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CASE REPORT

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Exacerbation of allopurinol-induced drug reaction with eosinophilia and systemic symptoms by teicoplanin: A case report

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Summary

What is known and objective: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare and potentially life-threatening drug reaction. Allopurinol is one of the most frequently reported drugs accounting for DRESS syndrome development. In contrast to allopurinol, DRESS syndrome induced by teicoplanin has not been reported frequently.

Case description: A 50-year-old woman was admitted to receive FLAG chemotherapy regimen (fludarabine, cytarabine (high-dose Ara-C), granulocyte colony-stimulating factor) for relapsed acute lymphoblastic leukaemia (ALL) treatment. Allopurinol was initiated at a dose of 300 mg per day 48 hours before chemotherapy regimen initiation, for tumour lysis syndrome prophylaxis. Seven days after allopurinol initiation, the patient presented with fever, dyspnoea, shortening of breath, facial oedema, generalized pruritus, erythema and macular rash affecting the face, abdomen, trunk, upper and lower limbs and an elevation in hepatic enzymes. Allopurinol was immediately discontinued and intravenous hydrocortisone was started concomitantly alongside other supportive measures. About 72 hours later, pruritus, erythema and rash were ameliorated and abnormalities in liver tests were improved. Afterwards, teicoplanin administration led to severe deterioration of pruritus, erythema and rash; subsequently, serum alanine aminotransferase increased again and episodes of worsening dyspnea occurred. Signs of hypersensitivity reaction were reduced by discontinuation of teicoplanin and supportive care.

What is new and conclusion: We report a case of allopurinol-induced DRESS syndrome, which was exacerbated by administration of teicoplanin. It can be suggested that the administration of drugs with high possibility of hypersensitivity reactions should be avoided during the acute phase of DRESS syndrome.

KEYWORDS

allopurinol, drug reaction with eosinophilia and systemic symptoms, teicoplanin

1 | WHAT IS KNOWN AND OBJECTIVE

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare and potentially life-threatening drug reaction. The overall incidence has been estimated to be between 1 in 1000 and 1 in 10 000 drug exposures and the mortality rate is about 10%.[1] It is characterized by fever, skin rash, enlarged lymph nodes, abnormality in blood count and visceral organ involvement. Delayed onset of symptoms (2-8 weeks after drug exposure), visceral organ involvement (single or multiple) and possible persistence or worsening after drug withdrawal are the features of this syndrome. The internal organs involved are liver, lungs and kidneys; however, it is not necessary to involve all of them for the diagnosis of DRESS syndrome.[2] It has been shown that aromatic anticonvulsants, sulphonamides, allopurinol, dapsone, minocycline and vancomycin are the most common agents associated with the development of DRESS syndrome.[3] Allopurinol, as an inhibitor of the xanthine oxidase enzyme, is frequently employed for the prevention of tumour lysis syndrome (TLS) in patients with haematologic malignancies. The accumulation of oxypurinol (one of the allopurinol metabolites) is believed to be a major reason for the development of allopurinol-associated DRESS syndrome.[4] Teicoplanin is a glycopeptide antibiotic with a mechanism of action similar to that of vancomycin, which is widely utilized for the treatment of invasive Gram-positive infections or empiric febrile neutropenia. In contrast to allopurinol, DRESS syndrome has not been reported with teicoplanin frequently.[5]

In this study, we report a case of allopurinol-induced DRESS syndrome, which was exacerbated by administration of teicoplanin.

2 | CASE DESCRIPTION

A 50-year-old 85-kg woman, with past medical history of B-cell acute lymphoblastic leukaemia (ALL) was admitted to the haematology ward of Shariati Hospital, Tehran, with complaints of persistent fever and weakness. The patient had undergone six cycles of chemotherapy regimen, with the last one being approximately 1 month ago. Laboratory examinations, peripheral blood smear and bone marrow aspiration and biopsy showed relapsed ALL. Meropenem 1 g TDS as a broad-spectrum empiric antibiotic was ordered immediately due to fever of unknown origin, and the diagnostic work-up for infection was done simultaneously. Three days later, the fever was ameliorated and the patient was prepared to receive FLAG regimen (fludarabine, cytarabine (high-dose Ara-C), granulocyte colony-stimulating factor) for chemotherapy. Allopurinol was initiated at a dose of 300 mg per day 48 hours before the start of induction chemotherapy for TLS prophylaxis. She was also receiving ciprofloxacin, fluconazole, acyclovir and pantoprazole orally.

