Antineoplastics

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Various toxicities: 3 case reports

In a case report 2 men and 1 woman, aged 40–68 years were described, who developed neutropenia, pneumatosis intestinalis (PI), neutropenic enterocolitis, neutropenic fever, coronavirus infection, *candida albicans* infection, upper respiratory infection, *Clostridium difficile* colitis, sinusitis, arsenic GI toxicity, sepsis, worsening of renal function and decreased urinary output, consolidations of the right pulmonary lower lobe, pneumomediastinum or pneumoperitoneum following chemotherapy with idarubicin, fludarabine, melphalan, panobinostat, sirolimus, tacrolimus, tretinoin or arsenic-trioxide for haematological malignancies [*dosages, routes, durations of treatments to reactions onsets not stated; not all outcomes stated*].

Case 1: The 67 year old woman, who was newly diagnosed with acute myeloblastic leukaemia (AML), was admitted to Moffitt Cancer Center in USA for initiation of induction chemotherapy with idarubicin. Fourteen days after admission, she developed PI. At the time of PI onset, she was febrile and was neutropenic with concurrent thrombocytopenia and anaemia since 9 days. Within 24 hours, she developed abdominal pain, haematochezia, nausea, vomiting, shortness of breath, cough and chills. The PCR test resulted negative for *Clostridia difficile* toxins. She was found to have neutropenic enterocolitis. She was therefore treated with metronidazole and cefepime, which was later switched to meropenem. She also received vancomycin, isavuconazonium, aciclovir, packed RBCs and platelets. Abdomen and pelvis CT scan revealed a thickened colon with air fluid levels and pneumatosis in the colon. The descending colon and the caecum were significantly dilated with air in the caecal wall extending into the ascending colon to the level of the splenic flexure. A diagnosis of PI was thus made. Giver her hypo-coagulable, immunocompromised and poor nutritional state, she was not surgically operated. One week later, she died in a hospice care [*immediate cause of death not stated*].

Case 2: The 40-year-old man, who was newly diagnosed with acute promyelocytic leukaemia (APML), was admitted to Moffitt Cancer Center in USA due to neutropenic fever, which began 7 days prior to the admission and PI. About 2 weeks prior to admission, he had started receiving tretinoin [all-trans retinoic acid] and arsenic trioxide, which were put on hold due to the neutropenic fever. Abdomen CT scan showed enterocolitis with intramural air within the right colon and mild air distension of the colon. He was considered to have experienced arsenic GI toxicity. He subsequently developed coronavirus infection, upper respiratory infection, *Clostridium difficile* colitis and sinusitis. The treatment was commenced with micafungin, metronidazole and piperacillin/tazobactam. On the same day, he developed sepsis, tachypnoea, tachycardia, worsening fever and worsening of renal function and decreased urinary output despite unspecified fluid boluses. He died one week later due to his illness (APML).

Case 3: The 68-year-old man, who had AML and had undergone allogeneic haematopoietic stem cell transplantation, was recently treated with melphalan and fludarabine. In a phase II trial, he received a combination of panobinostat, tacrolimus and sirolimus for GVHD. Shortly after his return to home, he developed a bout of diarrhoea, abdominal pain, productive cough, dizziness and shortness of breath. He presented to the local hospital in a state of hypotension (BP 89/56mm Hg) and tachycardia. ECG showed atrial fibrillation, which later reverted to a sinus rhythm. Chest CT showed focal consolidations of the right lower lobe of lung, pneumomediastinum with pneumoperitoneum and PI. He tested positive for *candida albicans* infection. He received antibiotic therapy for 2 days until he was transferred to the Moffitt Cancer Center in USA. Following treatment with piperacillin/tazobactam and metronidazole, his symptoms improved; although diarrhoea, abdominal cramping and productive cough persisted. He denied any chest pain, chills or fevers during the treatment and was able to tolerate food. He was later discharged after further improvement in the symptoms.

Author comment: "*Chemotherapy used to treat hematologic cancer patients results in prolonged neutropenia and mucositis, which increases the risk for a wide range of infections and end-organ damage.*" "*Here, we present 3 cases of PI that developed secondary to neutropenia in patients with hematologic malignancies.*"

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