Dermatology Case Reports

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Case Report

Drug Induced Hypersensitivity Syndrome Secondary to Allopurinol: A Case Report

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ABSTRACT

Drug induced Hypersensitivity Syndrome (DHS) is a rare but potentially lethal adverse drug reaction that classically manifest as morbilliform rash with associated fever, lymphadenopathy, hematologic abnormalities and multi-organ manifestation. The relevance of this case is that many patients will come to the Emergency room presenting with rashes but often misdiagnosed because the onset of symptoms typically occur at 2-6 weeks following the initiation of the offending agent, careful history taking and Physical Examination will help clinician rule out this disease and prevent end organ dysfunction.

The relevance of this case is that patients who present to the emergency room may likely be misdiagnosed and possibly a drug reaction missed as the onset of symptoms. A thorough history and physical examination will help a clinician properly diagnose, promptly intervene and prevent end organ damage.

Keywords: Drug; Hypersensitivity syndrome; Morbilliform; Infection; Hyperuricemia

INTRODUCTION

Drug induced hypersensitivity reaction is a rare type of drug reaction. It is more commonly associated WITH anticonvulsants and sulfasalazine. According to the literature about 0.4% is due to allopurinol. DIHS usually presents with fever, malaise, lymphadenopathies and skin eruptions. A telling feature is the delay in the onset of symptoms in relation to the exposure to the offending medication which would typically occur two-six weeks after of exposure to the offending agent. Medications taken for more than three months or initiated less than two weeks before the onset of DIHS are unlikely to be the culprit. Diffuse morbilliform rash with pruritus is the most common cutaneous finding [1].

OBJECTIVES

This case report aims to present a 59-year-old female with Drug induced Hypersensitivity syndrome secondary to Allopurinol**.**

CASE PRESENTATION

A 59-year old female was brought in to our institution after presenting with fever, generalized body malaise and rashes, patient was initially diagnosed as allergic contact dermatitis after having applied massage oils prior to symptoms. Morbilliform rashes were noted on the whole body after patient claimed to have massage with oils. Liver enzymes and kidney function tests were elevated. Allergic contact dermatitis seems unlikely in this case as areas where massage oils were not applied such as the face and other parts also developed lesions. The patient was prescribed with a medication however no rashes and other symptom was notice until after two weeks. It was known that the patient took antibiotics and anti-gout medications prior to onset of symptoms and from this the patient was diagnosed with Drug induced hypersensitivity reaction and was managed appropriately.

CASE SYNOPSIS

This is a case of a 59-year Filipino Married catholic housewife lives in Antipolo Rizal who came in our institution with a chief complaint of rashes, Two weeks prior to admission patient had noted fever and body weakness and dysuria patient consulted with private MD patient was given request for urinalysis and blood uric acid and urinalysis follow up consult after one day revealed urinary tract infection and hyperuricemia patient was prescribed with allopurinol and ciprofloxacin 500 mg/tab bid for Seven days Five days prior to admission patient noted to have fever episodes intermittent T_{max} 38 and body pains on lumbar area and upper and lower extremities, patient then went for massage with mentol and lime oil applied to her body, noted appearance of rashes in the lower extremity. Four days prior to admission still with body pains patient had another massage and rashes noted progressed covering her entire body hence brought to emergency department (Figure 1).

At the Emergency department patient appeared to be weak looking ambulatory, conscious coherent with vital signs revealed BP 110/80 Heart rate 120 Respiratory rate 22 cycles per minute temperature 36.5 oxygen saturation 97% at room air. Patient was

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given with paracetamol 300 mg IV, Diphenhydramine 50 mg IM, Hydrocortisone 300 mg IV was given and diagnostics were done [2]. The laboratory showed leukocytosis and thrombocytopenia there is elevation in the liver enzymes, and elevation on the serum creatinine (Table 1) there is also cervical-lymphadenopathy was appreciated as well [3].

Initial impression to the patient is Allergic contact dermatitis, upon admission patient was hook to PNSS 1 L × 60 cc/hr and was put to hypoallergenic diet and was started on Hydrocortisone 100 mg IV q6, Diphenhydramine 25 mg IV q12, Omeprazole 40 mg/cap OD, patient was then referred to derma service. Initial consideration was Steven Johnson Syndrome *vs* Toxic epidermal necrosis overlap patient was treated with diphenhydramine 50 mg IV q12, hydrocortisone 100 mg TIV q6 for 8 doses, Carnitine orotate, essential phospholipids, vitamin B tab BID due to transaminitis, and patient was hydrated with PNSS 1 L × 80 cc/hr, petroleum jelly was also applied in oral commissures three times a day due dryness in both oral commissures, On the 3rd day the rashes and swelling of the face noted to be decreased and repeat complete blood count, creatinine and sodium urinalysis was done which revealed elevated creatinine 109, Serum Sodium is 131 Compete blood count is interpreted with leucocytosis and thrombocytopenia. Urinalysis was showed persistence of pyuria (Table 2).