Seven days after allopurinol initiation, the patient presented with fever (38.7°C), dyspnea, shortening of breath, facial oedema, generalized pruritus, erythema and macular rash affecting the face, abdomen, trunk, upper and lower limbs, which involved more than 50% of the body surface area (BSA) (Figure 1). Physical examination showed remarkable enlarged cervical and axillary lymph nodes, and laboratory tests revealed a serum alanine aminotransferase (ALT) level of 129 U/L (greater than twice the upper limit of normal values), alkaline phosphatase of 232 U/L and total bilirubin of 1.7 mg/dL. The blood cell counts were as follows at the start of DRESS syndrome: WBC count was 2830/μL, platelet count was 21 000/μL and Hgb was 8.1 g/dL. The process of blood cell count reduction continued in subsequent days due to intensive chemotherapy regimen. Renal function tests, thyroid function tests and autoimmunity markers were all within the reference range. Hepatitis B surface antigen, hepatitis C antibody, CMV antigen, blood culture, urine culture, antinuclear antibody, antineutrophil cytoplasmic antibodies (cANCA and pANCA) and rheumatoid factor were all negative. The chest X-ray revealed bilateral pulmonary effusion with no signs of pneumonia.

Allopurinol was immediately discontinued with suspicion of drug hypersensitivity, and intravenous hydrocortisone (100 mg BD) was started concomitantly alongside other supportive measures. About 72 hours later, pruritus, erythema and rash were ameliorated and abnormalities in liver tests were improved. Nevertheless, due to increased concern regarding the possibility of infectious origin for fever, teicoplanin was administrated for coverage of Gram-positive microorganisms. Pruritus, erythema and rash were severely deteriorated after the first dose of teicoplanin (400 mg) (Figure 2); subsequently, ALT increased again and episodes of worsening dyspnea occurred. At that time, the WBC count was 1080/μL with a 12% eosinophil count.

Due to severe relapse of hypersensitivity reaction, teicoplanin was immediately discontinued in this patient. One week after discontinuation of teicoplanin, the symptoms and signs of hypersensitivity reaction were reduced significantly and they finally disappeared completely (Figure 3). Intravenous hydrocortisone was switched to oral prednisolone (25 mg/d) 6 days after the start of glucocorticoid therapy; it was continued for 12 days and then was tapered over 7 days. Liver function tests revealed no abnormalities 1 month following the acute hypersensitivity reaction.

Allopurinol is associated with a variety of hypersensitivity reactions including maculopapular rash, erythema multiforme, Steven-Johnson

