Multiple drugs

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Various toxicities: 3 case reports

In a case report, three patients (2 women and 1 man) aged 34–46 years were described, who developed invasive infections caused by *Candida tropicalis*, endemic Coronavirus (HKU1), *Toxoplasma gondii*, *Acinetobacter baumanni*, Cytomegalovirus (CMV), Adenovirus or Torque teno virus (TTV) during treatment with cytarabine, daunorubicin, cyclophosphamide, antithymocyte globulin or fludarabine for acute myeloid leukaemia or acute lymphoid leukaemia. One of these patients additionally exhibited lack of efficacy during treatment with cidofovir for Adenovirus and TTV infection [*dosages and routes not stated*].

This report describes a 38-year-old woman (case 1), who developed invasive infection caused by *Candida tropicalis* during treatment with cytarabine and daunorubicin: The woman with acute myeloid leukaemia achieved complete response following induction therapy with cytarabine and daunorubicin and two consolidations with high dose cytarabine. During chemotherapy cycles, she developed febrile neutropenia. Fluconazole was given in the first and second cycles of chemotherapy. Three months after the last consolidation cycle, she developed fever and malaise. Thus, she was admitted to hospital. On admission, an abdominal CT scan revealed solid lesions in the liver. Hence, voriconazole was initiated. Meanwhile, a liver biopsy was performed. In tissue, there was a mixed non-granulomatous inflammatory infiltrate without neoplasia, fungal, or bacterial elements. After 2 months, her symptoms remained, and new solid lesions were noted in the liver and spleen by CT scan. Therefore, caspofungin was added to therapy, and a sample of blood was collected to perform next-generation metagenomic sequencing (mNGS). The mNGS test revealed *Candida tropicalis*. Thus, treatment with caspofungin was continued, and 3 months after, her symptoms disappeared, and a significant reduction in all lesions was noted.

This report describes a 46-year-old man (case 2), who developed invasive infection caused by endemic Coronavirus (HKU1), *Toxoplasma gondii* and *Acinetobacter baumanni* during treatment with cyclophosphamide and antithymocyte globulin: The man with a T acute lymphoid leukaemia achieved a complete remission following induction therapy and was scheduled for an unrelated allogeneic stem cell transplantation. He received conditioning regimen with cyclophosphamide, antithymocyte globulin and total body irradiation. Subsequently, he underwent an unrelated allogeneic stem cell transplantation. Thereafter, he developed febrile neutropenia, and was treated with cefepime and vancomycin with a rapid resolution of fever. He recovered from neutropenia after 14 days, but a daily fever started after neutrophil recovery. Subsequent ECG revealed a tiny filamentous in the mitral valve. Meropenem and daptomycin were started. Concomitantly, acute graft-versus-host disease was noted. A few days later, he developed acute respiratory failure with a diffuse pulmonary infiltrate by CT scan. Amphotericin B liposomal and cotrimoxazole were added to the therapy. An endemic coronavirus (HKU1) was identified by multiplex-PCR in bronchoalveolar lavage (BAL). At this time, he started altering mental status. A blood sample was collected for mNGS and revealed the presence of *Toxoplasma gondii*, and cotrimoxazole therapy was maintained. New transoesophageal ECG was performed, and the previous mitral findings were no longer observed. Unfortunately, during toxoplasmosis treatment, he developed sepsis due to multiresistant *Acinetobacter baumanni* in the following days and died. He was *T. gondii*-seropositive before the transplantation.

This report describes a 34-year-old woman (case 3), who developed invasive infection caused by CMV, Adenovirus and TTV during treatment with cyclophosphamide and fludarabine, and exhibited lack of efficacy during treatment with cidofovir: The woman with acute lymphoid leukaemia in remission received a haploidentical peripheral allogeneic stem cell transplant from her brother following conditioning with cyclophosphamide, fludarabine and total body irradiation. Subsequently, she developed febrile neutropenia. She was initially treated with empirical cefepime and switched to meropenem and vancomycin due to the persistence of fever despite negative cultures. After 16 days of transplantation, her neutropenia recovered. On day 18, she reported urinary symptoms and gross haematuria. CMV disease was documented, and ganciclovir was started. During ganciclovir therapy, CMV viraemia was improved, but haematuria persisted. Two weeks later, she developed fever and respiratory symptoms. At this time, CT scan showed nodules, ground-glass infiltrates, and pleural effusion. Amphotericin B liposomal was started empirically, with a resolution of fever, respiratory symptoms and radiological improvement. On day 60, acute graft-versus-host disease was noted, and unspecified corticosteroid was started. Three weeks later, she experienced new episodes of fever with moderate to severe respiratory symptoms. A new CT scan revealed bilateral infiltrates, centrilobular opacities, and consolidations. Empirical therapies were then restarted, and a sample of blood collected to perform next-generation metagenomic sequencing (mNGS). The mNGS was positive for adenovirus and TTV. Cidofovir was started, but she developed sepsis, renal and respiratory failure, and in a few days, her condition worsened with haemodynamic instability. She died of sepsis, renal and respiratory failure, and haemodynamic instability.

Garnica M, et al. Metagenomic next-generation sequencing (mNGS) for diagnostically challenging infectious diseases in patients with acute leukemia. Brazilian Journal of Infectious Diseases 25: No. 2, Mar-Apr 2021. Available from: URL: http://www.sciencedirect.com/science/journal/14138670