Large bowel perforation associated with capecitabine treatment for breast cancer

Capecitabine is an oral fluorouracil prodrug which is licenced for treatment of metastatic breast and colorectal cancer [1, 2]. Toxic effects are similar to fluorouracil and include diarrhoea and hand–foot syndrome which resolve on drug withdrawal. We report two cases of large bowel perforation associated with the start of capecitabine treatment in the setting of breast cancer.

The first occurred in a 65-year-old woman with metastatic breast cancer who presented with a large thoracic paravertebral deposit (T3) causing spinal cord compression. Corticosteroids, radiotherapy (20 gray in five fractions) and capecitabine 2000 mg/m² twice daily were commenced. After 2 days of capecitabine treatment and one fraction of radiotherapy, the patient developed severe abdominal pain associated with peritonism, fever, tachycardia and hypotension. Computerised tomography (CT) imaging revealed free intra-abdominal air. Emergency laparotomy revealed a rectosigmoid perforation, possibly related to diverticular disease, which was treated with a Hartman’s procedure from which the patient recovered well.

The second case occurred in a 76-year-old woman with an invasive ductal carcinoma of the right breast which was oestrogen, progesterone and HER2 receptor negative. Significant medical comorbidities precluded wide local excision and standard i.v. chemotherapy. The patient commenced primary treatment with dose reduced capecitabine 1000 mg/m² twice daily. After two cycles, there was minimal tumour response without toxic effects and therefore the capecitabine dose was gradually increased to 2000 mg/m² over the next four cycles. After six cycles, the patient presented with septic arthritis and commenced i.v. antibiotics. Six days later, she developed abdominal pain with acidosis and renal impairment. CT imaging showed free intra-abdominal air. Laparotomy revealed a perforated ascending colon which was treated with right hemicolectomy. After a prolonged recovery, the patient underwent a mastectomy under local anaesthesia and remains well.

There is no published evidence of an association between capecitabine and intestinal perforation. However, the Medicines and Healthcare products Regulatory Agency have received two other reports of capecitabine-associated intestinal perforation in patients with colorectal cancer experiencing severe diarrhoea. Bowel perforation is a well-recognised rare complication of 5-fluorouracil (5-FU)- and bevacizumab-based chemotherapy for metastatic colorectal cancer. Risk factors for
bowel perforation in association with metastatic colorectal cancer treatment include having a primary bowel cancer in situ, recent colonoscopy or sigmoidoscopy and previous adjuvant radiotherapy [3].

None of these risk factors were present in our patients; however, one patient did have diverticular disease which may have increased their risk of bowel perforation. There was no evidence of breast cancer in either of the surgical resection specimens to explain the perforations. Even though the precise mechanism of bowel perforation is uncertain for majority of patients, capecitabine and 5-FU have significant toxicity to colonic cells. It is therefore likely that both perforations arose in areas of bowel that were either stressed or damaged and or undergoing normal regeneration, a process that was disrupted by capecitabine treatment which may have precipitated the perforations. Although uncommon, these cases highlight a potentially serious life-threatening complication of capecitabine treatment which clinicians should be aware of.

S. Cowman, J. Stebbing & M. Tuthill*

Department of Medical Oncology, Charing Cross Hospital, Fulham Palace Road, London, UK
(*E-mail: marktuthill@doctors.org.uk)

references


doi:10.1093/annonc/mdn397
Published online 18 June 2008