Unusual association of diseases/symptoms

An unusual case of DRESS syndrome due to leflunomide

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Summary

The DRESS (drug rash, eosinophilia and systemic symptoms) syndrome, is a type of drug hypersensitivity syndrome, is a severe idiosyncratic reaction to several drugs, mainly antiepileptics and antibiotics, which can occasionally produce acute hepatic failure. In this article, the authors report a case of DRESS syndrome with severe exfoliative dermatitis with acute hepatitis associated with intake of leflunomide. Rapid diagnosis with withdrawal of offending agent is crucial for survival of these cases.

BACKGROUND

Sometimes drug reaction may present as DRESS (drug rash, eosinophilia and systemic symptoms) syndrome which is a type of drug hypersensitivity reaction. A large number of drugs can cause this entity, the most common being sul-fasalazine, carbamazepine, phenobarbital, allopurinol and some antibiotics such as vancomycin and minocycline.^{1 2} Recently, bosentan has also been described as an inducer of DRESS syndrome.³ DRESS syndrome may be fatal in upto 10 % of cases.⁴ Here we first time report an unusual case of DRESS syndrome due to leflunomide. Early withdrawal of drug and appropriate measures led to successful outcome.

CASE PRESENTATION

A 40-years-old male was admitted to emergency department with high grade fever and redness of skin and rashes for 18 days. He also had backache with joint pains involving mainly large joints for last 3 months for which he was initially prescribed prednisolone and methotrexate but had no relief. For last 20 days, he was taking leflunomide 20 mg qd following which he developed the present complaints. Examination showed that the patient was in distress, there was diffuse erythema of body with white flakes (exfoliative dermatitis) (figure 1) with involvement of lips and oral mucosa (Stevens-Johnson syndrome (SJS)), jaundice, temperature 100.6°F and other vitals were

Figure 1 Diffuse erythematous rashes with white flakes over back of patient.

Figure 2 Oral candidiasis developed in the patient during course of his illness.

maintained. Rest of the examination did not reveal any finding.

INVESTIGATIONS

Investigations showed- haemoglobin-10.6 gm%, total leukocyte count-15000/mm³ with polymorphs-51%, lymphocytes-21%, eosinophils-28% and platelets 2.25×10⁵/mm³, urine-protein traces, blood urea-21 mg/dl, blood sugar random 89 mg/dl, serum bilirubin-9.0 mg/dl, alkaline phosphatase-399 IU/l, serum glutamic oxaloacetic transaminase-300 IU/l, serum glutamic pyruvic transaminase-1350 IU/l, absolute eosinophils count 4200/mm³ (normal <500/mm³) and antinuclear antibody-negative. Tests for hepatitis A, B, C, E and HIV 1 and 2 were negative. Ultrasound of abdomen showed pericholecystic cuffing with liver span of 14.8 cm.

DIFFERENTIAL DIAGNOSIS

Viral hepatitis.

TREATMENT

We withdrew leflunomide in the patient. Patient was started on tablet prednisolone 20 mg three times a day, anti-acids and tablet paracetamol as required. Patient improved over 4–5 days, rashes cleared, erythema decreased and oral ulceration subsided.

OUTCOME AND FOLLOW-UP

Patient however developed oral candidiasis for which he was advised clotrimazole lotion locally (figure 2). After stabilisation patient went home after 15 days.

Table 1 RegiSCAR inclusion criteria for DRESS syndrome.

(Three of the four starred criteria required for diagnosis)

Hospitalisation
Reaction suspected to be drug-related
Acute rash*
Fever > 38°C*
Enlarged lymph
Nodes of at least two sites*
Involvement of at least one internal organ*
Blood count abnormalities (lymphopenia or lymphocytosis*, eosinophilia*, thrombocytopenia*)

DISCUSSION

Drug reactions can vary from a mild skin eruption with pruritus to life threatening disorders such as SJS, DRESS syndrome and toxic epidermo-necrolysis. DRESS syndrome is characterised by drug rashes, eosinophilia and systemic symptoms and our patient fits into this category.

The systemic manifestations in DRESS syndrome most commonly involve the liver-80%, followed by the kidney-40% and pulmonary involvement in 33% of cases.⁵ The liver involvement can rapidly progress to acute hepatic failure and can prove catastrophic.

The manifestations in our case were due to leflunomide which he had been taking for 20 days. The hepatic manifestation in our case could therefore be due to DRESS syndrome or due to leflunomide which itself is hepatotoxic.^{6,7} To our information, this the first report of DRESS syndrome due to leflunomide. Prompt diagnosis with withdrawal of the drug and appropriate treatment enabled a satisfactory outcome in the case. It is therefore important to bear in

mind that these potent immunomodulating drugs should not be prescribed for trivial disturbances and should only be prescribed after careful consideration.

A RegiSCAR criterion has been proposed for DRESS syndrome⁸ (table 1). These criteria can be utilised to arrive at the correct diagnosis in such cases.

Learning points

- ▶ Drug reaction can have varied presentations.
- ▶ DRESS syndrome should be kept in differential diagnosis of severe drug hypersensitivity reaction.
- ▶ Here we report an interesting and rare case of DRESS syndrome due to leflunomide which unveils the toxic potential of this immunomodulatory drug.

Competing interests None.

Patient consent Obtained.

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