Case Report

Unusual case of DRESS syndrome with drug induced liver injury: A challenging overlap of immunology and hepatotoxicity in critical care practice

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Abstract

Background: A 33-year-old male developed severe Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome. The case highlights the critical care challenges of managing the overlap between immunological hypersensitivity and acute metabolic hepatotoxicity, requiring rapid recognition to prevent organ failure.

Key words: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome; Umbilical hernia repair

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Case Presentation

A 33 year's male with history of umbilical hernia repair in May 2025 12/05/2025- 14/05/2025- 3 days Piperacillin+ Tazobactam.

- November 28/2025- 09/12/2025- Surgical site infection.
- 29/11/2025- Laparoscopic adhesiolysis and mesh removal.
- POD2- Pseudo obstruction conservatively treated.
- Antibiotics- Piptaz from 28/11/2025- 05/12/2025.
- 06/12/2025- CAP- Antibiotics escalated to Meropenem.
- Discharged on 09/12/2025 with advice for 5 more days of Meropenem.

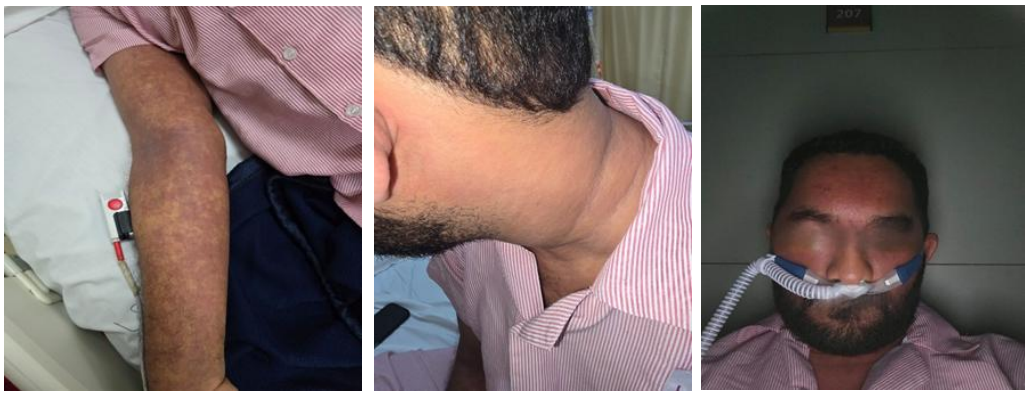
Post discharge patients had on and off fever and itching which was managed conservatively. Readmitted on 04/01/2026- with high grade fever and tiredness, breathing difficulty- Azithromycin 500mg started- past h/o salmonella titre positive. Iinitially started on Piptaz. Imaging showed: Normal CT chest and CT abdomen showed post-operative changes with fluid and air pockets and multiple enhancing mesenteric lymph nodes.

Antibiotics escalated to Meropenem and started on oral Vancomycin (C,Diff came negative).

- 07/01- Rash with itching – Azithromycin stopped.
- 08/01- Peripheral smear normal.
- 09/01/2026- Meropenem stopped as rash persisted.
- Antifungal added suspecting systemic fungal infection.
- On 12/01/2026- TC- 23000: Bilirubin- 6.5, Procalcitonin – 1.02.
- Peripheral smear- Normocytic normochromic anemia with Target cells, Leucocytosis.
- Tropical fever screening- Leptospira and Scrub typhus IgM negative.
- CMV, EBV, Measles screening- negative.
- ANA profile negative.
- General appearance- Rashes predominantly in extremities, eyelid, face and limb swelling.

