

## Multiple drugs

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**Various toxicities with lack of efficacy and off label use: case report**

A 52-year-old woman exhibited lack of efficacy following steroid therapy with ciclesonide and off label use of favipiravir for COVID-19 pneumonia. Additionally, she developed subcutaneous insulin resistance (SIR) syndrome following treatment with insulin-suspension-isophane/insulin for type 2 diabetes, and methylprednisolone and prednisolone for COVID-19 pneumonia. She also developed abdominal purpura following treatment with heparin as an anticoagulation [*not all dosages and routes stated*].

The woman had a history of type 2 diabetes for 10 years. Her concomitant medication included vildagliptin, repaglinide and metformin. She was suffering from fever, cough and dyspnoea from last 5 days, for which she was admitted to the hospital. Upon further investigation, she was diagnosed with COVID-19-associated pneumonia. Hence, she received ciclesonide, noradrenaline [norepinephrine] and off label treatment with favipiravir 3600 mg/day. However, no improvement was noted in radiological findings (lack of efficacy). Hence, she received mechanical ventilation and extracorporeal membrane oxygenation (ECMO) with heparin on day 4 and day 11 of hospitalisation, respectively. Later, she received IV pulse methylprednisolone 1000 mg/day from day 13 to day 15 of hospitalisation. Additionally, she received IV prednisolone 60 mg/day. Following it, on day 18 of the hospital stay, significant improvement was noted in her respiratory condition. Accordingly, ECMO was withdrawn. The dose of prednisolone was significantly tapered and later, it was discontinued on day 32. During ECMO, the albumin level decreased, and she had generalised oedema with extensive abdominal purpuras and increased plasma D-dimer levels during therapy which consisted of coagulation abnormalities. It was considered that the development of the abdominal purpura occurred because of heparin administered during ECMO. Looking out glycaemic control on admission, her all oral hypoglycaemic agents were discontinued. Further, multiple daily SC injections of regular and neutral insulin-suspension isophane/insulin [protamine Hagedorn (NPH) insulin] were started. On day 17 of the hospital, it was noted that her necessity for SC insulin was increased. Hence, she received 900 kcal/day enteral nutrition. It was attributed that the increased insulin requirement was not only due to insulin resistance induced by IV prednisolone and pulse methylprednisolone. Later, due to several extensive and excessive purpuras on the abdominal skin surface with skin bulging centred at the injection site, an IV infusion of regular insulin was initiated on day 18. Following it on day 20, the average blood glucose level decreased in response to 18 units/day insulin infusion and 118 units/day SC insulin (total of 136 units/day) under prednisolone 30 mg/day treatment. Therefore, insulin infusion was discontinued on day 21. Even after the daily insulin dose was unchanged from the previous day, her blood glucose level rapidly increased to 319 mg/dL. Hence, on day 22 hospital stay, infusion of insulin 40 units/day and SC insulin 118 units/day was restarted with prednisolone 15 mg/day. Following it, blood glucose level was reduced. Following the next 2 days, the blood glucose level remained under control. Later, SC insulin was decreased to 64 units/day. Upon findings, it was considered that SC insulin alone is not effective on hyperglycaemia, and it was attributed to SIR syndrome. Resistance to SC insulin was noted. However, sensitivity to IV insulin remains unchanged. Hence, she received additional IV insulin with rapid improvement of hyperglycaemia. On day 22 and day 24, a dose of prednisolone was decreased to 15 mg/day, later to 10 mg/day. Following it, IV insulin infusion decreased from 46 units/day on day 27 to 13 units/day on day 28 and 16 units/day on day 29. Subsequently, a good blood glucose level was noted in her condition. However, on day 29, the average daily blood glucose level was increased due to which persistence of the SIR syndrome-like pathological condition was considered. Hence, on day 30, IV insulin infusion was increased to 40 units/day with a decrease in prednisolone dose. Following it, significant improvement in her blood glucose level was noted. It was considered that due to a reduction in the prednisolone dose, hyperglycaemia improved. Later, her blood glucose level improved with sitagliptin and repaglinide on day 34 and day 35. On day 41, she received insulin degludec. Later, on day 42, IV insulin injection tapered and later withdrawn [*not all outcome stated and exact time to reaction onset stated*].

Satomura A, et al. Clinical features resembling subcutaneous insulin resistance observed in a patient with type 2 diabetes and severe COVID-19-associated pneumonia: a case report. *Diabetology International* 12: 474-479, No. 4, 1 Mar 2021. Available from: URL: <http://doi.org/10.1007/s13340-021-00500-x> 803623769