An unusual case of Acute Glomerulonephritis

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Professor & HOD,

Department of Nephrology

A 22 year old male patient, presented to the hospital with complaints of:

1. Ulcers over scalp and back for 20 days

2. Swelling of legs for 10 days

3. High coloured urine for 5 days

History of presenting illness :

C/O 2 ulcers, one on the back which has started 20 days back
 Started as a blister and has progressed to the present size
No H/O pain or discharge

An ulcer on scalp started 15 days back which is similar to the one on back

Patient noticed swelling in both feet 10 days before presenting to the hospital which has progressed upto calves then to face and hands then to abdomen.
Associated with mild SOB for 1 day

C/O high coloured urine for 5 days

Associated with decreased UOP

No H/O burning micturition/ abdominal pain / fever

No H/O NSAIDs or other drug abuse.

No H/O fever/ rash

No H/O cough/ chest pain/ cold

Past History :

H/O similar ulcers present since birth

N/K/C/O CKD, hypertension, type 2 DM, epilepsy, Asthma, Cardiovascular diseases.

Personal history :

Takes mixed diet.

Normal bowel and bladder habits

Normal sleep and appetite

Not a known smoker and no H/O alcohol consumption

No drug allergies.

Family history:

No H/O similar complaints in family members.

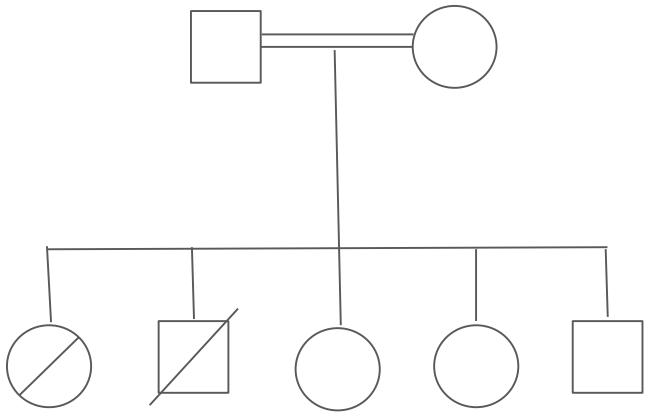
Patient’s parents had a 2nd degree consanguineous marriage and had 5 children.

First child was a female and died at the age of 6 due to an hepatic disease.

Second was a male child who has died at 2 months age during sleep, probably cot death.

Both 3rd and 4th children are females and have no health issues.

Patient is the 5th born



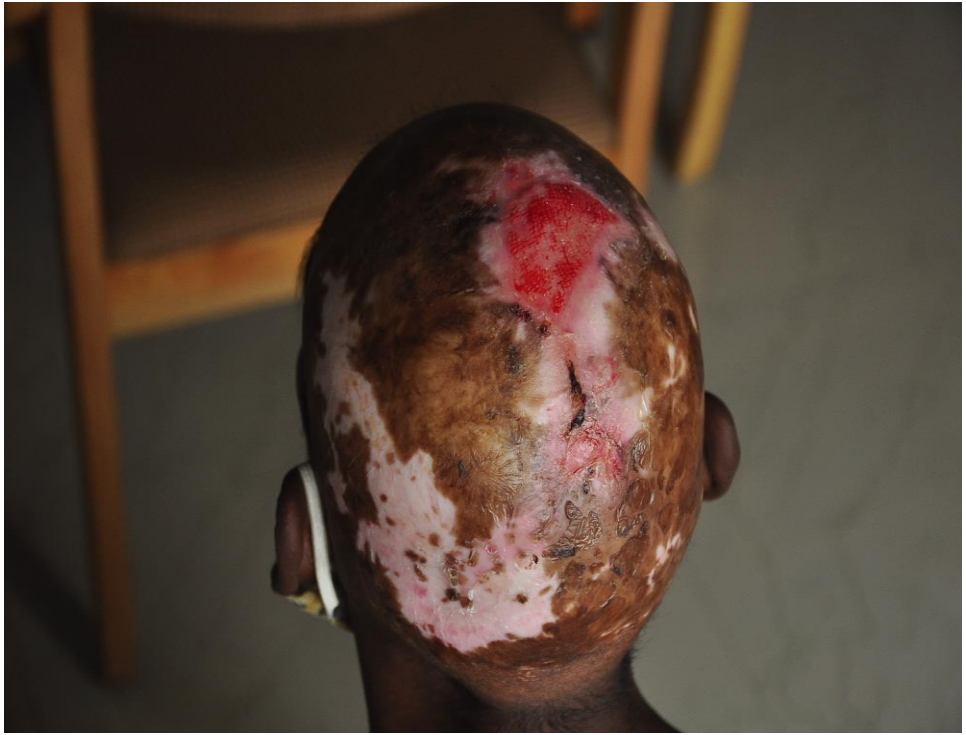
General examination :