2. Vital signs

Heart rate	94/min
BP	140/70 mm hg
Respiratory rate	18/min
SpO2	96% on room air
Temp	98.6F
Weight	89 kg
Respiratory system	Bilateral normal Vesicular breath sounds
Cardiovascular system	S1S2+, No murmurs
Abdomen	Soft, non-tender, Bowe sounds +
Central Nervous System	Conscious, oriented, No focal deficit
Skin	Erythema- blanchable on both hands and legs with interspersed purpuric lesions in both legs
Face	Erythema, ede



3. Differential diagnosis

1. DRESS/Drug induced liver injury
2. Sarcoidosis
3. Hemophagocytic lymphohistiocytosis
4. Autoimmune hepatitis
5. Tropical fever
6. Acute cutaneous LUPUS
7. Hyper eosinophilic syndrome
8. Viral infections

	13/01	**14/01**	**15/01**	**16/01**	**21/01**	**28/01**	**29/01**	**30/01**	**31/01**
Hb	11,2	11.2	10.4	9.0	10.6	11.2	10.60	9.1	10.00
Platelet	1.48L	1.48L	1.64L	1.55L	3.06L	2.02L	1.32L	1.92L	1.97L
WBC	17130	19480	19650	15470	10105	9230	7750	9900	6400
N %	37.5	77.6	53.3	43.2	49.5	45.6	76.1	71.6	78.5
L %	30.04	19.2	26.1	32.1	36.2	17.7	8.0	12.7	16.4
M %	**31.7**	2.6	**19.2**	**23.6**	8.7	0.65	1.9	5.2	4.1
E %	0.2	0.5	1.2	0.9	4.9	**28.5**	**13.7**	**10.3**	0.8
AEC	30	90	240	140	490	**2630**	**1060**	**1020**	50

	13/01	**14/01**	**15/01**	**16/01**	**21/01**	**28/01**	**29/01**	**30/01**	**31/01**
Creatinine	0.73		0.9		0.74	1.5	**2.11**		**1.43**
Sodium	128		136		135		134		
Potassium	4.4		4.4		4.8		3.6		
Bilirubin t/d	**9.2/8.1**	**9.7/8.3**	**12/10**	**9.7/8.4**	**2.9/2.3**	**2.9/2.0**	**2.1/1.5**	**1.3/1.1**	
ALT/SGOT	**351**	**125**	**130**	**110**	39	30	31	14	

AST/SGPT	**310**	**215**	**193**	**165**	**136**	**72**	**66**	**62**	
ALP	**865**	**855**	**749**	**595**	**368**	223	174	153	
GGT	**196**	**201**	**245**	**251**	**215**	**161**	**117**	**96**	
INR	3.21	1.39	1.09	1.17					
Albumin	**1.8**	**1.8**	**2.2**	**2.10**	**2.9**	**3.2**	**2.5**	**2.9**	

4. CT abdomen

- Moderate Hepatomegaly: GB wall edema.
- Enlarged portocaval, periportal, celiac and hepatic group of lymph nodes.
- Paraaortic, aortocaval, pelvic group of lymph nodes.
- Post operative changes.

Autoimmune work up	**Granulomatous disease**
ANA profile negative	Serum ACE level- 86.2 U/L
Anti-mitochondrial antibody- negative	24-hour urine calcium- 461 mg/day
Anti-smooth muscle antibody- Negative	Rule out rhabdomyolysis- CPK- 30
Autoimmune hepatitis panel negative	HLH work up-
Autoimmune encephalitis panel negative	LDH- 378
IgG- 2000 mg/dl	Triglycerides- 265
	Ferritin- 474

5. Histopathology

5.1. Skin biopsy

Epidermis showed stratified squamous epithelium with spongiosis and increased melanin pigment. Dermis shows perivascular lymphocytic infiltrate with neutrophils. No evidence of vasculitis/malignancy.

5.2. Liver biopsy

Architecture maintained. Hepatocytes show feathery degeneration, interface hepatitis, Cytoplasmic Cholestasis, apoptotic hepatocytes seen. Sinusoidal spaces show lymphoplasmacytic infiltration and hemorrhage; Periportal inflammation predominantly with lymphocytes followed by neutrophils and plasma cells. No granuloma or malignancy notes. RegiSCAR score 6.

6. Treatment given and course in the hospital

Broad spectrum antibiotics- Ceftazidime+ Avibactam 9 days, Anidulafungin for 7 days.

Steroids- Inj. Methyl pred- 125 mg once daily (13/01/2026- 17/01/2026) followed by 60 mg OD – 18 th. Tab. Wysolone 40 mg once daily (19/01/2026 to 21/1/2026) then 20 mg once daily till 26/01/2026 followed by 10 mg once daily. Topical steroid and antihistamines are given.

