CASE REPORT

Acyclovir-induced thrombocytopaenia in a patient with SLE

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SUMMARY

Acyclovir has been used in the treatment of herpes simplex and varicella zoster viral infections for over 30 years. The side effects of oral treatment at standard doses are rare and include headache, diarrhoea, dizziness and malaise. We report a patient with a new diagnosis of systemic lupus erythematosus (SLE) who developed thrombocytopaenia within days on a therapeutic dose with acyclovir. Prompt discontinuation of acyclovir and treatment with intravenous immunoglobulin resulted in reversal of the above potentially serious complication. Therefore a high index of suspicion should be exercised in patients with SLE who require treatment with acyclovir for herpes viral infections. In these patients regular platelet count measurement should be considered while on treatment with the above antiviral agent.

BACKGROUND

Acyclovir has been used to treat infections with herpes simplex and varicella zoster viruses for over 30 years. It is widely distributed in almost every organ in the body and is excreted in the urine. The drug has mild side effects at therapeutic doses as it is only absorbed by the virus infected and not the host cells. Common adverse effects include nausea, vomiting, malaise and diarrhoea. Less common adverse effects, usually related to high-dose intravenous administration, include neurotoxicity, renal, hepatic and psychiatric disorders, and rarely myelosuppressive complications and skin dyscrasias have been reported.[1 2]

We report a patient with a diagnosis of systemic lupus erythematosus (SLE) who developed severe isolated thrombocytopaenia within days following treatment at a therapeutic dose with acyclovir.

CASE PRESENTATION

A 54-year-old Caucasian female patient with no medical or family history of note was referred to the rheumatology department of our hospital with photosensitivity, malaise, high fever and oral ulcers. Shortly after admission she developed an acute severe hypertensive crisis with pulmonary oedema, pleural and pericardial effusions, and proteinuria. She also had evidence of non-erosive arthritis. Renal biopsy suggested the presence of diffuse proliferative nephritis. Her haemoglobin was 11.0 g/dL, white cell count was 2.16×10^9/L and platelet count was 176×10^9/L. Furthermore she had positive antinuclear antibodies, antidouble-stranded DNA, anti-Ro/SSA antibodies, IgA anticardiolipin, IgG and IgA anti-β2glycoprotein I antibodies. The diagnosis of SLE was made.[3] The patient was therefore treated with intravenous methylprednisolone (1 g/day for 3 days) and cyclophosphamide (1 g for 1 day). She was discharged home on a maintenance dose of prednisolone and made an uneventful recovery.

A month later she re-presented with a painful unilateral vesicular rash on the left side of the face and neck in keeping with herpes zoster infection affecting the branches of the left trigeminal nerve (figure 1). She also reported tingling sensation at the site of the rash but denied any constitutional symptoms like fever or malaise. At the time the patient was on treatment with prednisolone (1 mg per kg/day). She was apyrexial and the clinical examination was unremarkable. Her haemoglobin was 10 g/dL, white cell count was 6.64×10^9/L and platelet count was 275×10^9/L. The patient was therefore prescribed oral acyclovir 1 g once a day.

Five days after treatment with acyclovir, her platelet count dropped to 9×10^9/L. Her white cell count was 9.47×10^9/L, red blood cell count was 3.52×10^{12}/L and haemoglobin was 9.7 g/dL. She had no overt symptoms and no evidence of a purpuric rash or cutaneous haematomas. Due to the temporal relation between the introduction of the drug and the onset of thrombocytopaenia, the diagnosis acyclovir-induced thrombocytopaenia was made, likely to have been immune in origin. The patient had no symptoms related to the SLE and her autoimmune condition was quiescent. Acyclovir-specific antibodies are not available at our institution.

TREATMENT

Acyclovir was discontinued and the patient was promptly treated with intravenous IgG (0.4 g per kg/day for 4 days).

OUTCOME AND FOLLOW-UP

Three days later the platelet count recovered to 140×10^9/L. One year later the patient is completely asymptomatic on treatment with hydroxychloroquine (400 mg per day), prednisone (2.5 mg per day) and mycophenolate mofetil (2 g per day). Furthermore the platelet count remains stable at 270×10^9/L.

DISCUSSION

Our case report clearly demonstrates that the use of acyclovir to treat herpes zoster virus infection

