

Persistent Eosinophilia After DRESS Syndrome

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1. Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare, potentially life-threatening hypersensitivity reaction that may occur during treatment with various drugs. This report describes the case of a 57-year-old woman whose DRESS syndrome was successfully treated in our department. Because of the persistence of eosinophilia, we set up a diagnostic pathway to better frame it. As a result, we detected an unknown clear cell renal cancer which was then operated and led to the complete resolution of the eosinophilia.

2. Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare, potentially life-threatening hypersensitivity reaction that may occur during treatment with various drugs. Symptoms can include a skin rash accompanied by fever, hematologic abnormalities, lymphadenopathy and internal organ involvement. They tend to occur 2 weeks to 3 months after treatment start with the causative drug. Pathogenesis remains unknown, although a drug-specific immune response and virus reactivation are considered key factors [1,2,3].

3. Case Report

A 57-year-old woman presented to our emergency department with generalized pruritic skin lesions, worsening despite daily therapy with prednisone 25 mg and cetirizine 10 mg. Two weeks

before she had started amoxicillin and acetaminophen for otitis. After 7 days of therapy she developed skin rash without fever. At admission general examination revealed skin maculopapular rash, with confluent infiltrated erythematous plaques involving nearly 70–80% of the body's surface. There was no evidence of mucosal involvement (Figure 1). PCR test for Sars-Cov-2 was negative. Laboratory exams revealed severe eosinophilia ($3.2 \times 10^9/L$) associated with a slight increase in C reactive protein values (1.2 mg/dl). Liver and kidney function tests were normal. To rule out other causes of eosinophilia, an extended panel of laboratory markers was performed. Total IgE were 439 KU/L. Specific IgE to Penicilloyl G, Penicilloyl V, Amoxicilline and Cefaclor were negative. B-2-microglobulyn, thrombin time, C3, C4, anti-streptolysin O were normal. Rheumatoid factor was negative as well as anti-neutrophil cytoplasmic antibody, anti-citric-citrullinated peptide, double-strands DNA, extractable nuclear antigens, anti-transglutaminase, anti-thyroid peroxidase, anti-thyroglobulin and immunoglobulins. Antinuclear antibodies were 1:320 speckled pattern. Serological markers for Human Herpes virus 6, 8, Parvovirus B19, Cytomegalovirus virus, Epstein-Barr virus, Hepatitis B virus, Hepatitis C virus, Chlamydia pneumoniae, Mycoplasma pneumoniae, Echinococcus granulosus, Schistosoma mansoni were negative. Echocardiography showed mild pericardial effusion without clinical relevance. Neck echography showed bilateral reactive cervical lymphonodes and thyroid nodules. Being the ear-

ly clinical presentation indicative for a DRESS, we began treatment with intravenous methylprednisolone at a dose of 1 mg/kg, intramuscular Chlorpheniramine Maleate along with supportive care including intravenous fluids and omeprazole. For technical reasons, skin biopsy was performed on the second day of hospitalization and showed discrete dermal perivascular lymphomonocyte infiltrate, with scattered eosinophilic granulocytes and occasional activated lymphoid elements, findings compatible with our clinical diagnosis (Figure.2). Symptoms began to subside with brightening of skin lesions and slow decline of eosinophilia. Over the days it was possible to progressively taper steroid. However, after about 10 days, despite the complete resolution of the skin lesions, eosinophilic count kept being moderately high ($0,89 \cdot 10^9/L$). For this reason, we performed total body computerized tomography that showed in the middle third of the left kidney a mass of 18 mm, confirmed by abdominal magnetic resonance. Based on urological consultation, the excisional surgery of the solid mass was programmed and carried out after two months. Histology showed a clear cell renal carcinoma CD10+, CK7- pT1a, stage II WHO/ISUP, confined to renal parenchyma. No aspects of tumor necrosis or vascular infiltration were observed. After surgery, interestingly eosinophilic count was $0 \cdot 10^9/L$.



Figure 1: Clinical features.

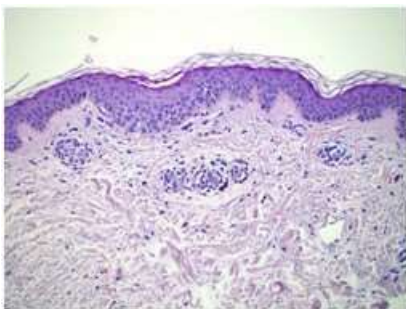


Figure 2: Histological features.

4. Discussion

In our case, despite the resolution of DRESS syndrome, we observed persistent peripheral eosinophilia due to concomitant clear cell renal cancer that had not yet been diagnosed. Eosinophilia usually occurs in conjunction with several medical conditions, such as tumors. It seems that cytokines such as interleukin-3, interleukin-5 and granulocytes macrophages stimulating factor released by the primary tumor can increase eosinophil's production. In renal cell

eosinophilia is extremely rare; only few cases have been reported. Interestingly after excisional surgery of renal solid mass, eosinophilic count became normal. According to our findings, resolution of peripheral eosinophilia following surgical resection of tumor was previously described in other studies. Furthermore, it has also been suggested that reappearance of eosinophilia may herald the onset of tumor recurrence [4,5].

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