Got readmitted with high grade fever after reducing the dose of steroid. Steroid dose modified and gradually fever subsided.

Discharged on 31/01/2026 with steroid tapering dose of 80 mg for 5 days than 60 mg for 10 days followed by 40 mg for 10 days than 20 mg once daily to continue. Planned to taper steroids over 12 weeks.

During course of stay had intense itching treated with antihistamines and topical steroids. Suggested patch test at a later date.

7. Drug reaction with eosinophilia and systemic symptoms (DRESS)/ Drug-induced hypersensitivity syndrome (DIHS)

Severe adverse drug reaction characterized by an extensive skin rash in association with visceral organ involvement, lymphadenopathy, eosinophilia, and atypical lymphocytosis.

Prolonged course flare ups even after cessation of offending drug. 2 to 8 weeks latency.

0.9-2/1,00,000 and 10-20 % hospitalized patients with adverse drug reactions.

8. Etiology and risk factors

- Drug exposure.
- Pharmacogenetic susceptibility - HLA polymorphism- high negative predictive value.
- CYP 450 and N Acetyl transferase polymorphism.

HLA alleles associated with susceptibility to DRESS[1-7]

Drug	HLA/genetic variant	Population
Allopurinol	B*5801	Han Chinese, European, Thai, Korean
Carbamazepine	A*3101	European, Japanese, Han Chinese
Dapsone	B*1301	Chinese
Nevirapine	DRB1*01:01	African, Asian, European
	CW*8, B14	European
	B*35	Asian
Phenytoin	B*13:01, B*51:01	Han Chinese, Thai
	HLA-A*24:02	European
Vancomycin	A*32:01	European
Raltegravir	HLA-B*53:01	African, Hispanic

DRESS: drug reaction with eosinophilia and systemic symptoms; HLA: human leukocyte antigen.

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Drugs implicated in DRESS[1-10]

High-risk drugs

- Allopurinol
- Aromatic antiepileptic agents:
  - Carbamazepine
  - Phenytoin
  - Lamotrigine
  - Oxcarbazepine
  - Phenobarbital
- Sulfonamides:
  - Sulfasalazine
  - Dapsone
  - Trimethoprim-sulfamethoxazole
  - Sulfadiazine
- Vancomycin
- Minocycline
- Nevirapine
- Antituberculosis agents:
  - Rifampicin
  - Ethambutol
  - Isoniazid
  - Pyrazinamide
- Mexiletine

Lower-risk drugs

- Beta-lactams:
  - Amoxicillin
  - Ampicillin
  - Piperacillin
- Others:
  - NSAIDs (celecoxib, ibuprofen, diclofenac)
  - Olanzapine
  - Fluoxetine
  - Imatinib
  - Sorafenib
  - Vemurafenib
  - Omeprazole
  - Raltegravir

DRESS: drug reaction with eosinophilia and systemic symptoms; NSAID: nonsteroidal anti-inflammatory drug.

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Image Source: *Haur Yueh Lee et al.*