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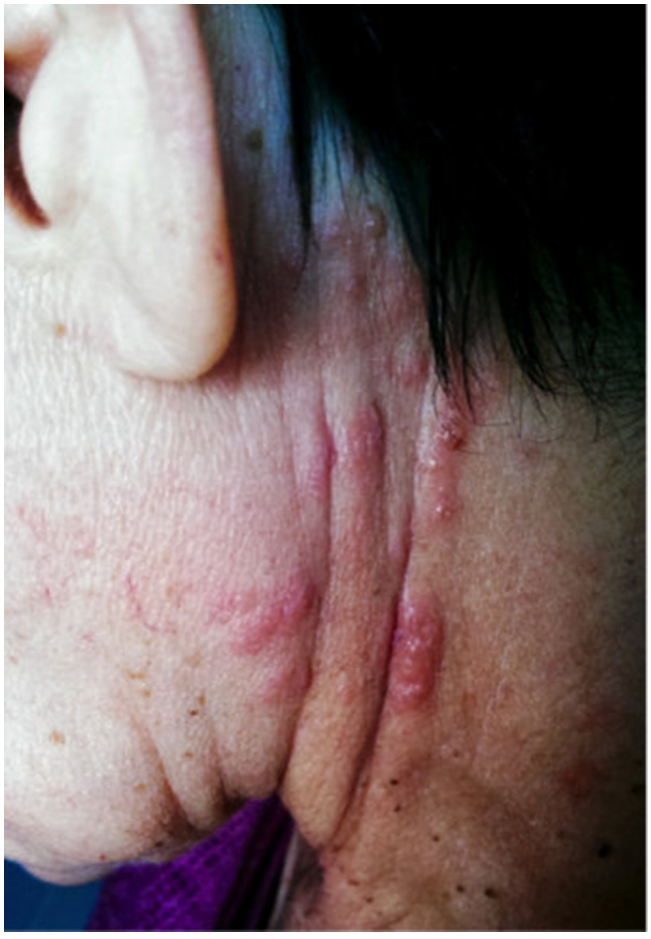

Figure 1 Unilateral vesicular rash on the left side of the face and neck suggestive of varicella zoster viral infection.

may lead to thrombocytopaenia, which unless recognised and treated promptly may lead to life-threatening complications. To our knowledge, this is the first case report of the above condition occurring after treatment with acyclovir in a patient with SLE.

Acyclovir is a purine nucleoside analogue antiviral drug which inhibits viral replication. Its mechanism of action involves three stages, the first of which involves metabolism by viral thymidine kinase and the last two stages by a cellular kinase, thereby converting acyclovir to acyclovir monophosphate, diphosphate and triphosphate, respectively. The active triphosphate form of the drug binds to viral DNA polymerase, inactivates it and inhibits further viral DNA chain growth.[1] Acyclovir is widely used to treat mucocutaneous herpes, herpes zoster, herpes encephalitis and genital herpes simplex. The drug has wide distribution in almost every organ of the body. It is only absorbed by the cells that are infected with the virus; hence, acyclovir has minimal side effects at therapeutic doses. However, high intravenous infusions may cause multisystem side effects and blood dyscrasias.

Drug-induced thrombocytopaenia is caused by either bone marrow suppression or by accelerated platelet destruction, usually immune-mediated.

There have been few reports on bone marrow suppression in the literature and a handful of case reports of acyclovir thrombotic thrombocytopaenic purpura.[4–6] Hong *et al*[5] reported a patient who developed immune thrombocytopaenia with tongue haematoma 10 days after intravenous acyclovir treatment. They postulated that in their patient with extensive purpuric rash and tongue haematoma, the presence of thrombocytopaenia was unlikely to be related to bone marrow suppression (as the haemoglobin and white cell count were unaffected) and more likely to be mediated by drug-dependent immune mechanism.

In our patient the likely diagnosis is one of acyclovir-induced immune thrombocytopaenia. This is based on the temporal relationship between starting acyclovir and the onset of thrombocytopaenia and the absence of any active clinical conditions, or the use of other pharmacological agents that are known to affect platelet count.

Learning points

- Acyclovir used for the treatment of varicella zoster viral infection in a patient with systemic lupus erythematosus (SLE) may cause severe thrombocytopaenia with potential life-threatening complications.
- A high index of suspicion should be exercised in patients with SLE who require treatment with acyclovir for herpes viral infections.
- In these patients regular platelet count measurement while on treatment with acyclovir should be considered.

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REFERENCES

1 Elion GB. Mechanism of action and selectivity of acyclovir. *Am J Med* 1982;73:7–13.
2 FDA. *Zovirax (acyclovir) prescribing information*, 2005.
3 Smith EL, Shmerling RH. The American College of Rheumatology criteria for the classification of systemic lupus erythematosus: strengths, weaknesses, and opportunities for improvement. *Lupus* 1999;8:586–95.
4 Katsenos S, Gkolias D, Nikolopoulou M. Acyclovir-Induced Immune Thrombocytopenia in a Patient with Herpes Zoster of the Trigeminal Nerve. *Pharmacotherapy* 2010;30:1085.
5 Hong X, Wang X, Wang Z. A rare case report of acyclovir-induced immune thrombocytopenia with tongue hematomas as the first sign, and a literature review. *BMC Pharmacol Toxicol* 2017;18:12.
6 Kamboj J, Wu F, Kamboj R, *et al*. A rare case of acyclovir-induced thrombocytopenia. *Am J Ther* 2014;21:e159–e162.

Unexpected outcome (positive or negative) including adverse drug reactions