MEDICINAL MISHAP

Severe adverse drug reaction to allopurinol

Grace Lucas
Immunology pharmacist[1]

Luke Droney
Clinical immunologist and immunopathologist[1,2]

[1]Princess Alexandra Hospital
[2]Royal Brisbane and Women's Hospital, University of Queensland
Brisbane

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Case

A 72-year-old Vietnamese man presented to hospital with a widespread rash, hypotension and diarrhoea. The patient had a history of hypertension treated with olmesartan for the past two years. Four weeks before presentation he had started allopurinol 300 mg daily for asymptomatic hyperuricaemia. Ten days after starting allopurinol the patient had noticed a pruritic erythematous rash on the abdomen, but was advised to continue allopurinol.

On examination the patient was febrile and hypotensive. He had a widespread morbilliform rash that spared the palms and soles. There were no mucosal lesions. Pathology testing revealed an acute kidney injury (creatinine 214 micromol/L, (baseline 130 micromol/L two years earlier)), liver injury (alanine transaminase 224 U/L and aspartate transaminase 224 U/L) and eosinophilia (peaking at 3.34×10^9/L five days after admission) with reactive lymphocytes on the blood film. The diagnosis on admission was drug reaction with eosinophilia and systemic symptoms (DRESS).

The patient was treated with high-dose corticosteroids (50 mg prednisolone for one week then reducing by 10 mg every two days until finished) and intravenous fluids. He improved over the following days, but kidney function was slow to recover and his liver function worsened before improving. The patient's rash also improved and he was discharged after five days. Allopurinol was not resumed.

As DRESS was suspected, he had HLA typing. This revealed HLA-B*58:01.

Comments

Adverse drug reactions can range from mild cutaneous reactions to very severe multisystem reactions that can be life-threatening. DRESS is a T-cell-mediated adverse drug reaction characterised by widespread rash with or without eosinophilia, fevers, lymphadenopathy and organ involvement (most commonly kidney or liver injury). It is a life-threatening condition with a mortality of 10%. The diagnosis is clinical, but the RegiSCAR score may be useful in considering the likelihood of DRESS.[1]

Human leukocyte antigens (HLAs), also known as the major histocompatibility complex, are central to immune function. They are involved in DRESS. There is widespread T-cell activation as a result of a drug altering the interaction between antigen-presenting cells and T cells.[2]

The most common drugs that induce DRESS are antibiotics (particularly beta lactams, sulfonamides and vancomycin), aromatic amine anticonvulsants and allopurinol.[1] The HLA alleles that predispose individuals to these T-cell–mediated reactions are common in particular ethnic groups so screening before prescribing these drugs has the potential to prevent life-threatening reactions.[2]

Identifying the culprit drug can be problematic in patients receiving multiple medicines. Often identification comes down to the temporal relationship between the drug and the reaction (usually 2–3 weeks after starting the drug), the prescription of known high-risk drugs and HLA typing when appropriate.

The culprit drug should never be prescribed again as future reactions may be more severe or fatal. Even small doses can precipitate another reaction so desensitisation is contraindicated.

Conclusion

DRESS is a potentially life-threatening adverse drug reaction. It occurs most commonly in association with particular drugs. In some cases, DRESS is associated with HLA alleles that are more common in some ethnic groups.

Allopurinol-induced DRESS is highly associated with the HLA class I allele HLA-B*58:01 which is of significantly higher prevalence in individuals of Asian descent. The risk of DRESS can be reduced by checking if these patients have HLA-B*58:01 and avoiding the drug in those who carry the allele.[3] The American College of Rheumatology guidelines also recommend screening African-American patients. No screening is required in patients of other ethnic or racial backgrounds.[4]

Patients should always be counselled on the risk of DRESS with allopurinol, particularly in the first eight weeks of treatment. They should stop the drug immediately and see their GP at the onset of symptoms. Allopurinol should be started at low doses (no more than 100 mg/day), especially in those with chronic kidney disease, then slowly titrated according to target serum urate concentrations.[4]

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FURTHER READING

Copaescu AM, Trubiano JA. The assessment of severe cutaneous adverse drug reactions. Aust Prescr 2022;45:43-8. https://doi.org/10.18773/austprescr.2022.010