#### Clinical meet- Department of Dermatology

- 1) Dr. Mohak Agarwal Intralesional 5-FU in the treatment of Basal cell carcinoma
- 2) Dr. Jayshree Ahuja Toxic epidermal necrolysis: Report of two cases
- 3) Dr. Anushka Rakesh A case series of three cases of pyoderma gangrenosum of the breast in the background of covid
- 4) Dr. Sriveni Bolisetti Comparative study of microneedling v/s microdermabrasion in females with periorbital melanosis

# Intralesional 5-fluorouracil in the treatment of basal cell carcinoma

## 56 Y/F, Shilpa Mohite, Farmer

Presenting complaints:

• Dark colored lesion - left side of face - 5 years

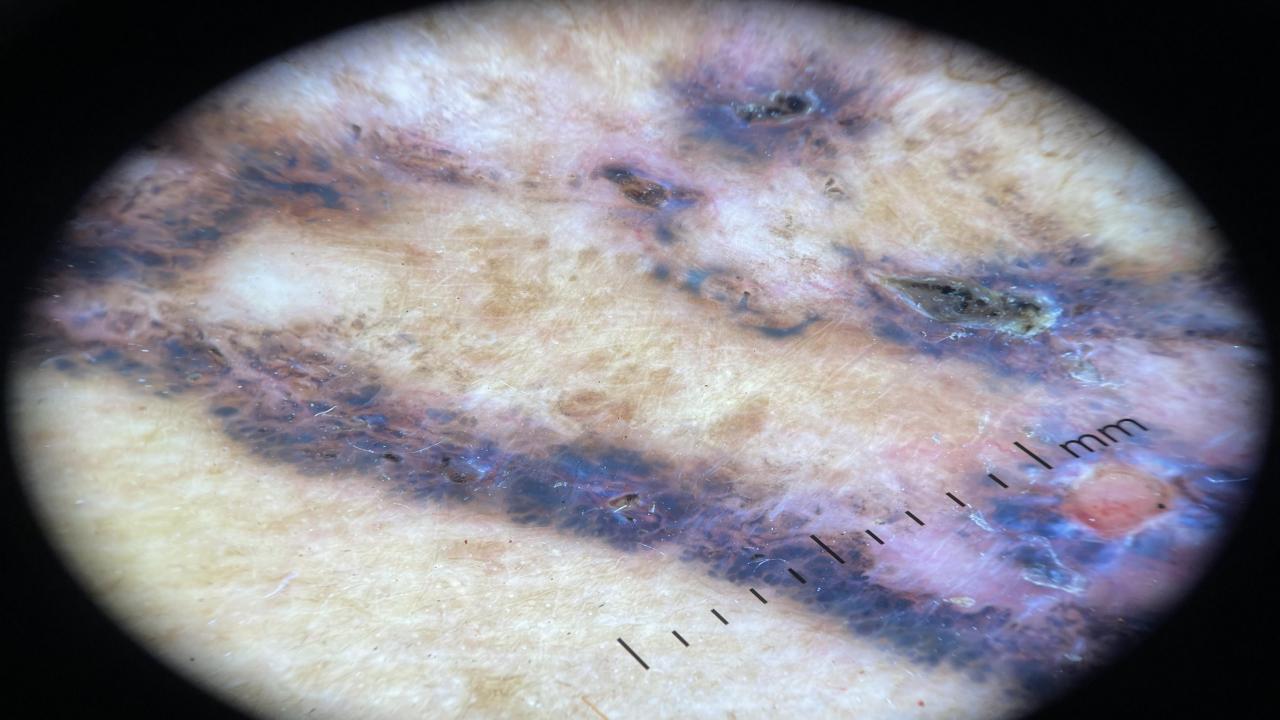
# History

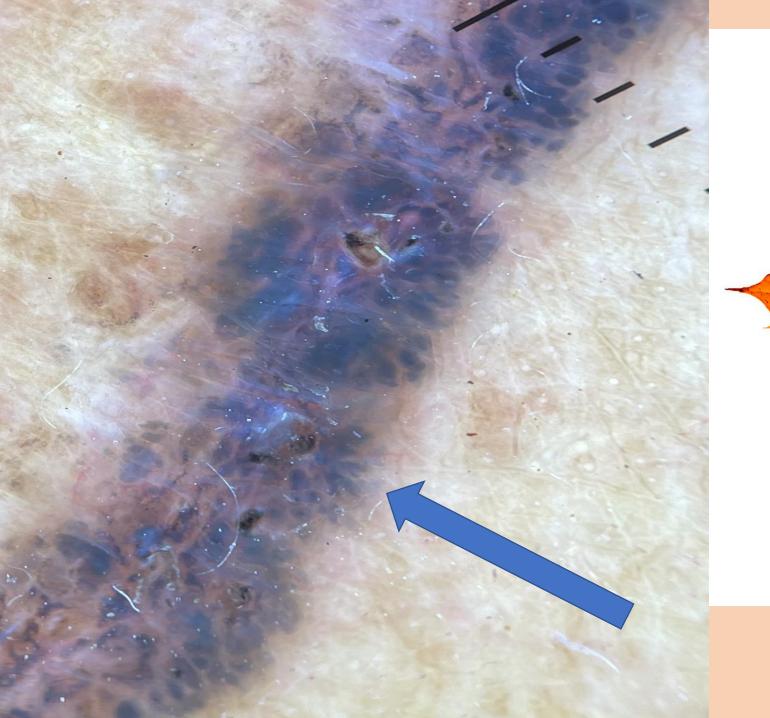
- Accidental acid burn left side face -10 years
  - raw areas topical t/t healed

• Increase burning on sun exposure over left side of face - 5 years











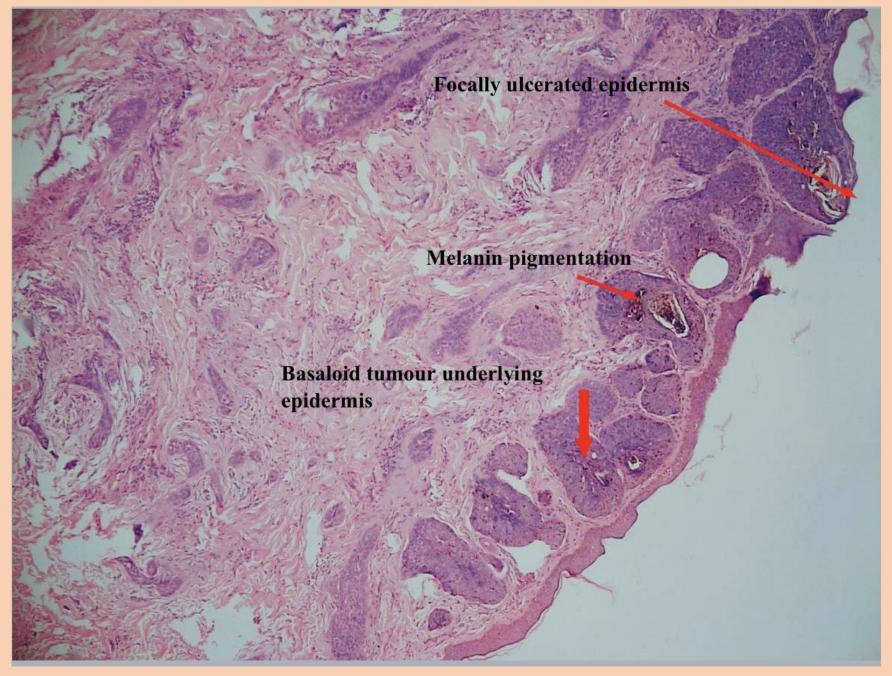
## Clinical diagnosis:

• Basal cell carcinoma

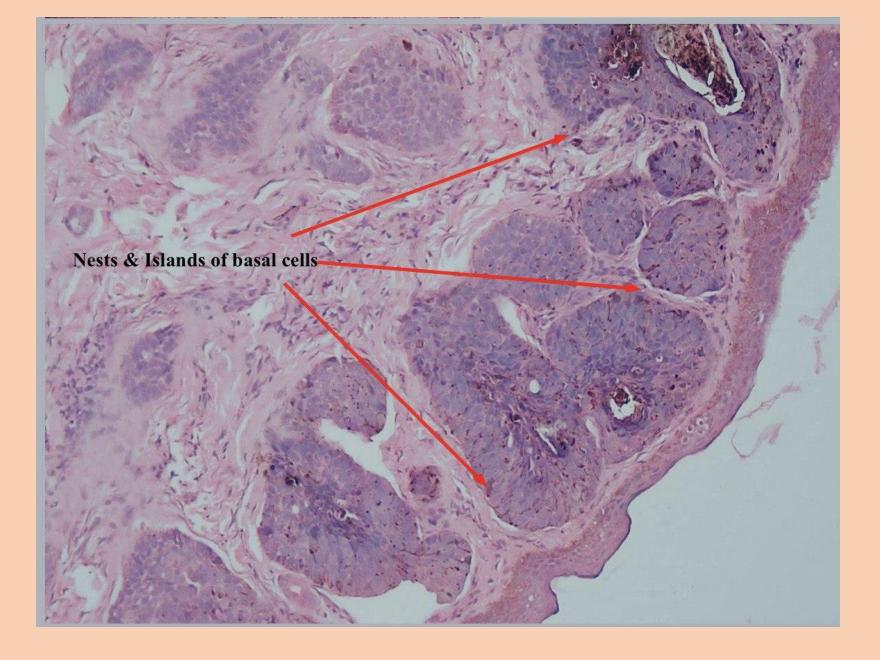
#### Differential:

