A RARE CASE PRESENTATION OF CARBAMAZEPINE DRUG HYPERSENSITIVITY SYNDROME IN A CHILD WITH MUCOPOLYSACCHARIDOSIS

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PRESENTATION OF CASE

An 11-year-old male child, k/c/o mucopolysaccharidosis, came to the skin OPD with reddish-raised lesions over both upper and lower limbs, chest, abdomen, back since 4 days, oral and genital ulcers since 4 days. Lesions were associated with fever since 8 days. Patient was relatively asymptomatic 8 days back when he developed fever and a few scattered blisters, then subsequently diagnosed as chicken pox (acyclovir and amoxicillin), 4 days later patient developed multiple reddish raised lesions over abdomen, which slowly progressed to involve bilateral upper limb, bilateral lower limb, chest, abdomen, back and face. It was associated with oral ulcers and genital ulcers.

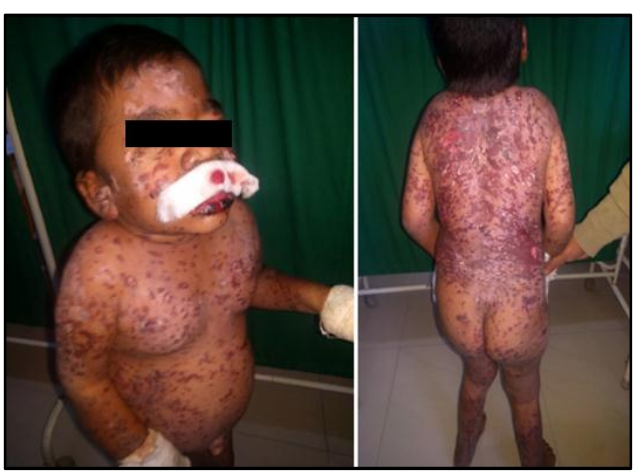

Figure 1. Child Having Crusted Papules to Plaques All Over Body with Few Discharging Erosions Involving Oral and Genital Mucosa As Well

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DIFFERENTIAL DIAGNOSIS

On the basis of clinical history; there may be a possibility of acute febrile neutrophilic dermatoses as a child has fever along with erythematous lesions, then patient skin can be sensitive to antipsychotic drugs. He is into like carbamazepine and risperidone, etc. an urticarial reaction secondary to drug intake can be present. Then, few lesions appear to be like target lesions with central crusting and a peripheral halo suggestive of erythema multiforme with fewer nodular eruptions like suggesting erythema nodosum as a next possibility. Few lesions present with superficial skin exfoliation suggesting generalised exfoliative dermatitis with some topical application and superadded irritant reaction (ayurvedic application) over few lesions. Fever with erythematous lesions of skin and oral mucosa also count towards the most probable diagnoses of viral exanthem such as measles. If associated vascular causes can be ruled out, then porphyria and related disorders can be suggested. A very few pustular eruptions suggesting pustular psoriatic variant can be sought. On the basis of clinical findings and proper investigations, the final clinical diagnosis comes as carbamazepine-induced drug hypersensitivity reaction.

CLINICAL DIAGNOSIS

There was history of difficulty in deglutition, painful micturition, stiffness of joints and oozing from lesions. This child is a known case of mucopolysaccharidosis (treatment details unavailable) since 4 years of age and a known case of psychiatric illness (behavioural disturbances) on treatment since 1 year (details unavailable). Patient was on Tab. Clonazepam 0.25 mg to 0.5 tablet b.d. since 1 month, Tab. Risperidone 0.5 mg half tablet b.d. since 1 month, Tab. Tegretol (carbamazepine) 100 mg half tablet h.s. for 25 days, then T. Tegretol (carbamazepine) 100 mg 1 tablet h.s. since 4 days (for increased irritability). On examination, the general condition of the child was irritable, febrile, patient was crying, vitals showed pulse rate of 100/min. and blood pressure of 90/60 mm of Hg. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy or pedal oedema. Systemic examination was within normal limits. Local examination showed multiple blisters over an erythematous base with few erosions and crusting present over both upper

and lower limbs, trunk, face and genitals. Oral cavity shows haemorrhagic crusts present over lips, erosions over buccal mucosa and genitals shows single erosion over prepuce.

PATHOLOGICAL DISCUSSION

Only few cases of DRESS syndrome has been reported in children. It is difficult to diagnose because of wide clinical spectrum and latent onset of 2 to 8 weeks after drug introduction may not meet the diagnostic criteria in children. It is potentially life-threatening. Therefore, early diagnosis and treatment is mandatory. Common antipsychotic drugs causing drug hypersensitivity reactions include antiepileptics (phenobarbitone, phenytoin and carbamazepine), allopurinol, sulphonamides and dapsone.

Criteria in Practice- DRESS includes skin rash (DR), eosinophilia (E), fever (SS), lymphadenopathy (SS) and hepatitis (SS). Bocquet's criteria require meeting these 3 features- Skin eruption, blood eosinophilia (>1.5×10^3/μL) or the presence of atypical lymphocytes, internal organ involvement, including fever, lymphadenopathies (>2 cm in diameter), hepatitis (liver transaminases values > twice the upper normal limit), interstitial nephritis and interstitial pneumonia or carditis.

