Allopurinol Induced DRESS Syndrome

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Abstract
A 45 years old female on allopurinol for 3 months presented with itching, rash, facial oedema and eosinophilia with hepatic and renal dysfunction. Skin biopsy revealed interface dermatitis, suggesting the diagnosis of DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) syndrome.

Introduction
Allopurinol is associated with generalised hypersensitivity disorders like diffuse maculopapular rash or exfoliative dermatitis as well as serious skin reactions like erythema multiforme, Steven Johnson syndrome and toxic epidermal necrolysis. DRESS syndrome is a multisystem condition associated with certain drugs in predisposed individuals characterised by fever, rash, internal organ involvement and eosinophilia. We report a case of 45 year old female who developed DRESS syndrome as a rare side effect of allopurinol treatment.

Case Report
A 45 year old female presented with complaints of intermittent fever, breathlessness class II-III associated with wheezing and oliguria since one month. She developed rash with itching and swelling over both lower limbs upto the thigh and puffiness of face with swelling of upper lip since 6 days. Her medications included tab. amlodipine, tab. glimepiride and tab. voglibose. Her general practitioner had put her on tab allopurinol 100 mg OD since 3 months for asymptomatic hyperuricaemia (sr.uric acid-8 mg/dl). She was febrile (temp-39°C). There was erythematous, papular rash over both lower limbs upto thigh, toes were swollen with blackish discolouration (Figure 1) and there was erythematous macular rash over cheek and swelling of upper lip (angioneurotic oedema) (Figure 2).

Blood cultures were negative. Ultrasound of abdomen showed normal size kidneys with increased renal cortical echogenicity. Urine showed proteinuria (24 hrs urinary albumin 1.2 gm) with abnormal sediment. Earlier investigations revealed rising AEC (absolute eosinophil count) sine 2 months.
from 128 to 1387 on admission and subsequently to 6324 a week later. Her allopurinol was stopped. She was put on diabetic diet, tab. amlodipine, tab. diethylcarbamazine and injectable chlorpheniramine, hydrocortisone, clarithromycin, frusemide. Blood sugar was controlled on insulin. Laboratory investigations revealed anaemia, eosinophilia, elevated SGOT, SGPT, sr.creatinine and sr.uric acid. HIV, anti HCV and HBsAg were negative. ANA was positive (1:80), anti dsDNA and p-ANCA were negative. C3 and C4 level were normal. On tapering hydrocortisone (day 7) she developed swelling of upper lip and complained of breathlessness and discomfort in the throat, respiratory rate of 36/min, bilateral coarse crepitations upto middle zones. She responded to oxygen, injectable hydrocortisone. Skin biopsy revealed superficial perivascular lymphocytic infiltration with focal basal cell vascularisation and mild focal spongiosis and parakeratosis and occasional eosinophils were scattered in the infiltrate suggestive of interface dermatitis (Figure 3) and diagnosis of DRESS syndrome secondary to allopurinol was established. She developed hyponatraemia (serum sodium 116 mEq/L) on day 11 with urinary sodium of 60 mEq/L, all suggestive of interstitial nephritis. Corticosteroid were continued for 2 weeks and tapered over 1 week. Her eosinophil count dropped over a period of 14 days to 21. Serum creatinine stabilised to 2.7 mg/dl. Her rash and discolouration of toes cleared in 3 weeks. She was discharged after 4 weeks.

Discussion

Differential diagnosis for skin rash, eosinophilia and hepatorenal involvement include acute infections (e.g. Hepatitis viruses, Ebstein Barr Virus, Cytomegalovirus, HIV Virus) collagen vascular disorder, drug reactions, lymphoma and hypereosinophilic syndrome.2

Our patient had erythematous maculopapular rash over both legs upto thigh, cheeks and facial oedema, progressive eosinophilia and hepatorenal involvement on the background of allopurinol intake for asymptomatic hyperuricaemia. The presence of interface dermatitis in skin biopsy clinched diagnosis of allopurinol induced DRESS syndrome.2

Skin reactions are common side effects of allopurinol with reported incidence of 2% of patients prescribed.3 Reported frequency of DRESS syndrome is about 0.4% patients treated with allopurinol.4 Apart from eosinophilia, the clinical triad of DRESS syndrome includes fever, rash, internal organ involvement within the first 2-8 weeks of exposure. It is not related to dose or serum concentration of drug. Re-exposure to the offending agent may cause development of symptoms within one day.5

The drugs associated with DRESS include anticonvulsants like lamotrigene, phenobarbital and phenytoin, long acting sulphonamides sulphamethoxazole, sulphadiazine, sulphasalazine, allopurinol, nevirapine, abacavir, dapson, minocycline and even vancomycin.

Skin eruptions are typically morbilliform and vary from mild to severe with exfoliative erythroderma. Facial oedema often accompanies the skin eruption and evolve to superficial pustules (esp. on face). Severity of skin changes does not necessarily reflect the severity of internal organ involvement which include liver (increased SGOT, SGPT to fulminant hepatic necrosis) kidney (haematuria, nephritis, acute renal failure) lung (ARDS, vasculitis, interstitial pneumonia) and central nervous system. Hypothyroidism and Coomb’s
negative anaemia can occur. Late sequelae possible with auto immune basis include SIADH, thyroiditis, grave's, SLE and DM.

If recognised early and culprit drug (S) discontinued the syndrome resolves over next few weeks. Rash disappears with mild desquamation. Symptoms in some patients may flare up 3-4 weeks especially after rapid withdrawal of a corticosteroid as was seen in our patient. Once the culprit drug is discontinued, organs initially involved may show progressive changes. The treatment include immediate withdrawal of culprit drugs, symptomatic treatment with anti histaminic and topical corticosteroid and systemic steroids usually prednisone at dose of 1-2 ml/kg/day. Cyclosporine and intravenous immunoglobulin is reserved for resistant cases.

**Conclusion**

Prevention is of prime importance, allopurinol should prescribe only for the right indication and the dose adjusted to renal function. Asymptomatic hyper uricaemia should not be treated.

**References**


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**Leptospiral Uveitis**

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**Abstract**

Leptospirosis is widely regarded as the most widespread zoonosis in the world. Systemic leptospirosis is a biphasic illness. Ocular involvement in leptospirosis has been reported to be extremely variable, ranging from 2% to 90%. Ocular involvement is seen both in the systemic bacteraemic phase as well as in the immunological phase. Leptospiral uveitis is a common entity in the tropical countries. However it remains underdiagnosed mainly because ocular manifestations are noted in the second phase of illness. The primary anatomical location of inflammation is either in the anterior segment or pan uveitis. We report the case of a 40 year old lady who had presented to us with leptospiral uveitis.

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**Introduction**

Leptospirosis is a spirochaetal disease. Leptospiral uveitis is a common entity in the tropical countries. However it remains underdiagnosed mainly because ocular manifestations are noted in the second phase of illness. There is a prolonged symptom free period that separates the systemic manifestations from detection of...