**Supplementary Table 3. Summary CIGH Case Reports: UK Yellow Card Data 1999–2017**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Sex, age (yr)** | **Clozapine dose (mg/d)** | **Clozapine duration (d)** | **Clinical features** | **Investigations** | **Treatment** | **Outcome** |
| M, 20-30 | - | 364 | Acute upper abdominal pain, nausea, vomiting haematemesis, loss of appetite, rigid abdomen | During laparotomy the whole of the gastrointestinal tract was found to be ischaemic and cyanosed with patches of dark green ischaemia. Diagnosed with peritonitis | Subtotal colectomy and colostomy (probably reversible). | During the operation had two cardiac arrests and was successfully resuscitated |
| F, 40-50 | 250 | 2242 | Hospitalised due to low haem­oglobin and severe constipation. Nausea. History of severe constipation | Found to have mega-bowel. Had advanced chronic kidney disease from obstructive uropathy due to chronic constipation | Ileostomy and haemodialysis | Loss of renal cortical mass and irreversible end-stage kidney disease. Patient experienced seizures after haemodialysis. Clozapine was to be continued at half the dose |
| M, 40-50 | - | - | Presented by ambulance with tachycardia, hypotension, Glasgow Coma Scale score of 3 | CT scan: obstructed large bowel caused by impacted stool at the end of the sigmoid colon (8 cm in diameter). No perforation detected. Sepsis secondary to bacterial translocation caused by fecaloma and associated kidney failure. The diagnosis was severe constipation leading to sepsis multi-organ failure. | Admission to ITU for continual enemas, laxatives, intubation and haemo­filtration. | Patient recovering following lengthy ITU admission |
| M, 40-50 | 700 | 3177 | Generally unwell with sepsis. | CT showed faecal loading consistent with chronic or sub-acute obstruction secondary to hypomotility. Over a few days’ patient became increasingly unwell and CT showed ischaemic bowel. Histopathology later confirmed ischaemic bowel and a dilated colon. | Sub-total colectomy with ileostomy formation and placement of intra-abdominal drains; 3-week stay on the ITU. Intubated for respiratory failure and pneumonia and received daily haemo­dialysis. Suffered dehiscence of his abdominal wound requiring placement of a drain and abdominal mesh. | Transferred to a general surgical ward, still requiring haemodialysis. |
| M, 30-40 | 325 | 1629 | Severe lower abdominal pain, anorexia, vomiting, and reduced bowel sounds. History of constipation. | Colonoscopy not performed due to risk of perforation. Chest X-ray showed massive bilateral air under the diaphragm indicating perforation (sigmoid colon). | Clozapine withheld and he was managed conservatively with fluids, hydrocortisone, noradrenaline, antibiotics via central line and tramadol. Respiration was supported with continuous positive airway pressure. Clozapine stopped. Underwent emergency subtotal colectomy and ileostomy and was in induced coma for one week following surgery. | Recovered. Clozapine discontinued due to risk of gut hypomotility. |
| M, 30-40 | 700 | 5475 | Vomiting, abdom­inal pain. Previous diarrhoea, vomiting and abdominal pain. Abdomen was soft and non-distended, but diffusely tender. White cell count and C-reactive protein elevated | Abdominal X-ray showed a dilated large bowel. Further urgent sigmoidoscopy showed acute necrotising colitis with ulcer slough and infarcted mucosa. The transverse colon grossly dilated (8 cm). | Managed conservatively, with i.v. fluids, i.v. antibiotics and a rectal catheter to improve mucosal circulation and decrease colonic dilatation. Laparotomy and colonic resection with stoma formation refused by patient. | Patient recovered. Clozapine discontinued and patient prescribed aripiprazole. |