Malignant melanoma

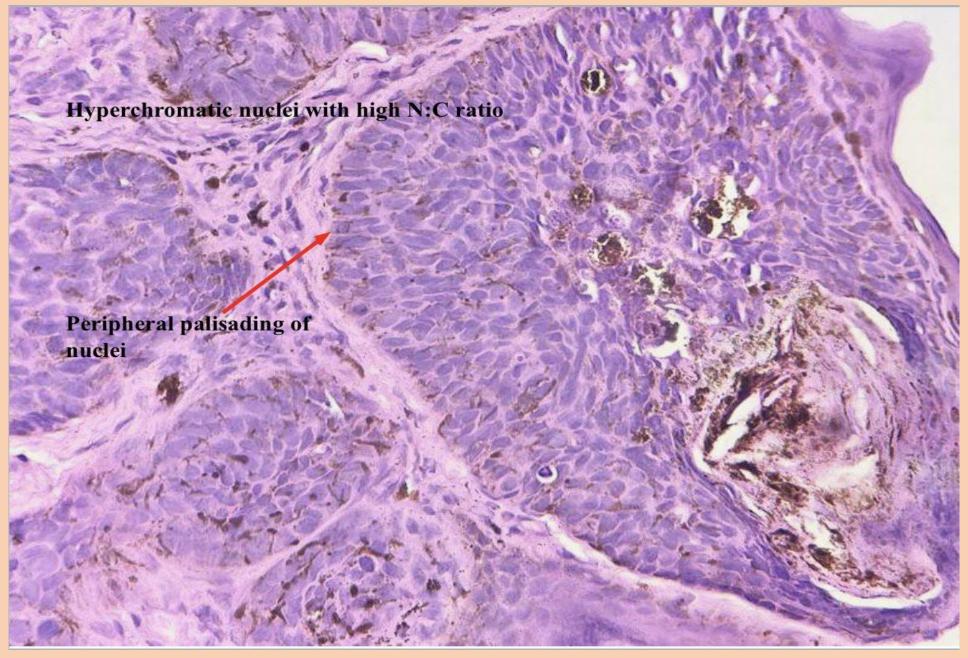
# Histopathology



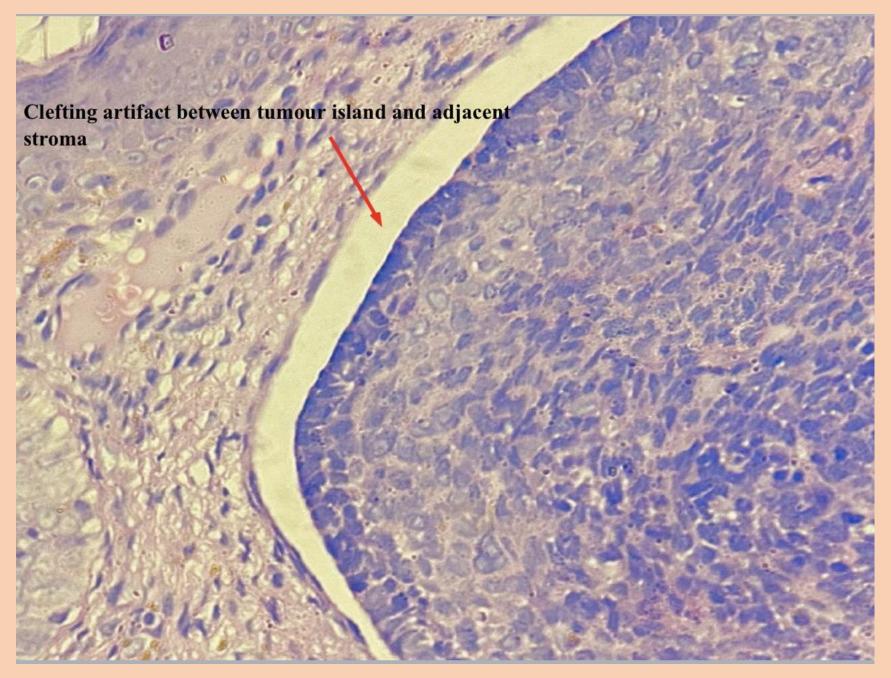
Photomicrograph of skin biopsy (H&E STAIN, 10X)



Photomicrograph of skin biopsy (H&E STAIN, 10X)



Photomicrograph of skin biopsy.(H&E STAIN, 40X)



Photomicrograph of skin biopsy (H&E STAIN, 40X)

## **MRI**

Showed no evidence of metastasis

# Diagnosis

## **Basal Cell Carcinoma**

(Type: pigmented)

# Treatment

• Intralesional 5 Fluorouracil (5-FU) 50mg/ml weekly

• Topical 5% 5-FU cream (daily twice application)



# Intradermal injection

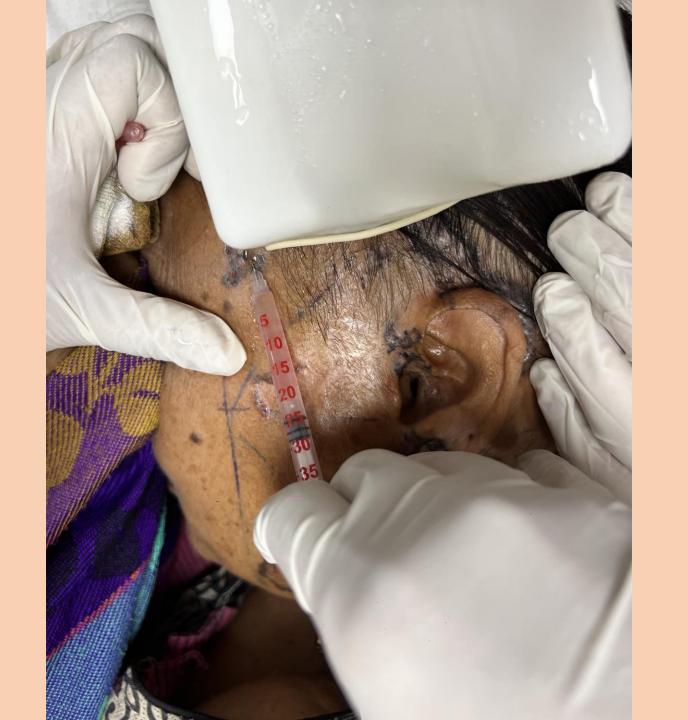
lesion divided into 4 quadrants



Injected @ 0.1ml/cm sq.

Plan: 8 weekly sittings

Till date: 7 given



# Adverse effects seen in the patient

#### During procedure:

- Burning sensation and pain
- Watering of eyes

#### Post procedure:

• Erythema over injection site.

(Pt. was kept under observation & monitoring overnight post injection)

O/E

• Erythema

Swelling

C/O

burning sensation

Post procedural photo @ 7th visit

# Discussion

• BCC → 74%

• SCC  $\rightarrow$  23%

Localized neoplasm

• Identified & treated before substantial morbidity is incurred

• Metastatic rates : < 1%

## Histopathological patterns of BCC include

- Superficial
- Nodular
- Infiltrative
- Micronodular
- Pigmented
- Morpheaform
- Basosquamous / metatypical

## Gold standard for t/t : Surgery

• Excision with flap reconstruction

Moh's micrographic surgery

# Intralesional or topical medications is an option:

• Palliative treatment

- Patients refuses surgery
- Unfit for surgery

Long-term follow-up is essential to monitor for recurrent lesions.

#### Efficacy of topical 5-fluorouracil in the treatment of BCC

S.NO.	Study	Regimen	Duration	Clearance rate %
1	5-FU 5% cream	BID	UA	<b>93</b> ( 105/113)
2	Gross	BID	11	90 ( 28/31)
3	Aggregate	n/a	n/a	<b>92</b> ( 133/144)

Chitwood K, Etzkorn J, Cohen G. Topical and intralesional treatment of nonmelanoma skin cancer: efficacy and cost comparisons. Dermatol Surg. 2013 Sep;39(9):1306-16. doi: 10.1111/dsu.12300. Epub 2013 Aug 5. PMID: 23915332.

#### Efficacy of intralesional 5-FU in the treatment of BCC

S. NO.	Study	Dose (mg)	Mean no. of t/t per tumor	Clearance Rate %
1	Avant	NR	4-14	<b>95</b> (20/21)
2	Kurtis	612.5	5.5	100 (2/2)
3	Aggregate	612.5	5.5	96 (22/23)

Chitwood K, Etzkorn J, Cohen G. Topical and intralesional treatment of nonmelanoma skin cancer: efficacy and cost comparisons. Dermatol Surg. 2013 Sep;39(9):1306-16. doi: 10.1111/dsu.12300. Epub 2013 Aug 5. PMID: 23915332.