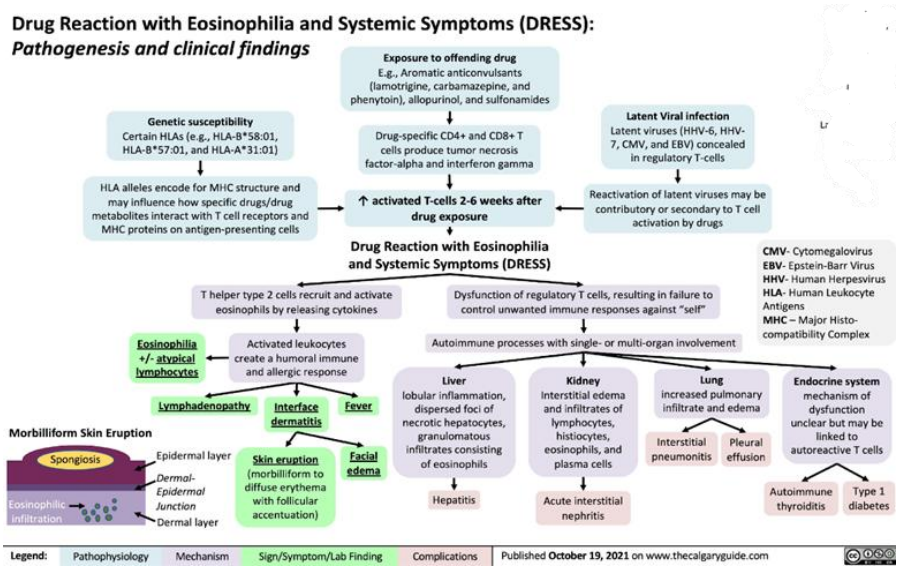
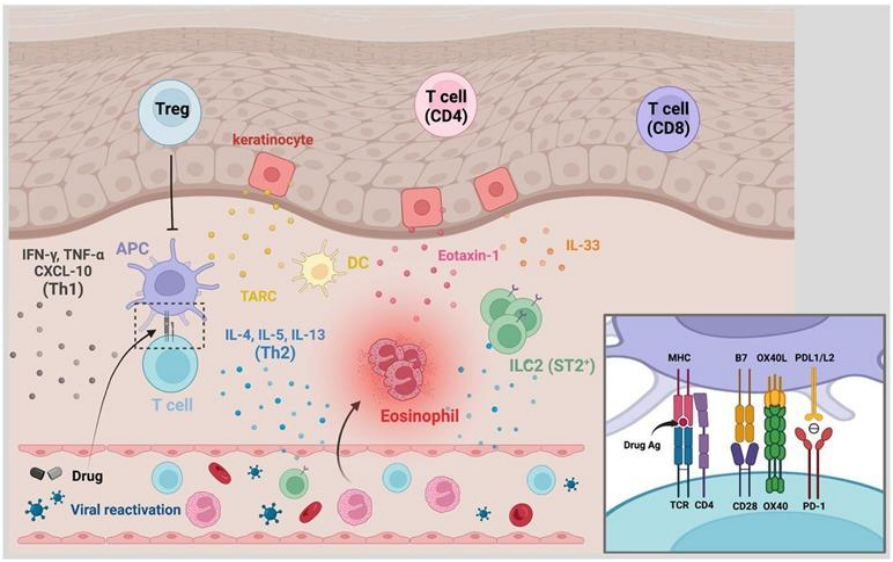


Image Source: *Lauren D. Lee et al*



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Discussion

The prodromal phase- fever, malaise, and lymphadenopathy. Cutaneous manifestations — most obvious and are often the first clue to the diagnosis. 3 percent of patients, the rash may be mild or absent.

- Morphology- polymorphic and evolving.
- Intensely erythematous maculopapular eruption that may progress to a coalescing erythema distributed on trunk and extremities.
- Additional findings may include purpura, infiltrated plaques, pustules, exfoliative dermatitis, and target-like lesions.
- Facial edema in 70% cases.

- Pruritis.
- Mild Mucosal involvement -50% cases.
- Fever ≥101.3°F or ≥38.5°C (75 to 90 percent).
- Lymphadenopathy (54 to 65 percent).
- Hematologic abnormalities.
- Eosinophilia >700/microL (82 to 95 percent, which may be absent in a subset of patients).
- Leukocytosis (95 percent).
- Neutrophilia (78 percent).
- Lymphocytosis (25 to 52 percent).
- Monocytosis (69 percent).
- Atypical lymphocytes (35 to 67 percent).
- Lymphocytopenia (45 percent), thrombocytopenia (25 percent), hemophagocytosis (5 to 24 percent).

