Progression of systemic lupus erythematosus associated with propofol administration: a case report

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SUMMARY

Propofol is a sedative-hypnotic agent used as a general anaesthetic with a good safety profile. However, the potential risk for patients with systemic lupus erythematosus (SLE) receiving propofol remains unclear. We report the case of a patient who received an intravenous infusion of propofol for painless gastroscopy which exacerbated acute SLE despite no history of allergies. The adverse effect might be because propofol increased T helper cells and triggered the induction of B cell differentiation and plasmablast formation, which further promoted the secretion of auto-antibodies. This case shows that propofol can exacerbate SLE symptoms in some patients and highlights the importance of identifying potential immune-related factors before propofol administration, especially in patients with autoimmune diseases. It is important to be aware of and differentiate this uncommon and non-specific SLE manifestation from a myriad of disorders presenting with a primary digestive disorder in the outpatient clinic.

BACKGROUND

Propofol is a short-acting intravenous sedative-hypnotic agent used for the induction and maintenance of sedation or anaesthesia. It is popular among gastrointestinal endoscopists because of its rapid induction and recovery times.¹ While generally safe and effective, the use of propofol is complicated by infrequent but life-threatening adverse events.² Reported propofol-related adverse effects have been largely attributed to cross-reactivity between the propofol solvent and some foods or to high doses and/or to long-term use of propofol causing, for instance, propofol infusion syndrome (PRIS).^{2–4} Adverse effects of propofol on the immune system, such as erythema, rarely occur and have not been clinically investigated. Therefore, we report here the case of a patient who had received an intravenous infusion of propofol for painless gastroscopy and developed severe symptoms of acute systemic lupus erythematosus (SLE) despite no history of allergies.

CASE PRESENTATION

A 56-year-old woman (height: 162 cm, weight: 59 kg) presented to the outpatient clinic complaining of a poor appetite for over 2 months accompanied by weight loss of about 10 kg and oedema of the left lower limb for 5 days. The patient stated that she had no history of food allergies and had not taken any medication before attending the clinic. She was scheduled for painless gastroendoscopic examination.

A single dose of propofol (1.5 mg/kg, Diprivan, batch no: MB851) was intravenously administered for general anaesthesia. The procedure was uneventful. However, approximately 3 hours after propofol administration, the patient developed a diffuse rash all over her body with itching, flushing and increased skin temperature. The rash was still present the next day and the dermatologist prescribed the antihistamine loratadine (10 mg, once daily), 10% calcium gluconate (1 g, once daily) and vitamin C (2 g, four times daily) (figure 1). The patient was then admitted to the gastroenterology ward for further examination. The rash persisted despite antianaphylactic treatment administered for six consecutive days. The clinical pharmacist considered it was probably an SLE eruption exacerbated by propofol administration.

INVESTIGATIONS

Laboratory examinations revealed anti-Sm antibody (+++), anti-dsDNA antibody 302.86 IU/mL (normal <100), anti-SS-A antibody (+++) and anti-SS-B antibody (+++), C3 0.36 g/L (normal 0.9–1.8), C4 0.07 g/L (normal 0.1–0.4), IgG 20.71 g/L (normal 7–14), IgA 5.45 g/L (normal 0.7–4), IgM 2.35 g/L (normal 0.4–2.3), ANA (positive, S type, 1:640), dsDNA D6 (positive, S type, 1:40), SSA (positive, +++), n-RNP/Sm (positive, +++), RHF 38 IU/mL (normal <20), ESR 40 mm/h (normal 0–20) accompanied by a decreased white blood cell count of $2.8 \times 10^9/L$ (normal $3.5\text{--}9.5 \times 10^9$) and proteinuria (425.08 mg/L, normal <100).

TREATMENT

In view of the probability of drug-exacerbated SLE, immunosuppressive drugs including methylprednisolone (80 mg, once daily), mycophenolate mofetil (0.5 g, twice daily) and hydroxychloroquine sulfate (0.2 g, twice daily) were prescribed.

OUTCOME AND FOLLOW-UP

The rash dramatically improved within 5 days. After 14 days of in-patient treatment, the patient's white blood cell count had increased from $2.8 \times 10^9/L$ to $5.46 \times 10^9/L$, platelet count had increased from $55 \times 10^9/L$ to $85 \times 10^9/L$ and urinary total protein had decreased from 425.08 mg/L to 144.38 mg/L. Anti-cardiolipin antibody and β_2 glycoprotein antibody were normal. The patient was discharged with oral medicine for subsequent treatment.