#### Adverse effects of intralesional 5-fluorouracil

- Ulceration
- Crusting
- Scarring
- Stinging & burning during injection
- Erythema
- Swelling
- Desquamation

### Intralesional injections –

- MTX
  @25 mg/mL, 12.5 mg/mL or 25 mg/mL
- Bleomycin
  @0.2 to 1.5 mg/mL
- IFNs (IFN $\alpha$ -2, IFN $\alpha$ -2a)
- IFN $\alpha$ -2b, IFN- $\beta$ , and IFN- $\gamma$

#### 5-fluorouracil

- Fluorinated pyrimidine analog with cytotoxic effect.
- Irreversible inhibitor of thymidine synthetase

#### FDA approved -

- Topical 5% cream is approved for -
- > Keratoacanthoma
- > BCC
- > SCC

Kathak

# Toxic epidermal necrolysis: Report of two cases

Dr. Jayshree Ahuja

#### Case 1- 37 Y/F, Mukta Gore, Homemaker

• Recently diagnosed with Rheumatoid arthritis - Sulphasalazine -15 days prior to presentation

#### Presenting complaints:

- Fever- 8 days
- Redness, peeling and blisters- 6 days

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#### Case 2- 27 Y/F, Poonam Ingavale, Homemaker

Recently diagnosed with Tinea cruris
 Griseofulvin -7 days prior to presentation

#### Presenting complaints:

- Raw areas in oral cavity- 10 days
- Blisters & redness 7 days
- Peeling 2 days

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## Case 1 - on admission



- Erythema
- Blisters
- Erosions
- Peeling
- Crusting

















## Case 2 - on admission



- Erythema
- Blisters
- Erosions
- Peeling
- Haemorrhagic crust







## **SCORTEN**

Prognostic factors		Points
Age (years)	> 40 years	1
Presence of malignancy	Evolving cancers or hematologic malignancy	1
Epidermal detachment	> 10% of BSA at admission	1
Heart rate (HR)	> 120 beats/min	1
Serum urea	> 10 mmol/L (27 mg/dL)	1
Serum glucose	> 14 mmol/L (252 mg/dL)	1
Serum bicarbonate	< 20 mmol/L (20 mEq/L)	1

## Predicted mortality rate of scorten

Score	Mortality (%)
0	1.2
1	3.9
2	12.2
3	32.4
4	62.2
5	85.0
6	95.1
7	98.5

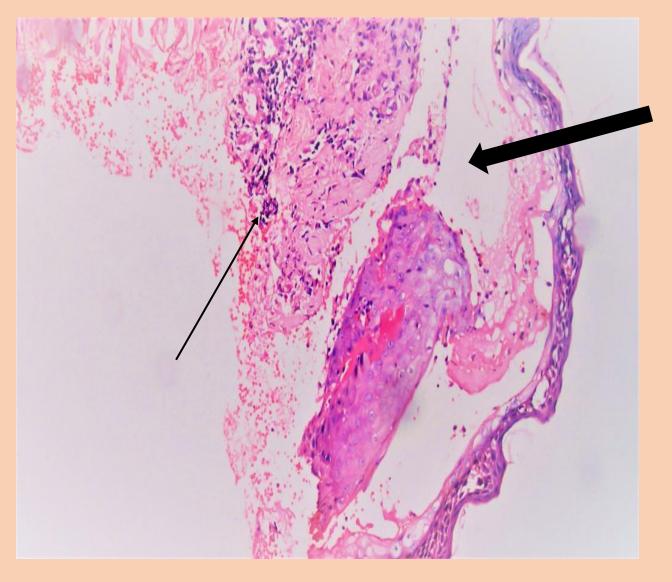
### Scorten in our cases

Prognostic factors	Case 1	Case 2
Age	37 yrs	27 yrs
Malignancy	none	none
Epidermal detachment	> 60% BSA	> 80 % BSA
Bicarbonate	31.2	14.9
Urea	25	63
Glucose	108	152
Heart rate	86	112
Total score	1	3
Predicted mortality	3.9 %	35.8 %

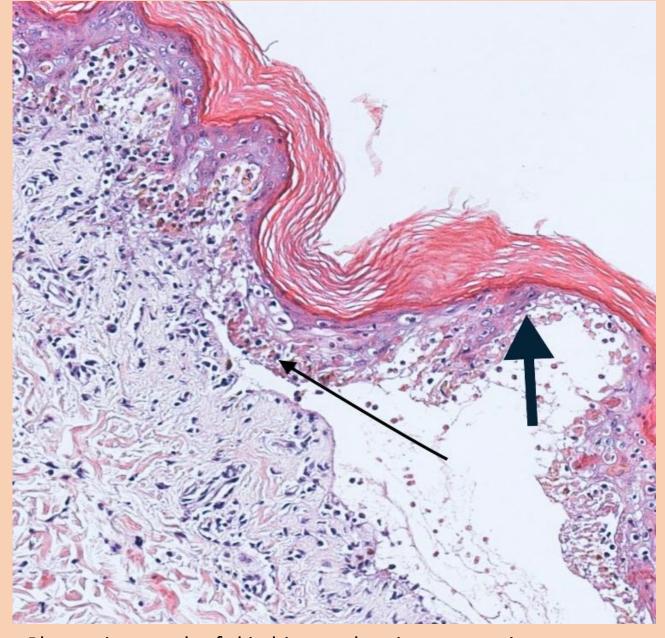
## Laboratory findings in our cases

Investigations	Case 1	Case 2
Hb	11.1	12.10
TLC	4000	4500
ESR/CRP	45/40	30/156
D-dimer	1422	3000
Procalcitonin	0.03	2.23
PT/INR	11/1.01	13.06/1.15
Urea/creatinine	25/0.55	63/1.08
Albumin/Globulin	3.0/3.44	2.86/3.41
Na/K/Cl	134/4.8/104	139/4.4/104

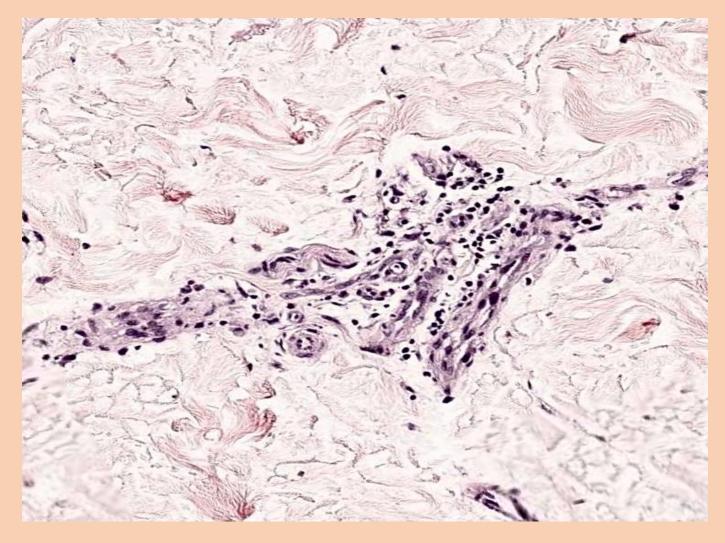
# Histopathology



Photomicrograph of skin biopsy, showing subepidermal bulla and intradermal inflammatory infiltrate (H&E STAIN, 100X)



Photomicrograph of skin biopsy, showing apoptotic keratinocytes and necrosis (H&E STAIN, 100X)



Photomicrograph of skin biopsy, showing perivascular lymphocytic infiltration (H&E STAIN, 400X)

# Diagnosis Toxic epidermal necrolysis

## Approach

Step 1- Withdrawal of the offending drug

Step 2- ICU admission- multidisciplinary approach



Steroids
Cyclosporine
Wet compresses
Paraffin bedding

#### General medicine

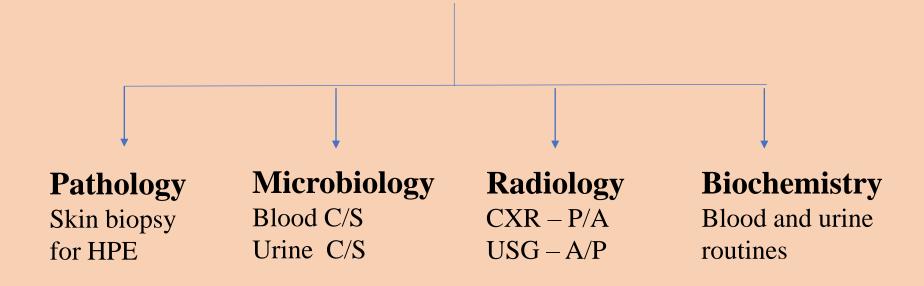
Fluid and electrolytes
Antibiotics
Anticoagulants

#### **Ophthalmology**

Glass rod -prevent synechiae Lubricants Antibiotic e/d

#### **ENT**

Oral & nasal rinse Clotrimazole mouth paint



## Case 1- Systemic medications

#### 1) IV Dexamethasone

```
4 mg-0-2 mg for 4 days
4 mg-0-0 for 10 days
3mg-0-0 for 2 days
Prednisolone 15 mg-0-0 for 2 days →
 10 mg-0-0 for 7 days \rightarrow stopped
```

#### 2) Concomitantly

Cyclosporine
100 mg-0-100 mg for 15 days
100 mg-0-0 for 2 days
Stopped

- 3) Minocycline 100 mg-0-100 mg for 7 days
- 4) Enoxaparin s.c 40 mg/day (0.4 cc) for 5 days

