

Case Report

DRESS syndrome secondary to pyrazinamide- A rare case report

Dr. Vijaya Patil, Dr. Ravindrakumar Pattar, Dr. Ravi Ichalakaranji*, Dr. L.S. Patil
and Dr. Umesh P.

BM Patil Medical Collage & Hospital, Bijapur, India

***Correspondence Info:**

Dr. Ravi Ichalakaranji
BM Patil Medical Collage & Hospital, Bijapur, India
E-mail: ravi.ichalkaranji@gmail.com

Abstract

Drug, rash, hypereosinophilia with systemic symptoms (DRESS syndrome) is life threatening drug induced hypersensitivity reaction. Pyrazinamide has been described as uncommon cause of DRESS syndrome. Here we report a 21 years old female patient had DRESS syndrome on 18th day of Pyrazinamide exposure. She had generalized pruritic maculopapular rash, fever, lymph node enlargement. Laboratory investigation revealed leucocytosis, eosinophilia, lymphocytosis, raised ESR, thrombocytopenia, raised liver enzymes. Urine examination revealed aseptic pyuria. She recovered completely 6 weeks after drug withdrawal. Here we report this as a rare case report of DRESS syndrome due to Pyrazinamide.

Keywords: DRESS syndrome, Pyrazinamide, corticosteroids

1. Introduction

Tuberculosis is a most common infectious disease in developing countries which can be totally cured by antitubercular drugs like Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. These drugs are associated with many adverse effects which lead to therapeutic failure. The major adverse effect of Pyrazinamide is hepatotoxicity. It may induce cutaneous pruritic maculopapular rashes which is very rare & still more uncommon is its association with DRESS syndrome.

DRESS syndrome is Type IV hypersensitivity reaction with overall mortality rate is 10%.¹ Defect in detoxification of drug, genetic viral infection are causative factor. Skin rash, hypereosinophilia, multiorgan involvement commonly liver, kidney and lungs are main manifestation.

2. Case Report

A 21 year old female patient presented to us with neck swellings, anorexia, weight loss and evening rise of temperature since 3 months. Physical examination revealed firm matted non tender posterior cervical and jugulodigastric lymphnode. No evidence of hepatosplenomegaly. Laboratory test revealed raised ESR 120 mm/hr and C-reactive protein 22mg/dl. Sputum test was negative for tubercle bacilli. Lymphnode biopsy was performed and histology revealed epithelioid and giant cell granuloma with central caseation. With this diagnosis of Tubercular cervical lymphadenitis was made and started antitubercular drugs (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol). On 12th day she developed fever, pruritic maculopapular rash initially over upper limb (Fig 1A), lower limb(Fig 1B) and later over the face (Fig 1C) associated with facial oedema, fever of 41^oc, generalized weakness, hepatomegaly, and enlargement of inguinal lymph node. Lab investigation revealed leucocytosis (16000cells/mm³), eosinophilia (3200cells/mm³), lymphocytosis (5500/mm³), thrombocytopenia (75000cells/mm³), ESR 130mm/hr. Abnormal LFT findings were ALAT- 180 IU/L, ASAT- 140 IU/L, alkaline phosphatase- 780 IU/L.

Fig 1: Showing maculopapular rash over upper limb (Fig 1A), lower limb (Fig 1B) and later over the face (Fig 1D)



1A



1B



1C

Urine examination showed 25-30 pus cells. Blood and Urine culture were sterile. Bone marrow aspiration was normal. No evidence of lymphoma or leukemia was detected by laboratory test. Blood examination for Brucella was negative. Serological test for Hepatitis B and C virus and Human immunodeficiency virus were negative. With this diagnosis of hypersensitivity to antitubercular drugs was made. There was no history of similar complaints in the past and in family members for these and any other drugs. The drugs were withdrawn and treated her with corticosteroids for 3 weeks, and antitubercular drugs were reintroduced one by one after taking consent of the patient. The reintroduction of Pyrazinamide resulted in reappearance of symptoms within 1 week and disappearance of symptoms 4 weeks after drug withdrawal and treatment with corticosteroids. This indicates the accountability of Pyrazinamide as a culprit drug due to positivity of drug challenge test and PATCH test as patient was not on any other drugs except vitamin supplements.

It took nearly 6 weeks for disappearance of skin lesions, lymph nodes, normalization of blood counts and Liver function tests after withdrawal of antitubercular drug. She recovered fully with corticosteroid treatment. Other antitubercular drugs excluding pyrazinamide along with quinolone were given to her.

3. Discussion

It is life threatening hypersensitivity reaction with mortality rate of 10%.¹ Its incidence is 1 in 10,000 with anticonvulsant drugs⁵ and also associated with calcium channel blockers, ibuprofen, gold, allopurinol, sulfasalazine.^{2,4} REGISCAR inclusion criteria for diagnosis of DRESS syndrome³:

- a) Hospitalization
- b) Drug induced skin rash
- c) Blood count abnormalities such as low platelets, raised eosinophils or abnormal lymphocyte count.
- d) At least one of the internal organ involvement hepatitis, interstitial lung disease, interstitial nephritis, myocarditis, pericarditis.
- e) Fever about 38 degrees Celsius
- f) Enlarged lymphnodes at two sites

The syndrome develops 2-6 weeks after initiation of treatment. In our case she had met all the 3 criteria of DRESS syndrome and she developed this in 2nd week after initiation of treatment. The diagnosis was suggested by disappearance of symptoms after withdrawal of pyrazinamide and recurrence immediately after resumption of pyrazinamide confirmed by drug challenge test. The exact pathophysiology of DRESS syndrome is not known but the hypersensitivity induced by the drug as a result of abnormalities in the production and detoxification of its active metabolites is one of the causative factors. Defect in detoxification of active metabolites which is also related to genetic abnormality, as risk increased by 25% with positive family history of slow acetylators and blacks^{6,7,8,9,10}. Viral etiology HHV6 infection has been incriminated recently in development of DRESS syndrome^{11,12}. Treatment of DRESS syndrome includes immediate withdrawal of drug and initiation of glucocorticoid therapy for several weeks¹³. Delaying this measure may be associated with worst prognosis. Treatment with high dose intravenous acetylcysteine, glutathione precursor which is involved in detoxification of many drugs has been proposed^{14,15}.

4. Conclusion

Pyrazinamide, antitubercular drug though a rare cause of DRESS syndrome should be reported to pharmacovigilance centers as its frequency of adverse reaction cannot be underestimated. Most important is early recognition of this entity and prompt withdrawal of culprit drug can save the life of the person.

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