Correction of electrolytes was done and 3rd generation cephalosporin was given, During the course in the ward, after thorough history and physical examination, history of allopurinol and use prior to admission and appearance of throat ulcers, slight monocytosis, elevated liver enzyme, elevated BUN and creatinine of the patient became significant and was diagnosed with Drug induced hypersensitivity syndrome (Figure 2). Patient was later discharged with antibiotics and slow tapering of steroids.

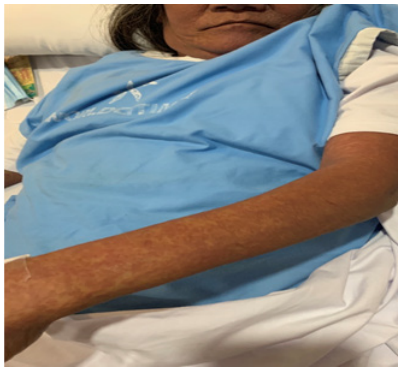

Figure 1: Rashes over skin of 59-year-old woman.

Table 1: Patient status before medication.

CBC	
Hemoglobin 164	Na 124.4
HCt .54	K 3.59
Wbc 10.80	BUN 13.10
Neutrophil .80	Creatinine 194
Lymphocyte .31	PT:
Monocyte 0.07	Control: 13.90 seconds
Eosinophil 0.02	Patient 13.80 seconds
Platelet 202	INR: 1.02
AST: 185	Percent activity: 96.90%
ALT 175	PTT:
Covid antigen test: Negative	Control: 31 seconds
CXR: Pneumonia both lower lobe	Patient: 39.50
ECG: Sinus tachycardia	Urinalysis: yellow/PH 5.0/leukocyte + 3/ Glucose Negative/Urine ketone negative/ Bilirubin Negative/Glucose Negative/Pus cells >50 HPF

Table 2: Patient report after medication.

Clinical feature		Present		Absent
Fever ≥ 38.5°C(101.3°F)		0		-1
Enlarged lymph nodes (>1 cm size, at least 2 sites)		1		0
Eosinophilia: ≥ 700 or 10% (leucopenia)	≥ 1500 or ≥ 20%	1	2	0
Atypical lymphocytes		1		0
Rash ≥ 50% of body surface area		1		0
Rash suggestive (≥ 2 of facial edema, purpura, infiltration, desquamation)		1		0
Skin biospy suggesting alternative cause (blood cultures, ANA, serology for hepatities virus, mycoplasma, chlamydia) ≥ 3 done and negative		1		0
Organ involvement: one	Two or more	1	2	0
Disease duration >15 days		0		-2
Investigation for alternative cause (blood cultures, ANA, serology for hepatitis virus, mycoplasma, chlamydia) ≥ 3 done and negative		1		0
Total score < 2, excluded; 2-3, possible; 4-5, probable; ≥ 6, definite				

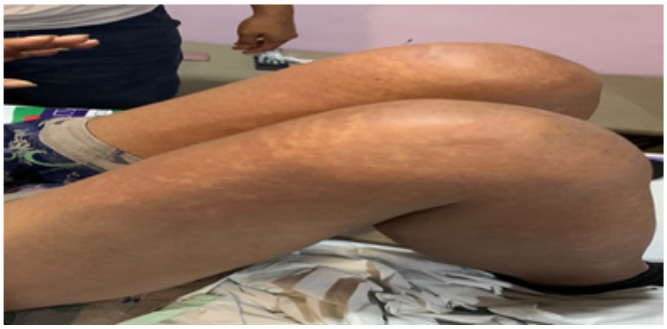

Figure 2: Rashes decreased shown in given figure.

DISCUSSION

Drug induced hypersensitivity syndrome often present rarely. It presents with systemic symptoms like fever, body malaise, and multiorgan manifestation and rashes. To get a diagnosis the important role of a good history taking and physical examination must be taken into account, Systemic manifestation like in our patient presents with generalized rashes with lymphadenopathy associated with Acute kidney injury, and started 2 weeks after ingesting antigout medication (Allopurinol). Anticonvulsants and sulfonamides are the most common offending agents and allopurinol is not common (Table 3)

Associated systemic symptoms other than fever, malaise and rash are directly related to the organ involvement, the liver is the most common organ affected involved, 60%-80%, renal involvement

Table 3: Drugs used while medication.

