The first case of severe drug-induced gastrointestinal injury related to levodopa is described. The 86-year-old patient experienced acute colitis temporally related to the intake of the drug with complete resolution of symptoms on levodopa withdrawal. Awareness of the possibility of a levodopa-related damage on colon biopsies performed for acute colitis is of paramount importance for pathologists. However, in order to exclude or confirm a drug-related damage an effective communications between clinicians and pathologists is always required.

Drug-induced gastrointestinal injury may represent a diagnostic challenge because it is frequently nonspecific both clinically and histologically. The diagnosis often depends on the pertinent clinical history and the exclusion of others conditions. A temporal relation with drug intake and drug withdrawal is essential to get to diagnosis.

Herein we describe the first case of severe, reversible acute colitis in a patient treated with levodopa for vascular Parkinsonism.

Rare cases of acute colitis have been reported in patients receiving alpha-methyldopa 1-4, an antihypertensive medication structurally related to catecholamines.

A 86-year-old man was admitted to hospital with a several weeks history of bloody diarrhoea and progressive weight loss. His past medical history included insulin-dependent diabetes mellitus, polymyalgia rheumatica, hypertension and atrial fibrillation. Vascular Parkinsonism had been diagnosed 3 months previously.

Medication recorded on admission were: warfarin, furosemide, canrenone, prednisone and insulin aspart. Levodopa plus carbidopa had been started 3 months previously. Blood tests showed mild anemia and neutrophilia, altered electrolytes level and a mild chronic renal failure. Stool cultures were negative. Colonoscopy showed a widely erythematous, friable mucosa with numerous microulcers from ileum to rectum. Multiple biopsies were taken.

The patient was on low-dose steroid therapy (prednisone 6.25 mg/day) for polymyalgia rheumatica; following the clinical and endoscopic suspicion of inflammatory bowel disease, he was put on high-dose steroid therapy (prednisone 80 mg/day) with no resolution of symptoms. Pathological evaluation of intestinal biopsies revealed a severe acute colitis. There was an intense inflammatory infiltrate in which neutrophils were prominent in the lamina propria and within some crypts in absence of both architectural distortion and basal plasmocytosis (Figs. 1-3). Numerous apoptotic bodies were present at the base of the crypts (Fig. 4). In the light of the acute pattern of intestinal injury together with apoptosis, the pathologist suggested to evaluate the possibility of a drug-related damage, after excluding clinically infections. It was felt that colitis might be related to levodopa treatment as the other drugs the patient was receiving do not generally cause a drug-induced intestinal injury. Levodopa was stopped with a rapid clinical improvement. One month later a repeated colonoscopy was totally normal with a complete histological restitution of intestinal mucosa. The temporal association between levodopa assumption and symptoms onset together with the rapid clinical, endoscopic and histological resolution of colitis after levodopa withdrawal suggests levodopa could be the cause of acute colitis. In the literature 1-4 cases of acute colitis have been reported in association with alpha-methyldopa, an antihypertensive medication structurally related to catecholamines. The
mechanism of colitis related to alpha-methyldopa is supposed to be a mediate immune reaction\textsuperscript{2,3}. Alpha-methyldopa and levodopa molecules have similar chemical features. Both alpha-methyldopa and levodopa contain a catechol (1,2-dihydroxybenzene) and an amino group. Alpha-methyldopa differs structurally from levodopa only in the presence of an alpha methyl group. After the first case of methyldopa-induced colitis by Bonkowsky and Brisbane\textsuperscript{1} in 1976, some cases have been reported\textsuperscript{2,3,4}. The histopathological features of alpha-methyldopa related colitis are those of an acute colitis reversible after cessation of drug administration. To the best of our knowledge, no cases of acute colitis related to levodopa have been described. Rare cases of lymphocytic colitis\textsuperscript{5} have been reported in patients treated with preparations containing either levodopa, carbidopa and entacapone or levodopa and benserazide. As levodopa was present in both preparations, it was supposed\textsuperscript{5} to be the causal agent of lymphocytic colitis.

Considering alpha-methyldopa and levodopa chemical structural similarities, we speculate a relation between acute colitis and levodopa administration. An etiologic link to levodopa is suggested by the temporal association between onset of symptoms and drug intake and by the rapid and persistent resolution upon levodopa cessation. Presumably levodopa related intestinal injury is far more common than is diagnosed, but insufficient clinical informations in addition to the frequently nonspecific histological pattern of injury make difficult to achieve the right diagnosis. As drug-induced gastrointestinal injury concerns, an effective communication between clinicians and pathologists is of paramount importance, as it was in our case, in order to get the correct and prompt diagnosis.
References

1 Bonkowsky HL, Brisbane J. Colitis and hepatitis caused by methyldopa. JAMA 1976;236;1602-3.