## Case 2- Systemic medications

1) IV Dexamethasone 8 mg stat on the first day

IV Methylprednisolone 1g for 3 days

2) Concomitantly

Cyclosporine

100 mg-100mg-100mg for 12 days

100 mg-0-100 mg for 2 days

0-0-100 mg for 2 days

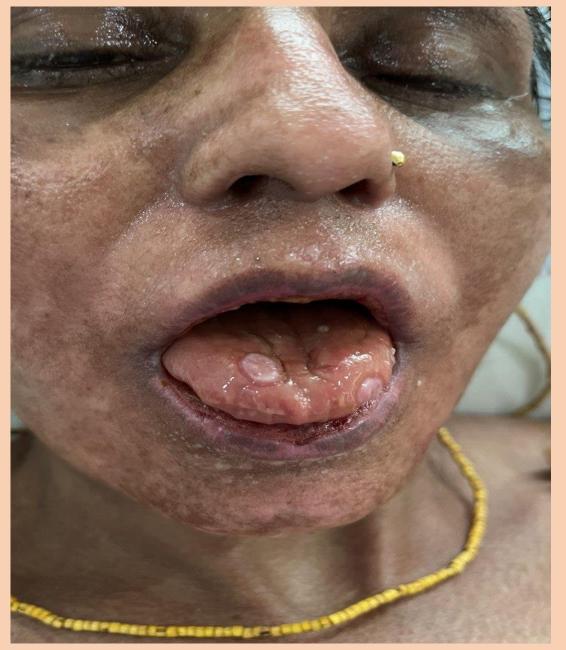
3) IV antibiotics as per C/S report

- Metronidazole 100 ml 8 hourly for 22 days
- Fluconazole 400 mg-0-0 for 14 days

- Meropenem 1 g 8 hourly for 12 days
- Tigecycline 100 mg stat → 50 mg 12 hourly for 13 days

# Case 1 After 17 days of treatment













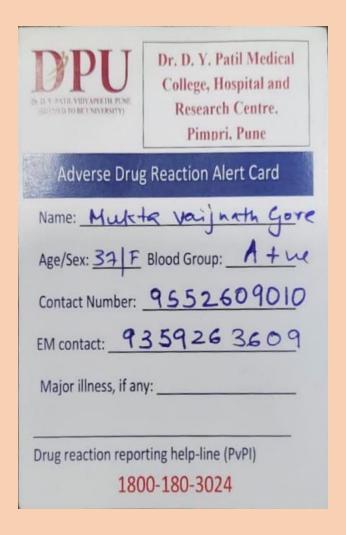




### Case 1

- Alert card was issued –
- Avoid sulfasalazine
  & other sulfa drugs like:

Sulfonamides
Cotrimoxazole
Sulfonylureas
Sulfadiazine
Sulfisoxazole

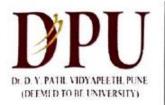


## Case 2 After 1 month of treatment



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Dr. D. Y. Patil Medical College, Hospital and Research Centre. Pimpri, Pune

#### Adverse Drug Reaction Alert Card

Name: Poonam Amar Ingavale

Age/Sex: 27/F Blood Group: B + Ve

Contact Number: 7447493880

EM contact: 9960284019

Major illness, if any: \_\_\_

Drug reaction reporting help-line (PvPI)

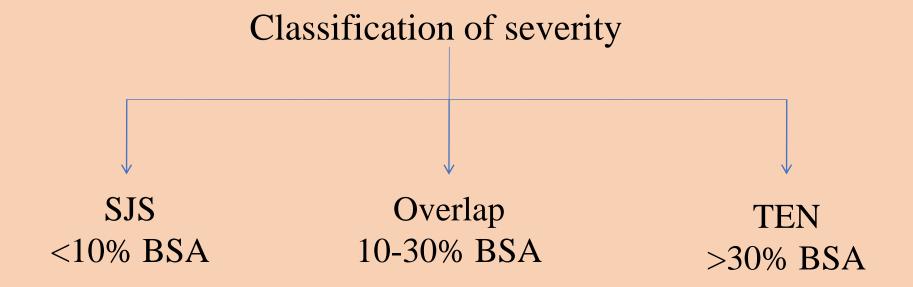
1800-180-3024

DRUG	REACTION	DATE
GRISEOFULVIN	TEN	26 07 2020
•		

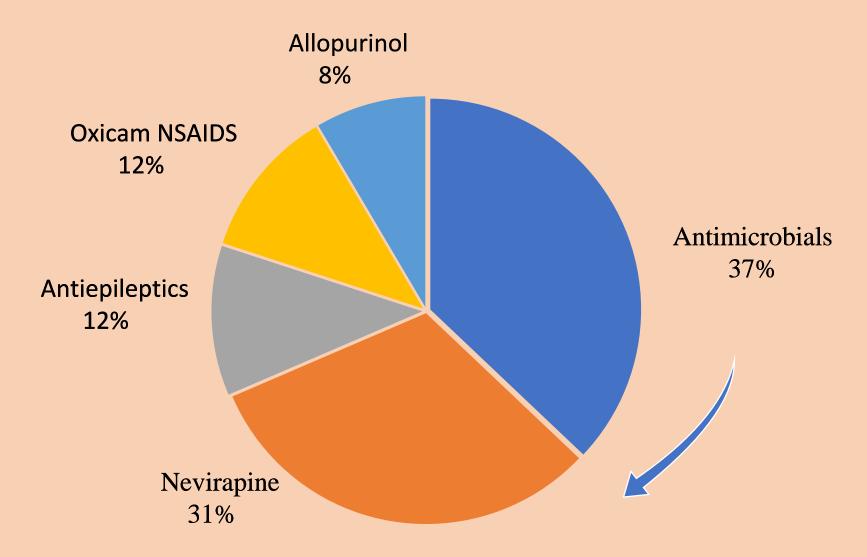
## Discussion

## Toxic Epidermal Necrolysis (TEN) Synonym- Lyell syndrome

• Latent period → 7 to 10 days (range 5-28 days)



#### Drugs implicated in TEN



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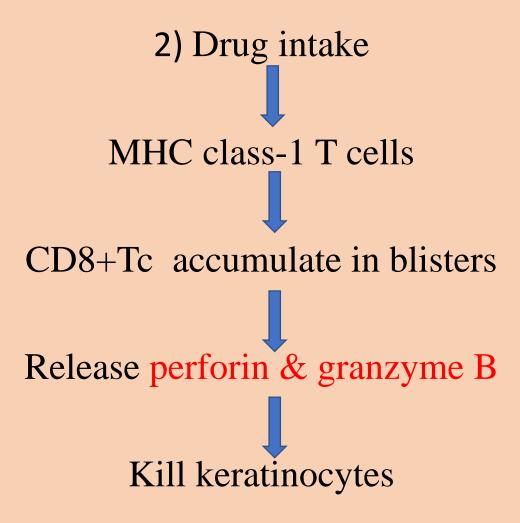
### Pathogenesis

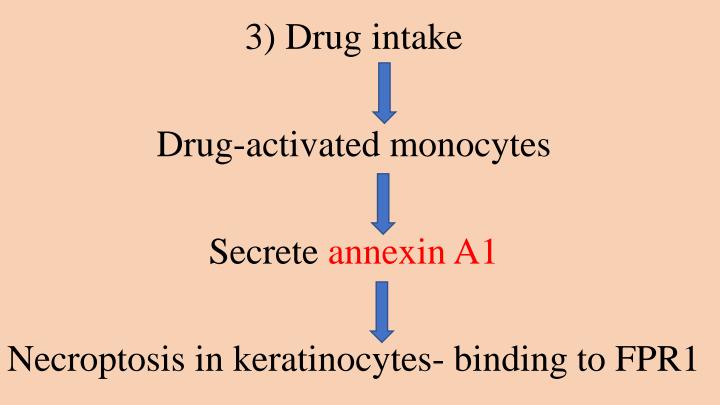
#### Mechanisms-

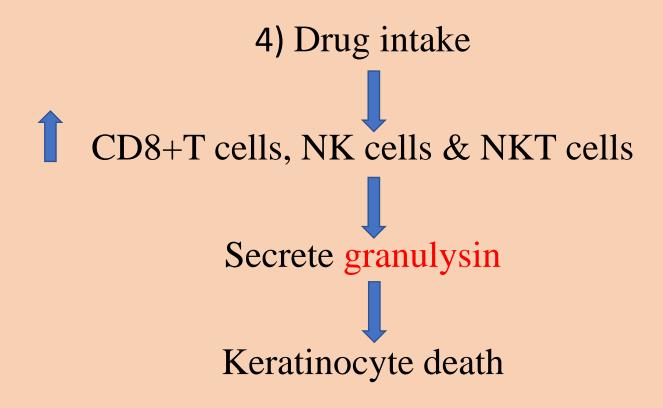
1) Drug intake

FasL - keratinocytes expressing Fas

Death receptor mediated apoptotic pathway







#### Acute complications

- Hypothermia
- Fluid depletion
- AKI
- Septicemia
- Hematological anemia, leucopenia
- Abnormal liver function
- Hypoalbuminemia
- Hyperglycemia
- Increased metabolic demand
- Bronchial erosions & airway obstruction

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#### Long term complications