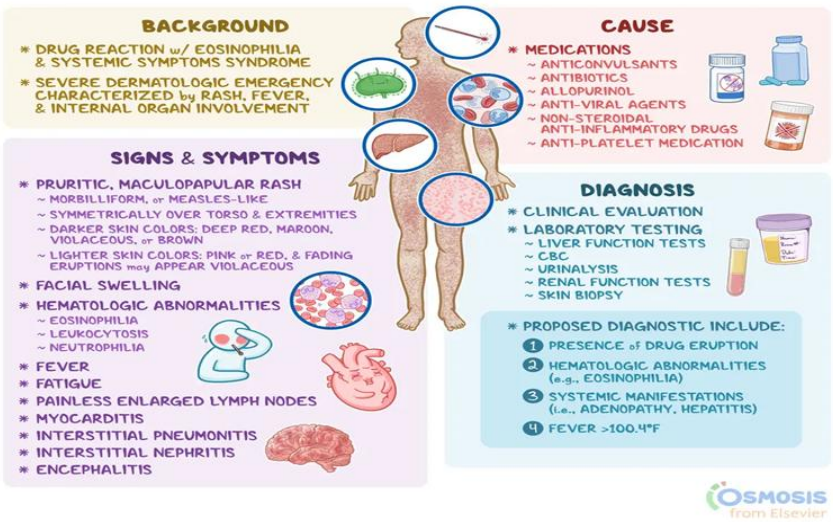

Image Source: *Lily Guo et al.*

Recommended laboratory and imaging investigations in patients with suspected DRESS

Confirmation of diagnosis	Exclusion of alternative diagnosis	Assessment of organ involvement
▪ CBC with differential including search for atypical lymphocytes ▪ Inflammation markers ▪ PCR for HHV-6, HHV-7, CMV, EBV	▪ Blood cultures ▪ Antinuclear antibodies ▪ Serology for viral hepatitis* ▪ Lymph node biopsy*	**Minimal screening**: ▪ Liver function tests ▪ Serum creatinine, urinary protein and cells ▪ Creatine kinase, troponin ▪ ECG **Additional investigations**: ▪ Prothrombin time/INR ▪ CT scan* ▪ Sonography* ▪ Endoscopy* ▪ Biopsy*

DRESS: drug reaction with eosinophilia and systemic symptoms; CBC: complete blood count; PCR: polymerase chain reaction; HHV: herpesvirus; CMV: cytomegalovirus; EBV: Epstein-Barr virus; ECG: electrocardiogram; INR: international normalized ratio; CT: computed tomography.

* Secondary investigations based upon suspected organ involvement.

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Scoring system for the diagnosis of DRESS

Clinical parameters	Score			Comments
	−1	0	1	
Fever ≥101.3°F (38.5°C)	No/unknown	Yes		
Lymphadenopathy		No/unknown	Yes	>1 cm, at least 2 sites
Eosinophilia ≥0.7 × 10^9 or ≥10% if leukopenia		No/unknown	Yes	Score 2 points if ≥1.5 × 10^9
Atypical lymphocytes		No/unknown	Yes	
Skin rash				
▪ Rash suggestive of DRESS	No	Unknown	Yes	Suggestive features: ≥2 facial edemas, purpura, infiltration, desquamation
▪ Extent ≥50% of BSA		No/unknown	Yes	
Skin biopsy suggestive of DRESS	No	Yes/unknown		
Organ involvement		No	Yes	1 point for each organ involvement, maximum score: 2
Disease duration ≥15 days	No/unknown	Yes		
Exclusion of other causes		No/unknown	Yes	1 point if 3 of the following tests are performed and are negative: HAV, HBV, HCV, mycoplasma, chlamydia, ANA, blood culture

Total score:
- <2: Excluded
- 2 to 3: Possible
- 4 to 5: Probable
- ≥6: Definite

ANA: antinuclear antibody; BSA: body surface area; DRESS: drug reaction with eosinophilia and systemic symptoms; HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus.

Adapted from:
1. Kardaun SH, Sidoroff A, Valeyrie-Allanore L, et al. Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: does a DRESS syndrome really exist? Br J Dermatol 2007; 156:609.
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Image

Source: *Haur Yueh Lee et al.*

9. Biomarkers

- Thymus and activation-regulated chemokine (TARC) levels may be useful as a diagnostic and activity biomarker. Levels are elevated in the acute stage of the disease and correlate with HHV-6 reactivation and eosinophilia.

- Adjunctive tests- Patch test or intradermal testing after 6 weeks to 6 months of resolution/1 month after stopping steroids.

- Drug Challenge is performed very rarely.