DISCUSSION OF MANAGEMENT

Investigations- SGPT- 45 units/litre, T. Blb 0.2 mg/dL, indirect blb 0.1 mg/dL, direct blb 0.1 mg/dL, Hb- 10 gm/dL, TLC- 4500/cu. mm, N 65%, L 26%, E 3%, M 6%, platelets- 2.27 lakhs/cu. mm, blood urea 15 mg/dL, S. creatinine 0.6 mg/dL, urine R/M- albumin trace (no signs of hepatitis, nephritis, pancytopenia and eosinophilia).

Treatment

Injection dexamethasone 2 mg IV 12 hrly. x 4 days, Tab. Prednisolone 60 mg in divided dosages x 3 days, Tab. Prednisolone 50 mg in divided dosages x 3 days, Tab. Prednisolone 40 mg in divided dosages x 3 days, Tab. Prednisolone 30 mg in divided dosages x 3 days, Tab. Prednisolone 20 mg in divided dosages x 3 days, Tab. Prednisolone 10 mg in divided dosages x 3 days, Syp. levocetirizine 2.5 mL h.s., calamine lotion LABD, lignocaine jelly 2% jelly (perianally), Vaseline jelly LABD + Fusion H ointment (lips), Betadine gargles LABD, eye drops Moxi q.i.d., Eye ointment Lacrigel LAHS, eye drop Extralube q.i.d.

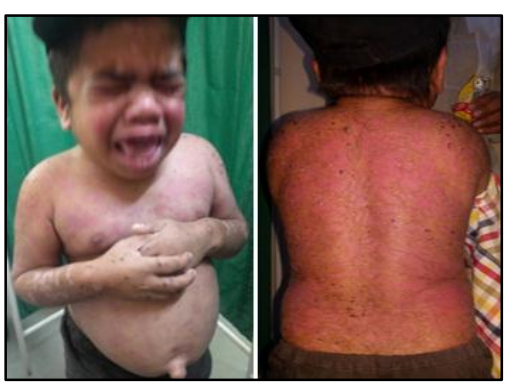

Figure 2. Resolving Erosions with Mild Eythema and Post Inflammatory Hyperpigmentation at Places

FINAL DIAGNOSIS

Mucopolysaccharidosis VI (MPS VI) or Maroteaux-Lamy syndrome (MIM #253200) is an autosomal recessive lysosomal storage disorder described in 1963 by Dr. Pierre Maroteaux and Dr. Maurice Lamy[1] and determined by mutations in the arylsulfatase B (ARS-B) gene located in chromosome 5 (5q13-5q14).[2] Pathogenic mutations of this gene result in reduced or absent activity of the enzyme arylsulfatase B (ARS-B) also called N-acetylgalactosamine 4-sulfatase (E.C.3.1.6.12) leading to incomplete degradation and cellular accumulation of the glycosaminoglycan(s) (GAG), (previously also known as a "mucopolysaccharide" dermatan sulfate (DS)) and cell injury. Another GAG, chondroitin 4-sulfate (CS) is also a substrate for ASB,[3,4] but is hydrolysed by hyaluronidase and β-glucuronidase to trisaccharides and higher oligosaccharides that also accumulate, but are not recognised as "classic storage material" (J Hopwood, personal communication). Clinical manifestations are related to progressive accumulation of DS GAG and sulfated oligosaccharides derived from both DS and CS in lysosomes, cells and tissues. The epidemiological studies of MPS VI are limited to publications describing birth prevalence, whereas no studies describing population prevalence are available. These birth prevalence studies are based on clinical identification of patients and regional birth rate.[5] They range from 1 in 43,261 births in Turkish immigrants living in Germany[6] to 1 in 1,505,160 births in Sweden.[7] Because these birth prevalence estimates are derived from patient referrals based mostly on clinical identification (except for a single publication that mentions prenatal diagnosis for one patient in Australia).[8]

Drug hypersensitivity syndrome (DHS), recently being also referred to as DRESS (drug reaction with eosinophilia and systemic symptoms) or DIDMOHS (drug-induced delayed multiorgan hypersensitivity syndrome) is increasingly being recognised as a distinct type of adverse drug reaction.[9,10] It was first associated with the Aromatic Antiepileptic Drugs (AEDs), viz. Phenytoin (PHT), Carbamazepine (CBZ), Phenobarbital (PB), lamotrigine and primidone (PRM).[11] The syndrome can also be caused by a variety of other drugs such as sulphonamides,[12] dapsone,[13] minocycline,[14] terbinafine,[15] azathioprine,[16] allopurinol,[17] gold derivatives, cyclosporine, captopril, diltiazem, felbamate,[18] metronidazole, nonsteroidal anti-inflammatory drugs-like ibuprofen and the antiretrovirals-like nevirapine and abacavir,[19] etc. It is usually defined by the triad of fever, skin rash and symptomatic or asymptomatic internal organ involvement.[18]

Carbamazepine hypersensitivity syndrome in a child with mucopolysaccharidosis with no sequelae.

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