DISCUSSION

Propofol is a short-acting intravenous sedative-hypnotic agent used for the induction and

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Figure 1 Propofol-induced diffuse rash in a female patient with no history of allergy

maintenance of sedation or anaesthesia. Previous reports and propofol labelling indicate that people allergic to soybean or egg may develop a propofol-induced acute reaction due to a cross-reactive allergen.^{3,4} However, a recent evidence-based study demonstrated no connection between allergy to propofol and allergy to egg, soy or peanut, which indicated that people without a food allergy history may also be at risk of developing an acute reaction to propofol.^{5–8} The safety of propofol has received wide attention in clinical practice.

In the present case, a 56-year-old woman initially experienced a severe rash with itching, flushing and increased skin temperature after administration of a single dose of propofol. A propofol related-allergy was suspected at first, but serum IgE levels were in the normal range. In most situations, acute anaphylaxis is mediated by IgE and can be resolved with an antihistamine drug or discontinuation of the suspected causative substance.⁹ However, in this case, the patient did not have a history of food allergy and had not taken any other medication except propofol. Antianaphylactic treatment for 6 days, including loratadine, 10% calcium gluconate and vitamin C, seemed to be ineffective (figure 1). As the skin eruption was not relieved until an immunosuppressive regimen was begun, the rash could not be simply considered a drug reaction. The results of laboratory examinations showed multiple positive immunological findings. Clinical symptoms included acute skin eruption, oedema of the lower limb resulting from venous thrombosis, decreased complete blood count and mild proteinuria. In light of the ACR classification criteria for SLE, we think that symptoms of SLE in this patient were exacerbated by propofol administration. Propofol was not on the risk list for causing lupus erythematosus in the past,¹⁰ but this case suggests that propofol can exacerbate SLE in some patients. The Naranjo probability scale for assessing causality had a score of 6, showing a probable relationship between propofol administration and the progression of SLE (supplementary table 1).

SLE is an autoimmune disease characterised by autoantibody production and a dysfunctional immune system resulting in

organ inflammation and consequent damage.¹¹ The pathogenesis of SLE is complex and has not yet been clearly elucidated. Patients with SLE have a dysfunctional immune system and multiple immunocytes are involved in the onset and course of SLE. A previous study found that patients who had received a propofol infusion had a higher percentage of T helper cells,¹² but the physiological significance of this has not been elucidated. Recently, researchers found a new type of cells called circulating T helper-like follicular cells in the blood of SLE patients.¹³ These cells shared similar phenotypic properties with germinal centre follicular helper T cells which could drive B cells to differentiate into IgG secreting plasma cells. The frequency of these cells in blood was related to levels of serum anti-dsDNA antibodies and ANA in SLE patients.¹⁴ Therefore, we hypothesised that propofol increased the number of T helper cells and triggered induction of B cell differentiation and plasmablast formation, which could further promote the secretion of auto-antibodies. This could be the main reason why some patients are at higher risk of developing SLE in the presence of propofol.

There are few articles reporting the potential risks for patients with SLE undergoing general anaesthesia.^{15–17} The major concern during the perioperative period is to protect the kidneys and the cardiovascular and central nervous systems from damage and to maintain stable haemodynamic conditions in patients.¹⁶ Administration of a steroid hormone could improve the safety of surgery in patients with SLE.¹⁸ Usually, investigations need to be carried out before embarking on anaesthesia. However, identifying and managing SLE is a challenge in the outpatient department. Our patient's initial clinical presentation was similar to a primary digestive disease rather than SLE, which can present with butterfly erythema, arthralgia or fever. Due to the complexity of the diagnosis in new-onset SLE, special attention should be paid to patients when propofol is used as an anaesthetic in clinical practice. The current patient was cured by immunosuppressive therapy. For patients with autoimmune diseases, such as SLE, rheumatoid arthritis, systemic vasculitis and scleroderma, special attention should be paid when propofol is administered for advanced endoscopic procedures.

In conclusion, we report for the first time that the general anaesthetic propofol can exacerbate SLE symptoms in some patients. This case highlights the importance of identifying potential immune-related factors before propofol administration.

Contributors YY and HG contributed equally to the preparation and checking of the manuscript. KX collected the clinical information on the patient. XF, YY and HG contributed to the literature search. JH reviewed the manuscript and supervised the entire process.

Learning points

- We present a case of exacerbated acute systemic lupus erythematosus (SLE) in a patient who had received an intravenous infusion of propofol for painless gastroscopy despite no history of allergies.
- Identifying potential immune-related factors before propofol administration, especially in patients with autoimmune disease, is of great clinical importance.
- It is important to be aware of and differentiate this uncommon and non-specific SLE manifestation from a myriad of disorders presenting with a primary digestive disorder in the outpatient clinic.

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Competing interests None declared.

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