Skin	Nail	Hair
Dyspigmentation/scars	Onychomadesis	Telogen effluvium
Eruptive melanocytic naevi	Dystrophy	
Abnormal photosensitivity	Permanent anonychia	
Reduced sweating	Ridging	
Pruritus	Nail bed - pigmentation	
Oral – Gingival synechiae Dysgeusia		

Ocular	Vulvovaginal	GIT	Psychological	Pulmonary
Symblepharon	Dyspareunia	Strictures	PTSD	Bronchiolitis obliterans
Entropion/ trichiasis	Genital adhesions	Intestinal ulceration		
Corneal ulceration				

#### Treatment protocol

- Withdraw culprit drug
- Resuscitation- ICU/burns unit
- Multidisciplinary approach

#### Supportive

- Ambient temperature (25-28 °C)
- Air bed
- Topical therapy & dressings
- Fluid replacement & nutrition
- Analgesia
- Preventing/treating infections

#### Definitive treatment

In early stages of acute phase-

1) IVIG (0.5-1 g/kg/day for 3-4 days)

or

- 2) Systemic corticosteroid
- Prednisolone 0.5-1 mg/kg/day

or

- IV methyl prednisolone 500 mg 3 days or
- 3) Cyclosporine 3 or 4 mg/kg/day in divided doses



# A series of three cases of pyoderma gangrenosum of the breast in the background of Covid

#### Introduction

- Cutaneous necrotizing neutrophilic disorder
- Non-infectious

- Rapidly spreading
- Tender ulcer
- Preceded by inflammatory papule / nodule/ pustule
- Most commonly → pretibial areas

#### Case 1: Usha Gore, 37Y/F, Housewife





Two painful raw lesions on left breast since 5 months & 10 days respectively.

#### Case 2: Ruchita Yadav, 40Y/F, Housewife



Ulcer on right breast since 20 days

#### Case 3: Manisha Wadmare, 42Y/F, Saloon employee

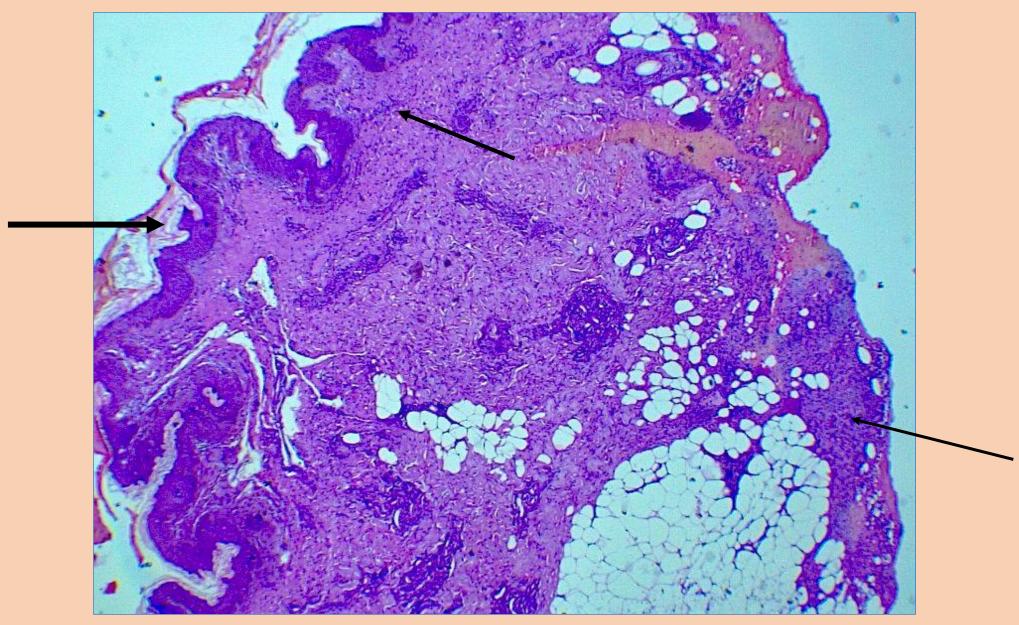




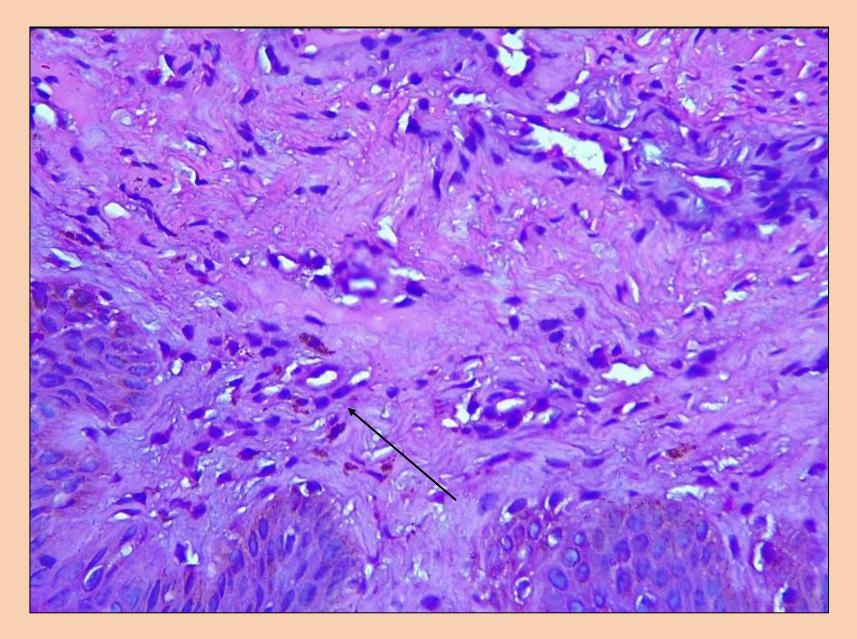
Ulcer on left breast since 2 months

	Case 1	Case 2	Case 3
	Obesity	Ι	-H/o I & D
Risk factors	Covid-19 vaccination		Covid-19 infection (RT-PCR+)
	10days	15days	Unvaccinated
Comorbidities	Pemphigus vulgaris [Dsg3 108.13 RU/ml]	SLE [ANA (positive) 1: 100 dsDNA ,U1-SnRNP, Ro 52/60]	Hypertension
Lab investigations	Hb 10 TLC 13200 DLC N74 E1 B0 L20 M5 ESR 53 CRP 15.5	Hb 10.3 TLC 11900 DLC N91 E0 B0 L7 M2  ESR 87 CRP 86  Urine R/M trace protein	Hb 11.1 TLC 3900 DLC N51 E4 B0 L25 M20  ESR 72 CRP 35 D dimer 4800 Urine R/M trace proteins

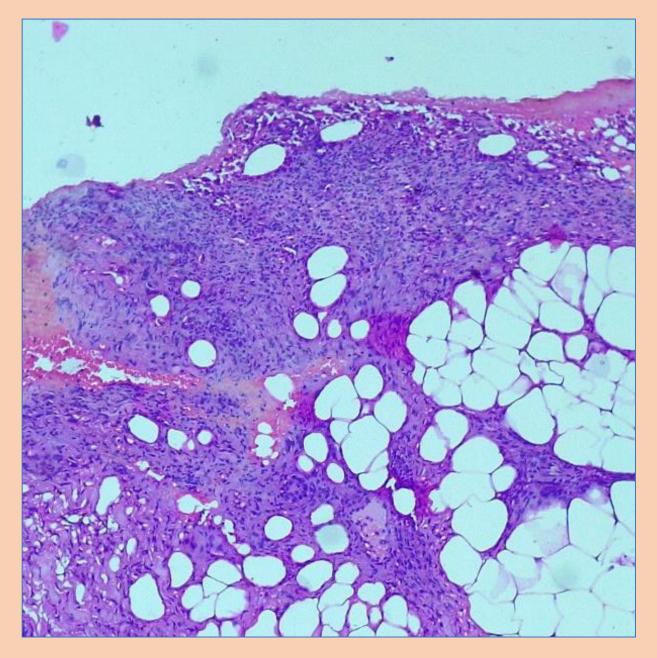
## Histopathology



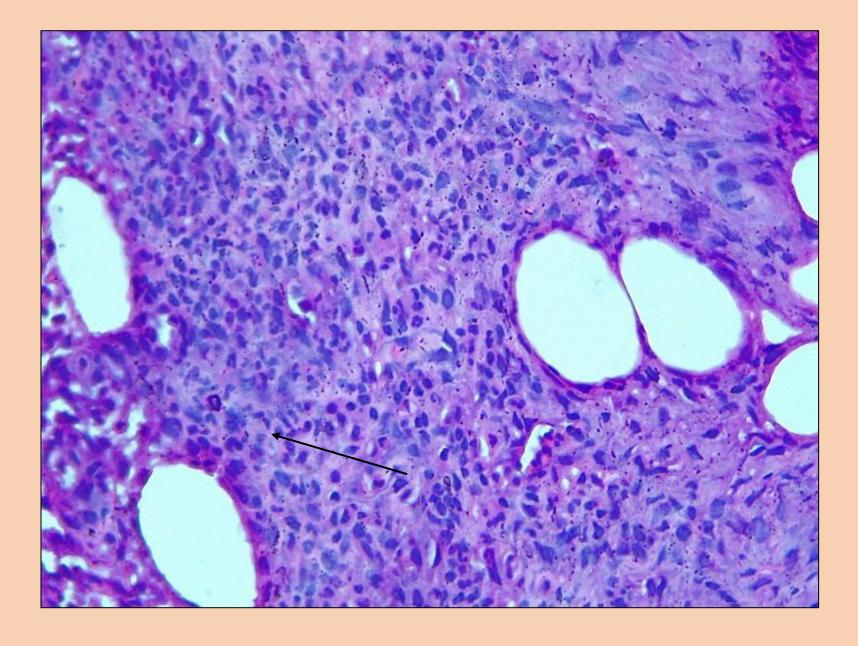
Photomicrograph of skin biopsy, (H&E STAIN, 10X)