- Invitro tests: Lymphocyte transformation test, Drug induced cytokine assay.

Evaluation of generalized skin eruption suspicious for cutaneous drug hypersensitivity reaction

NSAID: nonsteroidal anti-inflammatory drug; SJS: Stevens-Johnson syndrome; TEN: toxic epidermal necrolysis; DRESS: drug reaction with eosinophilia and systemic symptoms; AGEP: acute generalized exanthematous pustulosis; ACE: angiotensin-converting enzyme.

* Symptoms suggesting anaphylaxis include:
- Glossal/pharyngeal edema, hoarseness, stridor, sense of choking
- Dyspnea, tachypnea, wheezing, cyanosis
- Hypotension, tachycardia (or sometimes bradycardia), palpitations
- Nausea, vomiting, diarrhea

¶ ACE inhibitors specifically induce angioedema, not associated with urticaria, that may begin even after months or years of treatment.

Δ Most cases of cutaneous vasculitis are not drug induced.

Adapted from: Brockow K, Ardern-Jones MR, Mockenhaupt M, et al. EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity. Allergy 2019; 74:14.

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Image Source: *Haur Yueh Lee et al.*

10. Mild DRESS

DRESS with or without modest liver involvement, such as elevation of liver transaminases <4 times the upper limit of normal, in the absence of clinical, laboratory, or imaging evidence of renal, pulmonary, or cardiac involvement.

10.1. Moderate DRESS

- DRESS is classified as moderate if any of the following parameters are fulfilled:
- Hemoglobin 7 to 10 g/dL and/or neutrophils 500 to 1500/microL.
- Platelets 50,000 to 100,000/microL.
- Creatinine >2.99 mg/dL (264 micromol/L) or 1.5 times the upper limit of normal.
- Liver enzymes 4 to 15 times the upper limit of normal and/or alkaline phosphate three to five times the upper limit of normal.

10.2. Severe DRESS

- DRESS is classified as severe if any of the following parameters are fulfilled:
- Major isolated cytopenias (hemoglobin <7g/dL, neutrophils <500/microL, or platelets <50,000/microL).
- Pancytopenia.
- Hemophagocytosis.
- Rapidly progressive and/or severe eosinophilia (≥1500/microL).
- Rapidly progressive and/or severe atypical lymphocytosis.
- Acute kidney failure or rapidly progressive oligo/anuria.
- Liver enzymes >15 times upper limit normal and alkaline phosphatase >5 times upper limit normal and/or factor V <50 percent.
- Involvement of any other organ (eg, heart, lungs, nervous system)/multiorgan involvement.

11. Management

- Drug withdrawal, supportive treatment and monitoring.
- Supportive care includes fluid, electrolyte, and nutritional support. Adjunctive measures include gentle skin care with emollients and warm baths/wet dressings.
- Serial clinical, laboratory, and imaging monitoring and timely consultation with specialists.
- Mild DRESS- symptomatic treatment with topical steroids.
- Moderate DRESS- Topical steroids with a course of systemic steroids.

- Severe DRESS- Systemic steroids.
- 1mg/kg of Prednisolone tapered over 8 to 12 weeks with or without pulse dose steroids for 2-4 days.
- Corticosteroid refractory DRESS-Cyclosporine.
- Oral cyclosporine at a dose of 3 to 5 mg/kg divided twice daily for seven days, followed by a taper over the next 7 to 14 days.
- JAK inhibitors like Tofacitinib.
- Anti IL5- Benralizumab, Mepolizumab, Reslizumab.
- IVIG- less evidence.
- Anti-viral- Routinely not recommended due to spontaneous resolution.
- Gancyclovir /Valgancyclovir recommended when- PCR + for CMV, EBV, HHV with high viral load.
- Proven Viral induced organ damage or severe disease.

12. Clinical course

- The clinical course is variable.
- No reliable markers at presentation to predict outcome.
- viral reactivation and, in particular, cytomegalovirus (CMV) reactivation detected during the course of the disease is associated with poorer outcomes.

