Dipyrone/filgrastim

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Neutropenia, agranulocytosis and lack of efficacy: 3 case reports

In a case series, two women and one man aged 33-53 year were described, who developed neutropenia or agranulocytosis during treatment with dipyrone. Additionally, a 53-year-old woman exhibited a lack of efficacy during treatment with filgrastim for neutropenia [*not all routes, dosages, duration of treatment to reaction onset and outcome stated*].

Case 1: A 33-year-old woman developed neutropenia during treatment with dipyrone for abdominal cramps. The woman was admitted to the department 1 week post her 5th normal vaginal delivery. Following delivery, she suffered from mild abdominal cramps, for which she took over the counter paracetamol and dipyrone [metamizole] a few times per day during the previous week prior to the admission. On admission, her physical examination and vital signs found to be normal. Her lab tests revealed leucocytes of 2750 cells/µL with absolute neutrophils count of 700 cells/µL, haemoglobin of 11 g/dL and normal thrombocytes level. She was positive in a polymerase chain reaction (PCR) of nasopharyngeal swab for SARS-CoV-2, indicating COVID-19. Also, dipyrone associated neutropenia was considered and her treatment with dipyrone was discontinued. She was followed for 2 days and had spontaneous resolution of neutrophil counts.

Case 2: A 53-year-old woman developed neutropenia and agranulocytosis during treatment with dipyrone for fever; she also exhibited a lack of efficacy during treatment with filgrastim for neutropenia. The woman had a medical history of smoking, migraine and a autoimmune haemolytic anaemia. She received unspecified corticosteroids. She had abnormality of elevated cholestatic liver enzymes 2 weeks before admission to the hospital. On admission, her vital signs were normal. Lab tests revealed normal absolute neutrophil count of 7500 cells/µL. Following various investigations, she was diagnosed with COVID-19 along with splenomegaly. Liver biopsy showed results compatible with reactive process, most probably viral infection. Bone marrow biopsy revealed mild erythrophagocytosis with normal granulocytic lineage. On day 3 of hospital admission, she became febrile and received dipyrone [metamizole] as needed. On day 10 of hospitalisation, she received oral dipyrone at a dose of 1g and became severely neutropenic with absolute neutrophil count of 300 cells/µL which further decreased to zero. Treatment with dipyrone was discontinued because of a clear temporal association and thus a suspicion of dipyrone-associated agranulocytosis was raised. She was treated empirically with piperacillin–tazobactam, vancomycin and isoconazole due to fever in the presence of agranulocytosis. Post 2 weeks of hospitalisation, she developed severe pulmonary manifestations of COVID-19, including severe respiratory failure. She also received treatment trial with filgrastim; however, she had no recovery of neutrophils counts. She had a subsequent marked progression of hypoxemic respiratory failure requiring mechanical ventilation. Eventually, she died of hypoxemic respiratory failure.

Case 3: A 53-year-old man developed neutropenia during treatment with dipyrone for high grade fever; The man, who had severe mental retardation with a medical history of Barret's oesophagus presented to the emergency department 10 days after diagnosis of COVID-19. He had productive cough, dyspnoea and high grade fever. At presentation, he was febrile with a body temperature of 39°C. Lab tests revealed leucocytes of 1600 cells/µL with an absolute neutrophil count of 1500 cells/µL, haemoglobin level of 10 g/dL and thrombocytopenia of 112 000 cells/µL. He received off-label treatment with dexamethasone for COVID-19. He also received unspecified low molecular weight heparin. He then received IV dipyrone [metamizole] at a dose of 1g due to high grade fever. On day 2 of his hospitalisation,he had severe hypoxaemic respiratory failure that required the use of high-flow nasal cannula. Repeated lab tests showed a leucopenia of 1000 cells/µL and a neutropenia of 900 cells/µL with no significant changes in other blood lineages. The neutropenia was considered secondary to dipyrone. Thereafter, his neutropenia did not improve. Further, he suffered from septic shock associated with electrolytes imbalance, acute kidney injury and mixed hypercapnic–hypoxaemic respiratory failure, which resulted to his death.

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