Drug category	Drug name
Anticonvulsant	Carbamazepine, lamotrigine, phenobarbital, phenytoin, valproic acid, zonisamide
Antimicrobial	Ampicillin, cefotaxime, daposone, ethambutol, isoniazid, linezolid, metronidazole, minocycline, pyrazinamide, quinine, rifampin, sulfasalazine, streptomycin, trimethoprim-sulfamethoxazole, vacnomycin
Antiviral	Abacavir, nevirapine, zalcitabine
Antidepresent	Bupropion, fluoxetine
Antihypertensive	Amlodipine,captopril
Biologic	Efalizumab,imatinib
NASAID	Celecoxib, ibuuprofen
Miscellaneous	Allopurinol, epoetin alfa, mexiletine, ranitidine

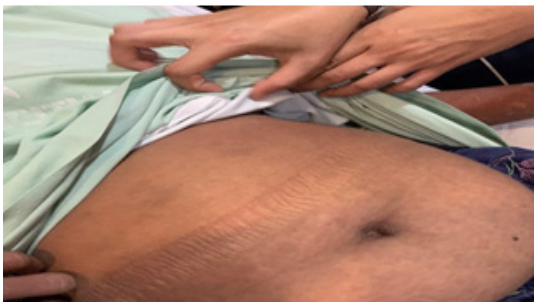

Figure 3: 59 year old female who presented with rashes and fever.

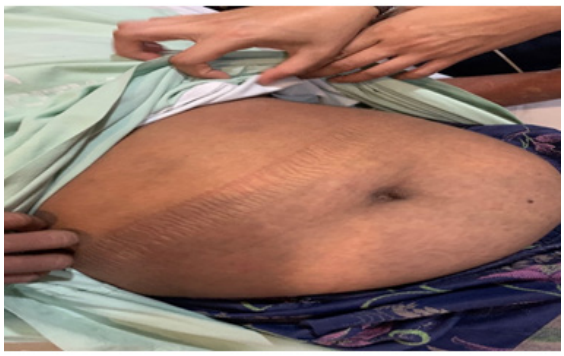

Figure 4: The above figure shows the swelling near stomach region.

10%-30% of cases, hepatic necrosis with fulminant liver failure is the most common cause of mortality. No reliable standard for the diagnosis of DIHS syndrome diagnostic criteria are based on clinical and laboratory findings [4]. The most commonly used in the United States and Europe is known as Registry of Severe cutaneous adverse reaction (RegisCAr). For patient to be definitive with diagnosis of DIHS, patient must fulfilled six of the criteria suggestive of a DIHS.

- Acute rash
- Fever >38
- Involvement of one or more internal organs (liver, Kidneys)
- Blood count abnormalities
- Cervical-lymphadenopathy

Diagnosis of Drug induced hypersensitivity reaction syndrome should be made clinical and skin biopsy is only use if we are trying to rule out other causes Cornerstone of treatment is prompt diagnosis discontinuation of the offending medication aggressive supportive therapy and high dose steroids, current clinical recommendation are systemic steroids at a dose equivalent at least 1 mg/kg/day with increased dosing based on lack of clinical response or when there is significant organ involvement [5]. Prognosis of the disease is associated to the complications related to organ involvement. Most patients like this case recover completely in the weeks to months from withdrawal to the offending drug and appropriate therapy (Figures 3 and 4).

CONCLUSION

In summary this is a case of 59 year old female who presented with rashes and fever may be diagnosed as simple allergic reaction but noted with organ involvement and the rash appeared as delayed onset after taking the offending medications. For this case it is usually admitted to Intensive care unit common due to its consequence if not diagnosed will provide with end organ dysfunction and may cause multi organ failure that may lead to shock or DIC. Usually liver failure is the most common cause of death, other complications are electrolyte imbalances, secondary bacterial infections and sepsis related to break down of the skin barrier.

This patient was diagnosed early and was manage early that it provides favorable outcomes and no severe complications as mentioned above.

We presented a 59 year old female who presented with rashes, fever and systemic symptoms suggestive of organ involvement secondary to allopurinol. This patient was diagnosed early and managed accordingly resulting in a favorable outcome with no severe complications. Detailed history particularly of drugs, thorough physical examination, correct diagnosis and immediate proper management cannot be overemphasized in this case.

CLINICAL RECOMMENDATION

Drug induced hypersensitivity syndrome should be considered as a diagnosis in patients who present with rashes, facial edema, lymphadenopathy and systemic symptoms/organ involvement. Careful history taking particularly drug intake is crucial for correct diagnosis and treatment and in so doing prevent further organ involvement in identifying diagnosis and obtaining essential laboratories and imaging if there is suspected organ involvement can lead in diagnosis for early treatment.

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