Multiple drugs

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DRESS-syndrome and rebound effect: case report

A 36-year-old man developed DRESS syndrome during treatment with carbamazepine, morphine, paracetamol and dipyrone. Additionally, he experienced a rebound effect following the dose reduction of prednisolone for DRESS syndrome [*routes and exact durations of treatments to reactions onsets not stated*].

The man, who had a history of obesity, hepatic steatosis, hypertension, panic disorder and alcohol addiction and under treatment with carbamazepine 400 mg/day, escitalopram, amlodipine, losartan and nebivolol, presented on 1 April 2020 for mild to moderate abdominal pain, diffuse, associated with dyspepsia, belching, with no nausea, vomiting with fever. On day 3, the pain worsened and was described as left thoracolumbar colic, radiating to the periumbilical region and testicles, associated with important abdominal distension. He was checked in the hospital with normal temperature, preserved peristalsis, no change in urinary or intestinal functions, non-nodular liver, palpable at 3.0cm from the costal margin and non-palpable axillary, inguinal or cervical lymph nodes. In addition to oral rehydrating solutions, the prescribed treatment included fexofenadine [fexofenadine hydrochloride], paracetamol 1500 mg/day, dipyrone 1000 mg/day, codeine, scopolamine 30mg and dipyrone 750 mg/day. On the same day, he underwent total abdomen CT that revealed hepatic steatosis, kidney stones, bowel loops normal in diameter, normal peritoneum, retroperitoneum, gall bladder and bile ducts. On day 7, a cholangioresonance confirmed hepatic steatosis, and showed that the liver was slightly enlarged, with sparse infracentimetric cysts, adenomyomatosis at the bottom of the gall bladder, intra and extrahepatic bile ducts with no dilations, normal pancreas, pancreatic ducts, and spleen, normally positioned kidneys, bilateral single kidney microcysts, calyceal system with no dilations and single lymph node in the hepatic hilum. On day 8, the molecular diagnosis of COVID-19 was confirmed. From day 8 to day 14, he had lip fissures, painful and numerous aphthous ulcers that limited food intake, flatulence, diarrhoeal white stools, with no jaundice, anal fissures, and haemorrhoid with droplets of blood. A treatment with lidocaine ointment in association with hydrocortisone [hydrocortisone acetate], zinc oxide, aluminum subacetate and triamcinolone [triamcinolone acetonide] was prescribed. On day 11, he complained about loss of taste and pronounced oedema of the face and limbs. On day 12, these gastrointestinal symptoms were followed by dermatological manifestations, although he had no history of dermatoses. From day 12, monomorphic vesicles dispersed in the trunk and limbs were observed as a first alteration, evolving to maculopapular rash, initially erythematous and delimited, then violet and coalescent, also affecting the palms of the hands and the soles of the feet, associated with desquamation, sparse fissures, and burning pain. On day 29, these dermatological manifestations reached such a proportion that he was transferred to the semi-intensive care unit, following the isolation protocol. At this moment, the possibility of toxidermia, which they attributed to the use of morphine was suspected. A final diagnosis of DRESS syndrome secondary to carbamazepine, morphine, paracetamol and dipyrone was made.

The man was started on prednisolone 40 mg/day. He was discharged from the hospital in a better condition on day 35. However, on day 37, he had recurrence of the cutaneous lesions, then aggravated, presenting with putrid odor on the skin, sparse pustules and chills when the axillary temperature reached 38.9 °C. Skin culture was positive for *Staphylococcus aureus* and fungal infection was ruled out. On day 37, he received treatment with cotrimoxazole [sulfamethoxazole and trimethoprim] for 10 days. Periodical complete blood counts showed: red series with no changes either in count or in shape throughout the clinical course; eosinophilia 1132 /mL on day 8 and 3198 /mL on day 14 in the most acute phase of the rash; mild leukocytosis 13 610 /mL, with a shift to the left, during *staphylococcal* co-infection and corticosteroid administration; gamma-glutamyl transferase 309–590 U/L; alanine aminotransferase 113–574 U/L; aspartate amino transferase 31–89 U/L; alkaline phosphatase 162–169 U/L; increased serum C-reactive protein 2.95–3.40 mg/dL; bilirubins, glucose, lipase, amylase, calcium, magnesium and creatine phosphokinase remained normal throughout the clinical evolution. Tests for dengue, hepatitis A, hepatitis B, cytomegalovirus, syphilis, and AIDS were nonreactive. The attempt to taper-off corticosteroid therapy worsened the dermatological condition, with lichenification, pigmentation and skin fissures over the joints. Weight loss, loss of muscle mass, generalised myalgia, weakness and fasciculation in the limbs made his walking difficult. The magnitude of the skin lesions and the acute hepatitis in the presence of SARS-CoV-2 infection, in addition to the use of carbamazepine, led to the conformation of pharmacotoxicity. Therefore, carbamazepine discontinuation started on day 43, with marked improvement of the rash and progressive skin recovery. He did not show any respiratory changes since the onset of symptoms, maintaining O2 saturation around 98%. On day 49, COVID-19 IgG/IgM was found non-reactive. The treatment finished on day 80 of symptom onset, with normalisation of liver and kidney functions, great weight loss and gradual recovery of activities of daily living.

Cruz VB, et al. Does sensitization by SARS-CoV-2 immune complexes trigger DRESS syndrome?. Brazilian Journal of Infectious Diseases 26: 102337, No. 2, Mar 2022.
Available from: URL: http://www.sciencedirect.com/science/journal/14138670
803653320