Patient’s conscious and oriented

Moderately built and nourished

On head to toe examination the following were the findings :
Pallor +
Icterus -
Cyanosis -
Lymphadenopathy -
B/L pedal edema + (pitting)

A 15X 7 cm superficial ulcer on scalp, with granulation tissue
Loss of hair over the scalp simulating scarring alopecia



A 35X 7 cm superficial ulcer on center of the back, similar to the one on scalp

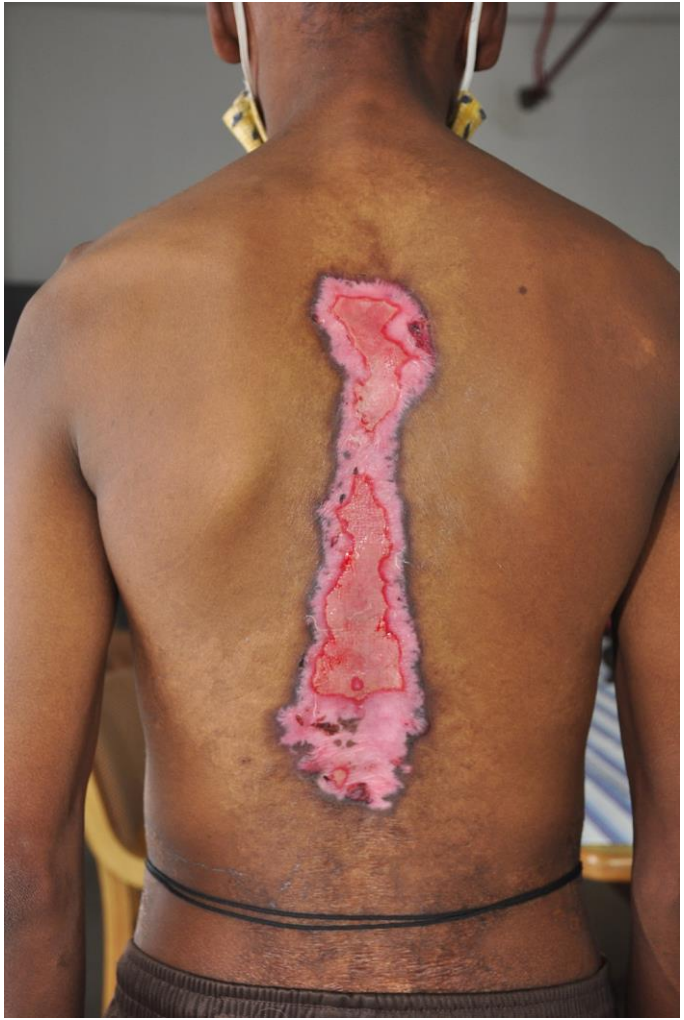
multiple healed scars on trunk and scalp