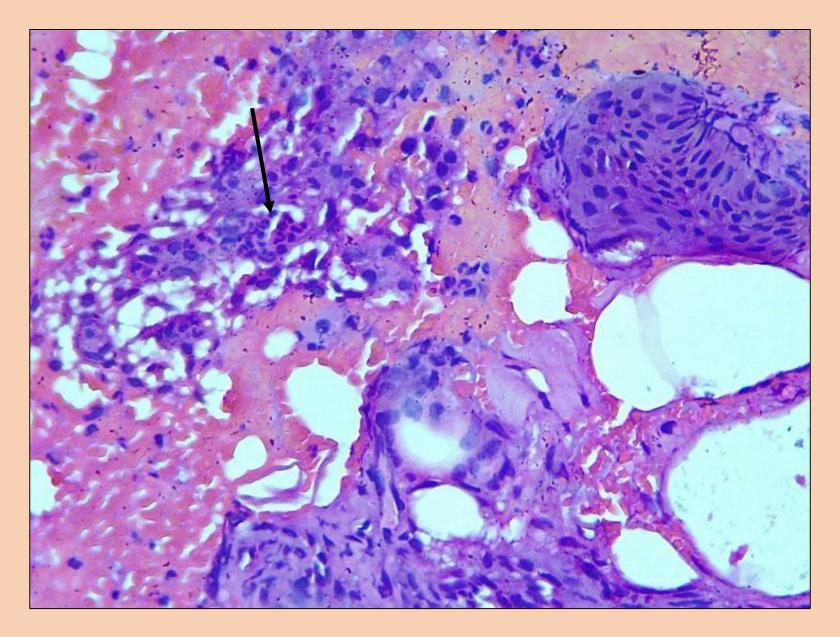
Photomicrograph of skin biopsy, showing perivascular region showing lymhocytic infiltrate. (H&E STAIN, 40X)



Photomicrograph of skin biopsy, showing deeper planes (H&E STAIN, 10X)



Photomicrograph of skin biopsy showing marked inflammatory infiltrate H&E STAIN,( 40X)



Photomicrograph of skin biopsy, showing collection of neutrophils (H&E STAIN, 40X)

	Case 1	Case 2	Case 3
Treatment	Prednisolone 30 mg/day PO (tapered →5 wks)  Dapsone 100mg PO BID for 10days	IV Methylprednisolone 250mg/day for 3days  + IV Cyclophosphamide 500mg 2weekly (6 cycles)  HCQS 200mg/day PO	IV Dexamethasone 6mg/day for 6wks (tapered 4wks)  Prednisolone 30mg/day PO for 4wks  IL TAC 10mg/ml  Cyclosporine 200mg/day PO for 4wks (discontinued)  Lugol's Iodine

## Regression of lesions

#### Case 1





Day 7





Day 14 Day 21





Day 28 Day 35

#### Case 2





Day 30



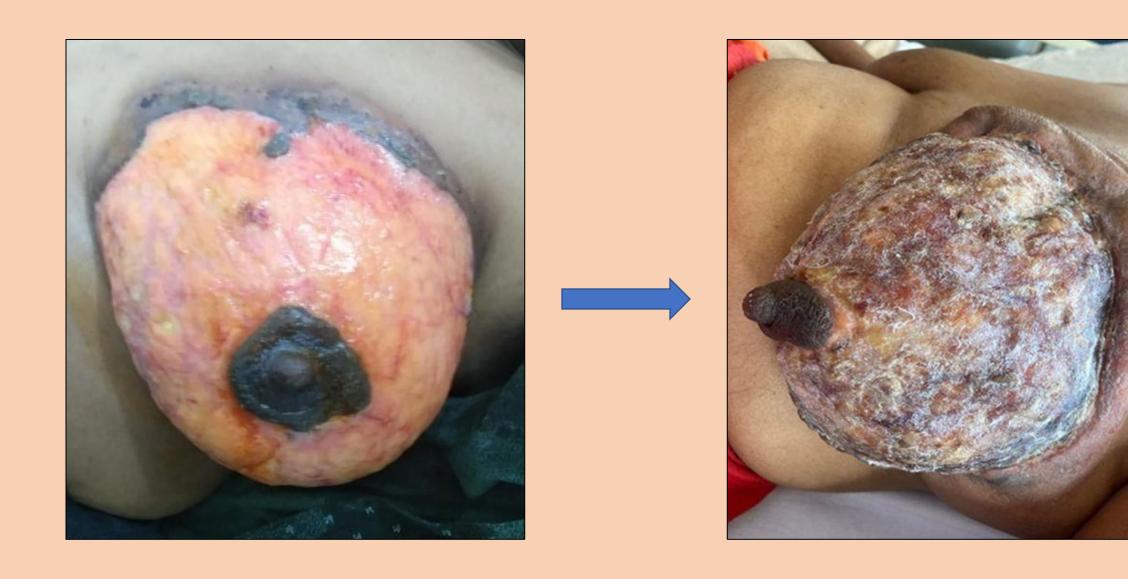
Day 60

# Case 3





Day 15



Day 30 Day 75

# Discussion

# Clinical variants

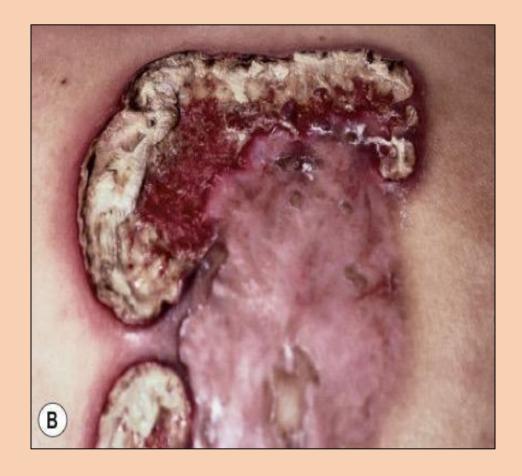
- Ulcerative
- Vesiculobullous



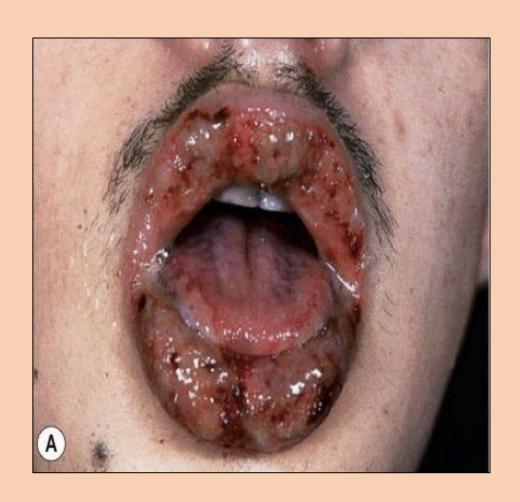
#### • Pustular



# • Vegetative



# • Pyostomatitis





# Diagnostic criteria

- **Major criteria:** 1) Rapid progression of painful, necrolytic ulcer with irregular, violaceous and undermined border
  - 2) Other causes of cutaneous ulceration have been excluded

Minor criteria: 1) H/o pathergy / cribriform scarring

- 2) Systemic disease associations
- 3) HPE (sterile dermal neutrophilia, ± mixed inflammation, ± lymphocytic vasculitis)
- 4)Treatment response (rapid response to systemic corticosteroids)

# Differential diagnosis

#### Vascular:

- Venous stasis
- Vasculopathy
- Arterial occlusive disorder, Vasculitis, APLAs

#### **Infection:**

- Bacterial (Ecthyma gangrenosum),
- Mycobacterial /atypical mycobacterial,
- Deep fungal infection (Blastomycosis, sporotrichosis, aspergillus, cryptococcus),
- Rarely- tertiary syphilitic ulcer, amoebiasis, herpes

#### Drugs:

- Hydroxyurea
- Halogenoderma

#### Others:

- Dermatitis artefacta
- Calciphylaxis
- Necrotizing insect bite
- Malignant rheumatoid disease
- Cutaneous lymphoma

# Associations

• **IBD** (20-30%) - Crohn's disease and ulcerative colitis

• Inflammatory arthritis (10%)

Hematological d/o -Monoclonal gammopathy, acute myelocytic leukemia,
 (5-7%) myelodysplastic syndrome, polycythemia vera,
 essential thrombocytosis, myelofibrosis,
 leukemoid reaction, Hodgkin lymphoma,
 non-Hodgkin lymphoma, cutaneous T-cell lymphoma

Visceral malignancy – Breast, ovaries, bladder, prostrate, colon,
 (5%)
 carcinoid, bronchus

Hidradenitis suppurativa

• **Drugs** - Granulocyte-colony stimulating factor

# Correlation of Covid-19 infection/Covid-19 vaccination with pyoderma gangrenosum

• PG is associated with increase in pro-inflammatory cytokines (IL-12, IL-23, IL-6, TNF∝,)

• Increased secretion of pro-inflammatory cytokines (IL-1,IL-2R, IL-6, TNF∝) also plays a role in covid-19 infection and in response to covid-19 vaccine.