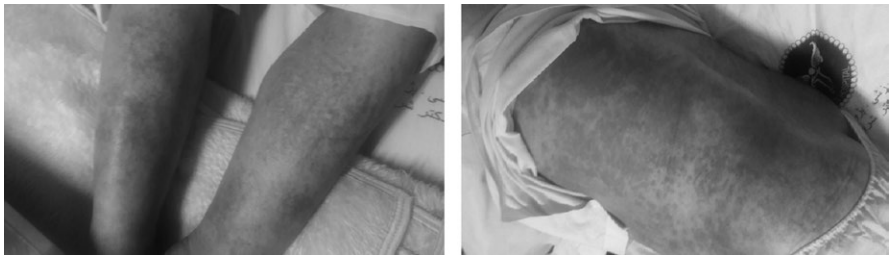

FIGURE 1 Skin rash followed by allopurinol administration

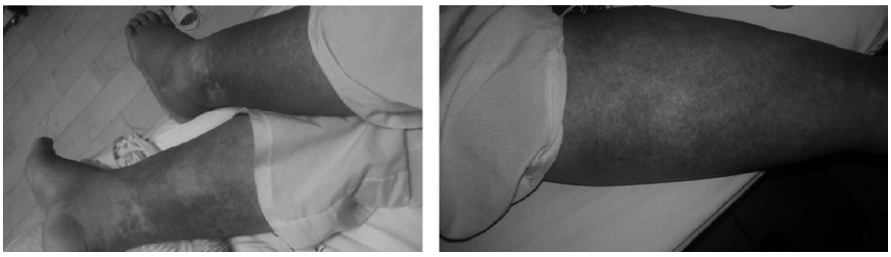

FIGURE 2 Exacerbation of skin rash followed by teicoplanin administration

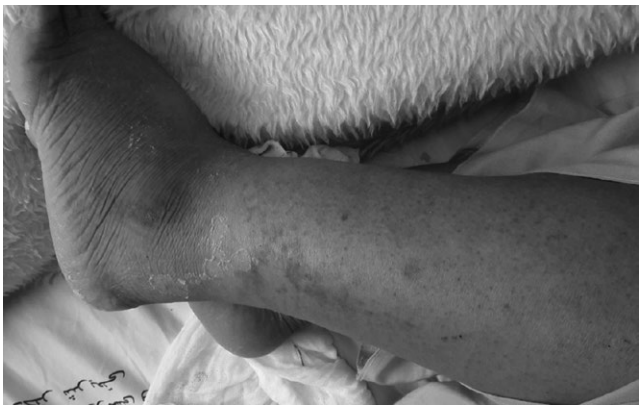

FIGURE 3 Disappearance of skin rash after management

syndrome (SJS), toxic epidermal necrolysis (TEN) and DRESS syndrome.[6,7] Besides allopurinol, carbamazepine, phenobarbital, phenytoin, lamotrigine and vancomycin are the most frequently reported drugs for the development of DRESS syndrome.[3] Allopurinol as a xanthine oxidase inhibitor has been widely utilized for prevention of TLS in patients with haematologic malignancies.[8] Given that DRESS syndrome may be life-threatening, immediate diagnosis and management is necessary. According to neutropenic conditions, atypical lymphocytes and probable lymphadenopathy in patients undergoing chemotherapy for treatment of ALL, the confirmation of DRESS diagnosis is more difficult in this population. The most common diagnostic criteria for classification and diagnosis of DRESS syndrome are RegiSCAR scoring system[9] and scoring system published in 2007 by Kardaun et al.[10] The diagnosis of allopurinol-induced DRESS syndrome was suspected in our patient based on fever (more than 38.5°C), skin rash which involved more than 50% of BSA, enlarged lymph nodes (more than 1 cm, in at least two sites), facial oedema and liver and lung involvement. The diagnosis of allopurinol-associated DRESS syndrome was definite and probably based on Kardaun and RegiSCAR scoring systems, respectively. Although other life-threatening drug reactions like SJS and TEN may cause similar complications, we did not observe any mucosal involvement (lips, oral cavity, conjunctiva, nasal cavity, urethra, vagina or gastrointestinal tract) that are common in patients with these severe drug adverse effects. Also, we observed favourable results after allopurinol discontinuation and corticosteroid administration, which is one of the DRESS syndrome characteristics.[11] Although DRESS syndrome as a type 4 hypersensitivity reaction is characterized by delayed onset of disease after drug exposure (2-8 weeks),[2] in our patient clinical symptoms of hypersensitivity reaction emerged 7 days after allopurinol therapy commenced. It can perhaps be explained by the fact that the patient had received allopurinol for prophylaxis of TLS in previous chemotherapy cycles approximately 1 month earlier. Also, cases of DRESS with short onset have been reported. A retrospective study which reviewed sixty cases of DRESS showed that the average interval time to drug reaction was 20.7 days (range, 3-76 days).[12] One case of chloral hydrate-induced DRESS syndrome with short onset (3 days) in the second episode of administration (after 3 weeks) has been reported.[13]

Allopurinol is one of the leading causes of DRESS syndrome (36.7% in Chiou et al., 31.7% in Chen et al. and 27% in Eshki et al.),[12,14,15] but other concomitant medications in this patient are not on the list of drugs strongly associated with SJS, TEN and DRESS.[12,14-16] On the other hand, the complications were improved after allopurinol was ceased; therefore, the diagnosis of allopurinol-induced drug reaction was suspected in our patient.

Teicoplanin flared up the symptoms and signs of hypersensitivity reaction just after the first dose, while receiving high dose of glucocorticoid. Eosinophilia was observed besides the deterioration of skin rash, liver enzymes abnormality and dyspnea, after teicoplanin administration. It should be noted that the eosinophil count was not checked at the start of the allopurinol-induced DRESS syndrome; therefore, it was not considered for a diagnosis of DRESS in Kardaun and RegiSCAR scoring systems.

Reports about teicoplanin-induced DRESS syndrome are limited; however, vancomycin as another glycopeptide is one of the most frequently involved drugs in DRESS syndrome development. Considering a similar chemical structure and mechanism of action between teicoplanin and vancomycin, high incidence of cross-reactivity between glycopeptides and high possibility of vancomycin-induced DRESS syndrome,[3,5] the exacerbation of hypersensitivity reaction after initiation of teicoplanin can be explained.

3 | WHAT IS NEW AND CONCLUSION

We report a case of allopurinol-induced DRESS syndrome, which was exacerbated by administration of teicoplanin. We concluded that the administration of drugs with high possibility of hypersensitivity reaction should be avoided during the acute phase of DRESS syndrome.

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ETHICAL CONSIDERATIONS

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy) have been completely observed by the authors.

CONFLICT OF INTEREST

The authors declare that there are no conflict of interests.

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