13. Resolution of the acute phase

- Rash takes at least 15 days; usual time is 7 weeks and up to 90 days in 20 percent cases.
- Flare ups in 25% cases. Median duration is 4.5 months which are cutaneous most of times.
- Common due to rapid steroid tapering.

14. Prognosis and follow up

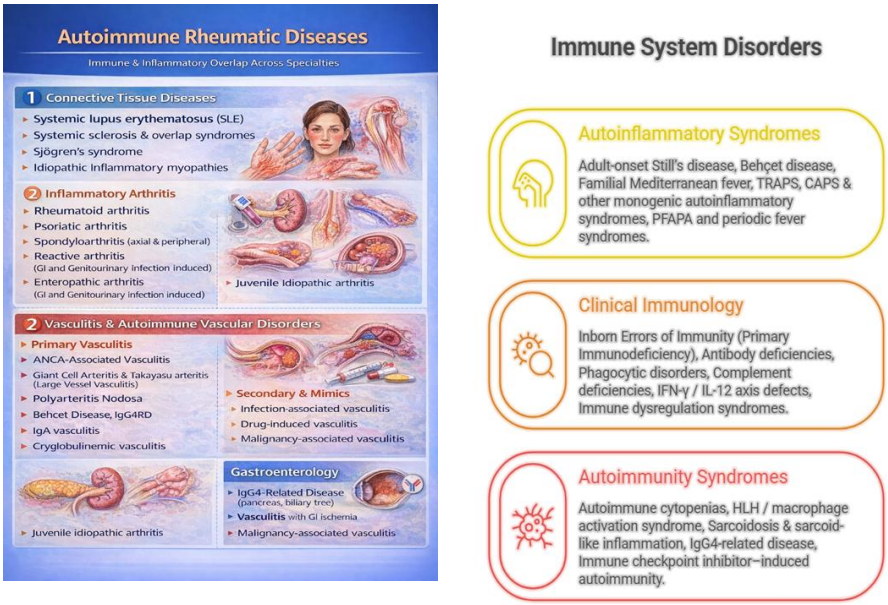
- Most patients recover completely from weeks to months after drug withdrawal.
- should undergo long-term monitoring for the development of autoimmune sequelae.
- Relapses can happen due to structurally different drugs also. Reason for cross reactivity is unknown.
- Immune hyperactivation triggered by the initial episode of DRESS that leads to polysensitization to multiple drugs.

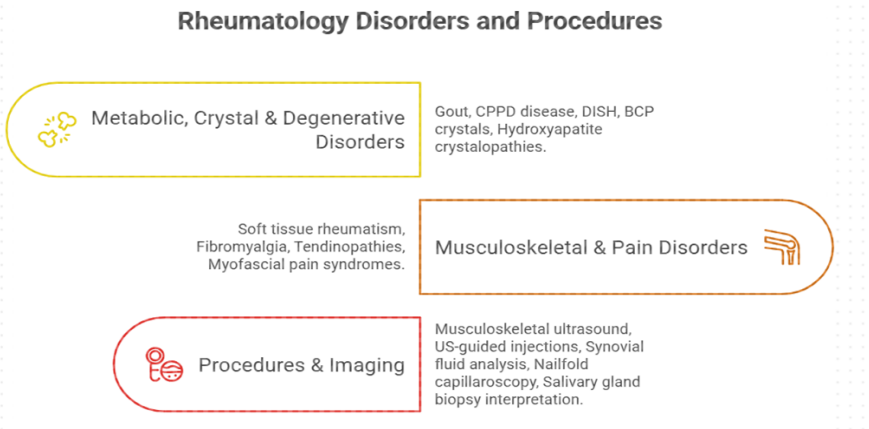
Long term sequelae

- Autoimmune thyroiditis, vitiligo, alopecia areata/universalis, autoimmune hemolytic anemia, lupus erythematosus, and type 1 diabetes.
- Mortality- 2-10%.
- Older age, severe organ involvement, and multiorgan failure are the main predictors of mortality.
- Primary and secondary prevention:
    - Avoid exposure to unnecessary drugs
    - Genetic screening
    - Avoid reexposure to causal agent

15. Acknowledgement

Dr Abhishek, Consultant Rheumatologist, Kauvery Hospitals





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