• Dysregulation of JAK-STAT pathway which has also been implicated in PG, plays a major role in covid-19 infection.

• Covid-19 spike protein may serve as an immune trigger for PG.

#### Literature reviews

Covid-19: Infection → 8 cases prior to PG (1 breast)
 Vaccination → 6 cases (none on breast)

• Breast PG  $\rightarrow$  146 cases (70% associated surgical intervention)

• SLE  $\rightarrow$  23 cases (none on breast)

• Pemphigus vulgaris  $\rightarrow$  1 case (lower limb)



# Comparative study "Microneedling / Microdermabrasion" with 20% vitamin C serum in Females with Periorbital Melanosis

Periorbital melanosis - cosmetic concern and difficult-to-treat entity.



#### Aim:

To compare the efficacy of microneedling (MiN) with vitamin C serum and microdermabrasion (MDA) with vitamin C serum in the treatment of POM.

#### Selection of patients:

60 female pts (20-50 yrs) with POM randomly divided -2 groups -30 each

#### Exclusion criteria:

- Chronic debilitating disease
- Generalized pigmentation of the face
- Pregnancy

#### Pre-procedure:



- Priming done with vitamin C serum application once daily at night for 7 days.
- Strict photoprotection

#### Schedule:

Both procedures repeated @ interval of 21 days for 4 sittings.

#### Post-procedure:

- Photoprotection
- Adequate sleep
- Reduce screen time

# Regimen 1

Topical anesthetic



#### Dermaroller 0.5mm

rolling - horizontally and vertically



Vit.C serum (1ml,20%) applied @ periorbital area



# Regimen-2

MDA - diamond probe

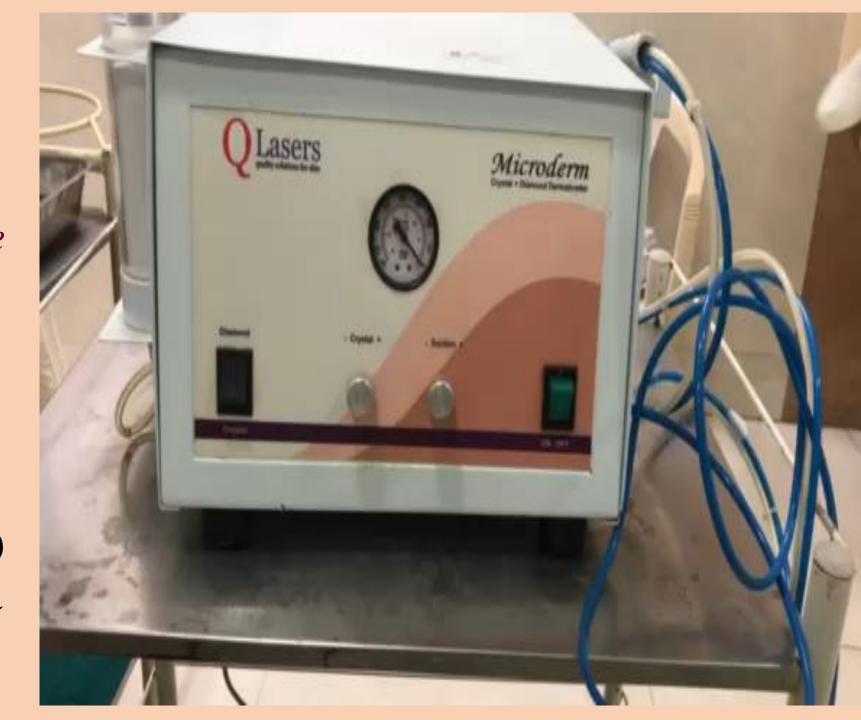


Two passes

@20mm Hg pressure



Vit.C serum (1ml,20%) applied periorbital area



# Grading of response

Improvement was graded every 3 weeks as:

```
    I - Slight (<25%)</li>
    II - Moderate (25-50%)
    III - Obvious (50-75%)
    IV - Marked (>75%)
```

Finally, the results were analyzed and compared.

# Comparison

1	MiN with Vit.C serum		MDA with Vit.C serum	
grade				
	No. of pts.	%	No. of pts.	%
I	7	23.3	14	46.7
II	8	26.6	11	36.7
III	13	43.3	5	16.7
IV	2		_	_
Total	30		30	

# Microneedling with vitamin C serum



AFTER 12 WEEKS



# Microdermabrasion with vitamin C serum





# Discussion

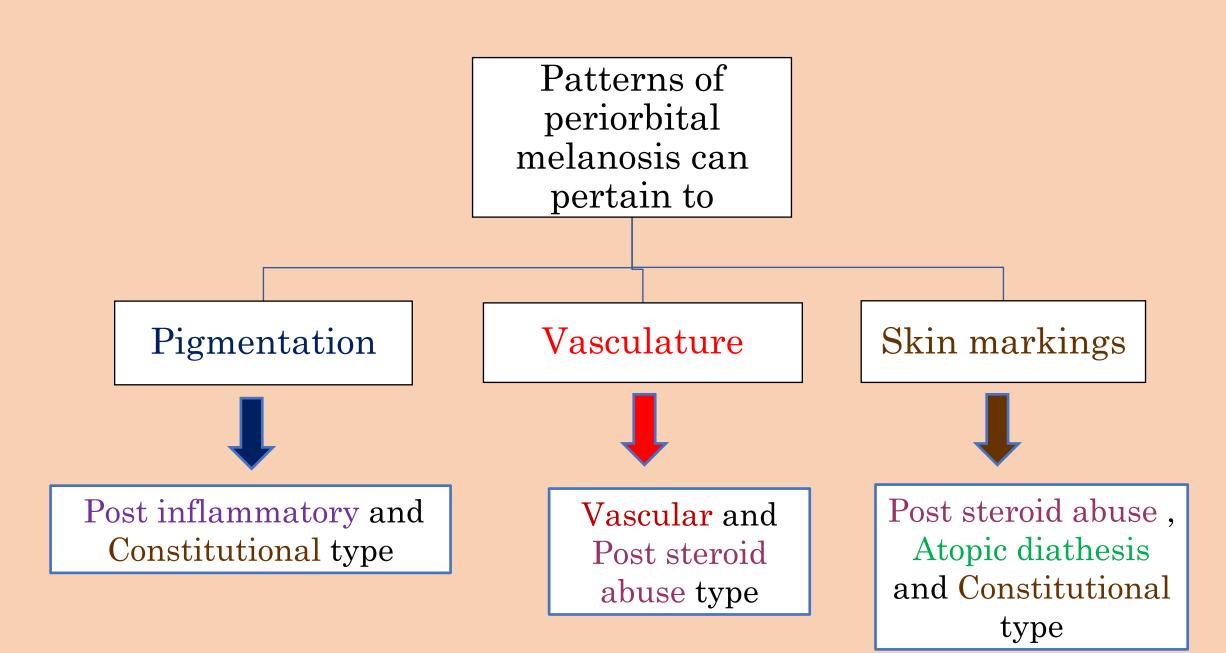
• The tendency of POM to **respond poorly** to treatment is widely acknowledged.

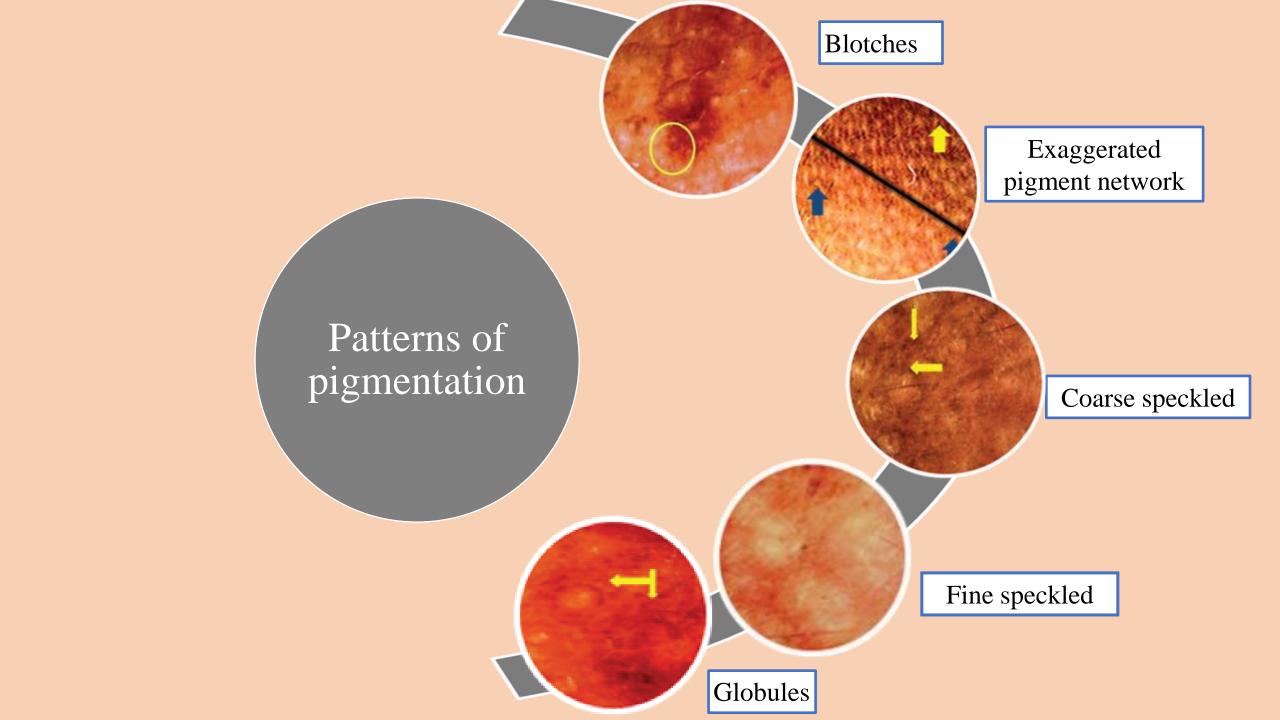
• The **result** of the treatment of the skin with dark circles is most often **gradual** and **rarely durable**.

