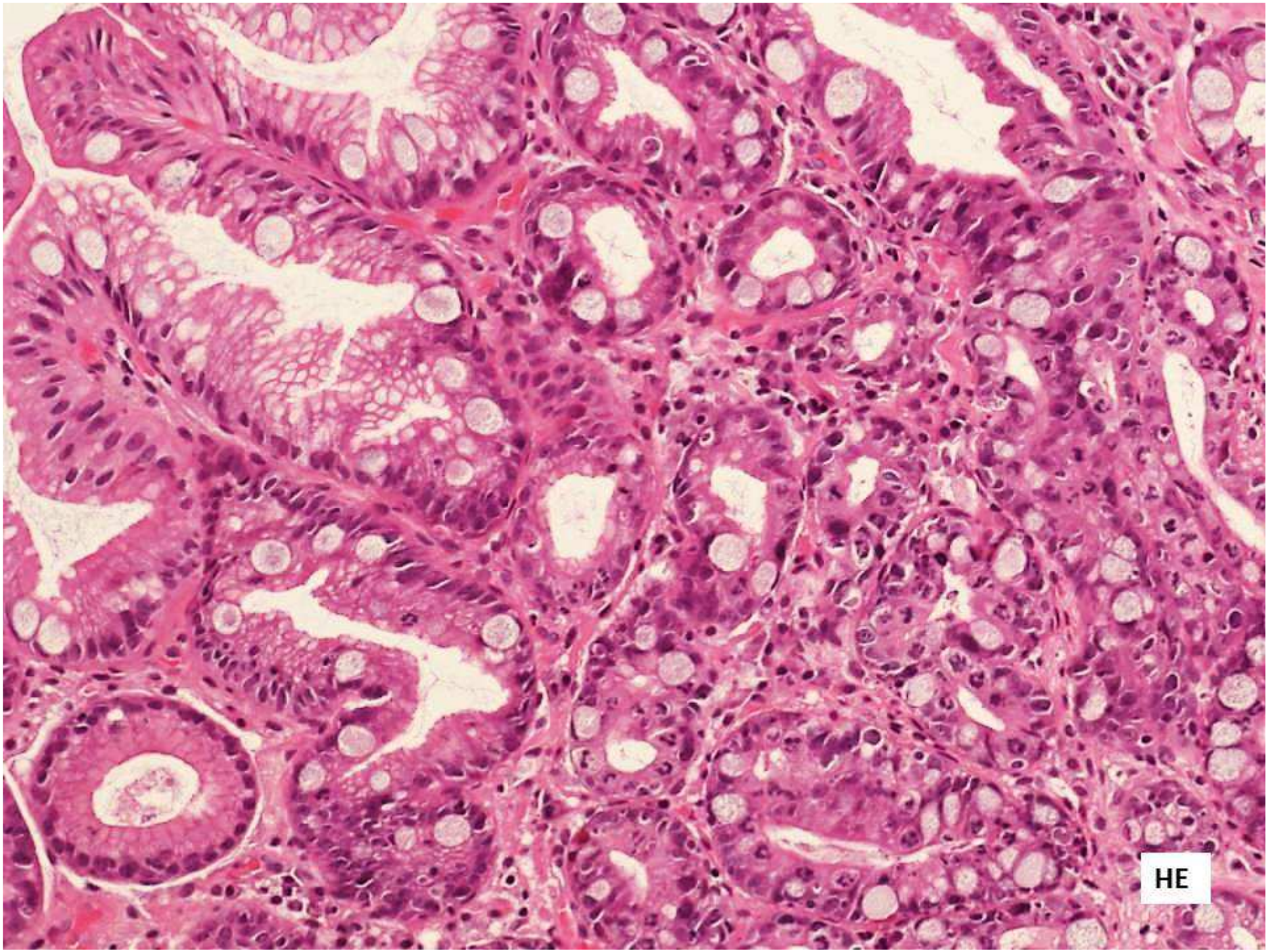
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Taxane-induced injury of the GI tract

Some chemotherapeutic agents are associated with different side-effects. Among them, Taxanes -Docetaxel (TaxotereTM) and paclitaxel (TaxolTM)- have been shown to have several cytotoxic-induced GI and non-GI side-effects, such as myelosuppression, neuropathy, myalgia, alopecia, fatigue, mucositis, diarrhoea, and skin and nail changes.
In the GI tract, Taxol has been associated with mucosal injury in the form of cell necrosis, gastritis, duodenitis, diarrhoea, neutropenic enterocolitis, and colonic perforation. The development of pseudomembranous colitis in some patients receiving these drugs is due to different grades of inflammation and necrosis of the colonic mucosa, with alteration of the intestinal flora. Methotrexate has been the most common implicated agent, but Taxanes and platinum-based drugs can also cause extensive inflammatory changes in the colonic mucosa, with a favorable environment for the overgrowth of Clostridium difficile (C. difficile) and production of its exotoxins.
Taxanes induce unique histologic changes within the epithelium of the GI tract. The effects are secondary to early damage of the cell, since the drug binds to the □-subunit of tubulin with microtubule assembly and stabilization of the polymers that blocks depolymerization. This leads to cell-cycle arrest due to centrosomal impairment. Taxol activates apoptosis inducing Bcl-2 phosphorylation, thus Bcl-2 does not bind to BAX. It also induces p53 and p21/WAF-1. Docetaxel also induces angiogenesis.
Morphologically there is an increased apoptosis with ring mitosis that evolve into cell necrosis. The drug acts on the mitotically active cells of the mucosa, such as those in the proliferative compartment of the GI tract. Ring mitoses and accompanying apoptosis are seen within the proliferative region of the mucosa.
The differential diagnosis among Taxol-associated changes are true dysplastic epithelial changes. The presence of ring mitoses resulting from mitotic arrest are not seen in true dysplastic epithelial changes. Besides, in Taxol mucosal injury, there is a surface maturation of the epithelium, which is scarcely seen in dysplasia. Pathologists should be aware of these changes, since it could lead to false diagnosis of different grades of dysplasia or intraepithelial neoplasia. Besides, Ki-67 and p53 may not help to its distinction.

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