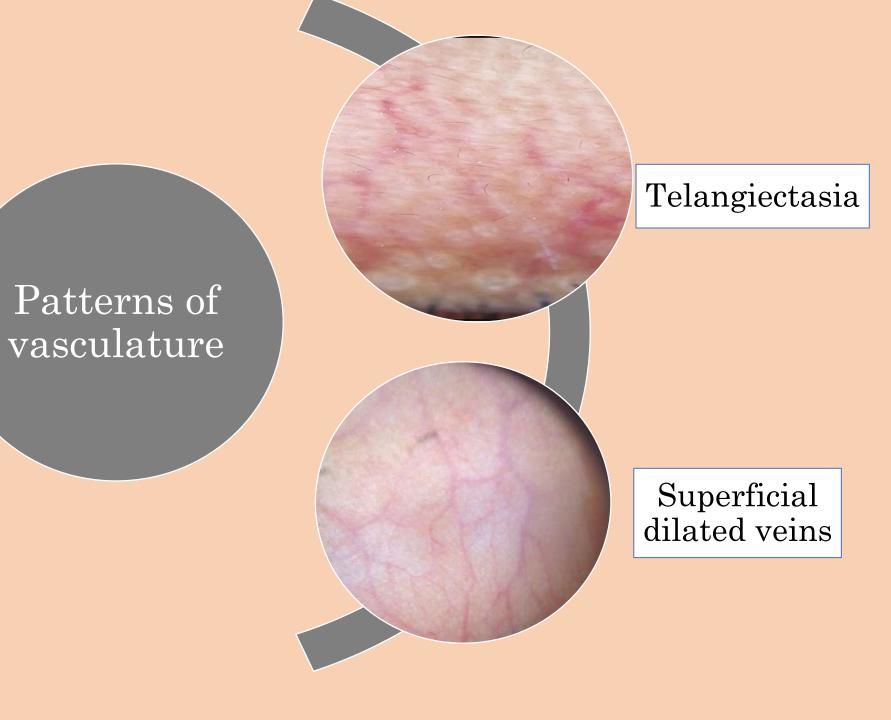
• Since the physiopathology of this type of hyperpigmentation involves **individual predisposition** to pigmentation along with the **vasodilating phenomena**.

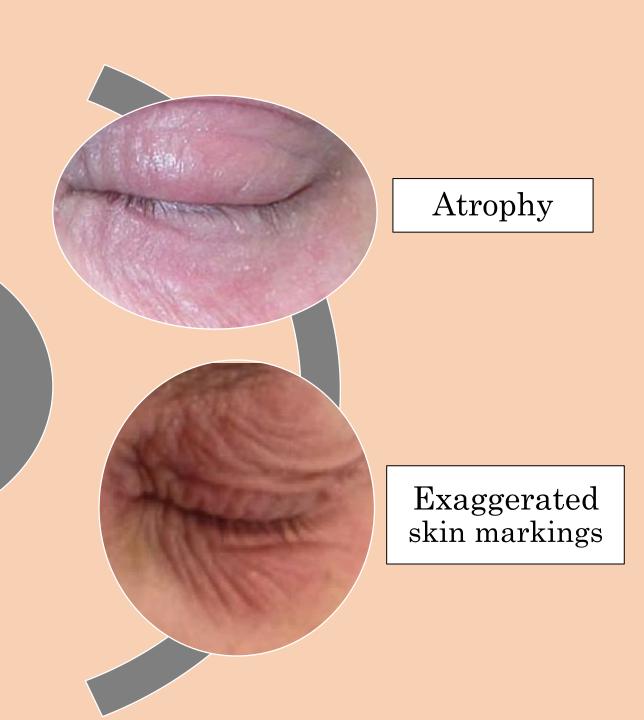
# Causes

Endogenous	Exogenous		
<ul> <li>Genetics</li> <li>Excessive vascularity</li> <li>Advanced age</li> <li>Vitamin K deficiency</li> <li>Facial anatomy</li> <li>Chronic sinusitis</li> <li>Local swelling</li> </ul>	<ul> <li>Allergies (contact and airborne)</li> <li>Fatigue</li> <li>Post inflammatory hyperpigmentation</li> <li>Hormonal therapy</li> <li>Sun exposure</li> </ul>		









Patterns of skin markings

#### Vascular

A variety of pathologic and age-related processes



permeability of the local vasculature



extravasation of hemoglobin breakdown products such as hemosiderin and biliverdin



# Dermaroller 0.5mm











# Mechanism of action – Triphasic

### Inflammatory phase - 1-2 days

Microneedle penetration upto upper dermal layer

Proliferative phase

Remodelling phase

Inflammatory phase

Damaging vessels and collagen

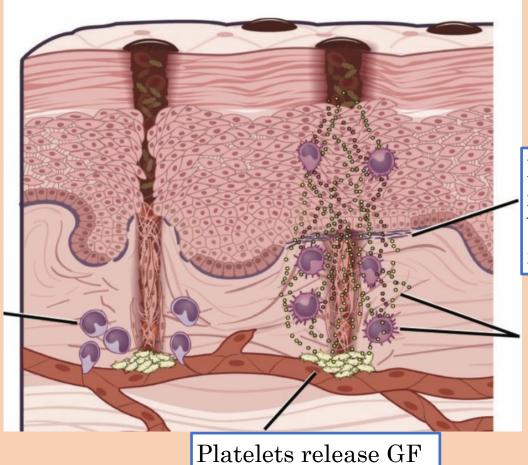
Keratinocyte migration

Fibroblast chemotaxis and proliferation

Release of platelets and neutrophils

Bleeding

# Proliferative phase – 2-4 days

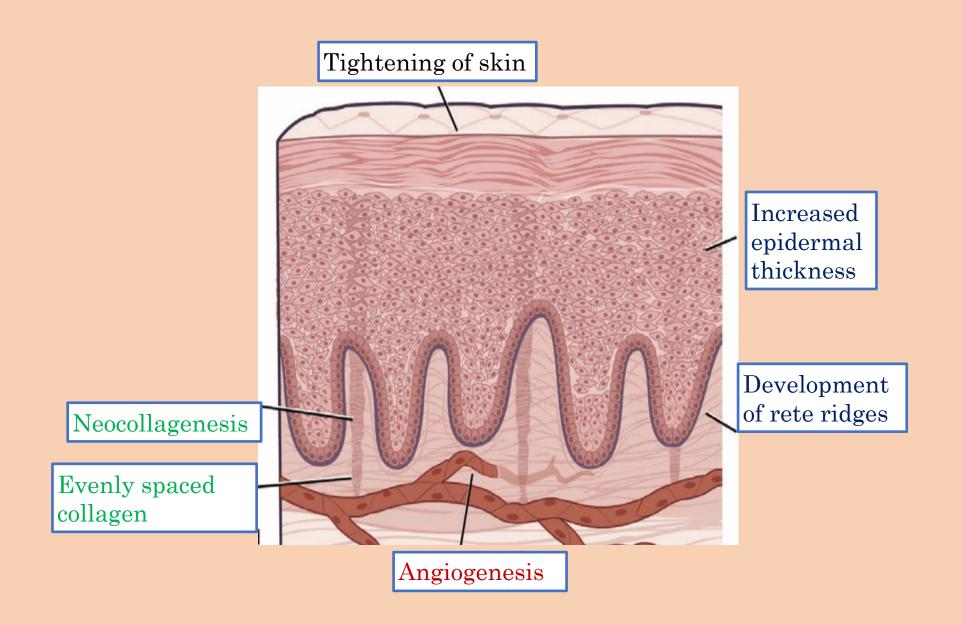


Keratinocytes
re-establish
basement
membrane

Monocytes transform into **Mφ** and release GF

Monocytes infiltrate replace neutrophils

# Remodelling phase – **5-24** days



# Microdermabrader



Microdermabrasion

Exfoliation

Cellular growth

# Conclusion

• At the end of 3 months, pigmentation showed improvement with both MiN with vitamin C serum and MDA with vitamin C serum.

• Though **microneedling** with Vit.C serum was more effective, the same was not statistically significant.

• Larger studies are needed to know better about the outcome.