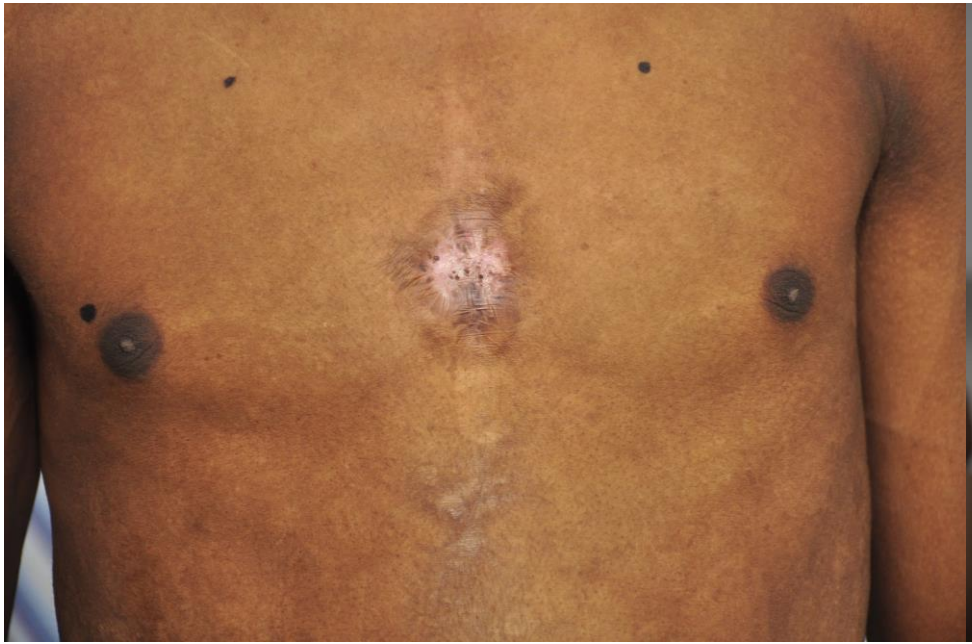
Inability to open mouth completely was noted and multiple dental caries were noted in the oral cavity.

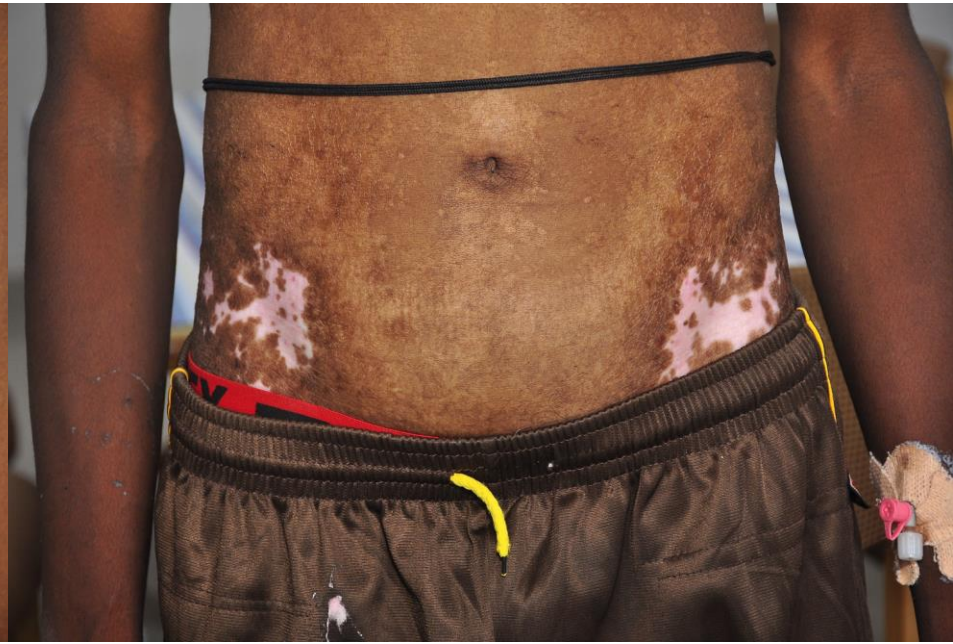
Complete absence of finger and toe nails was seen .

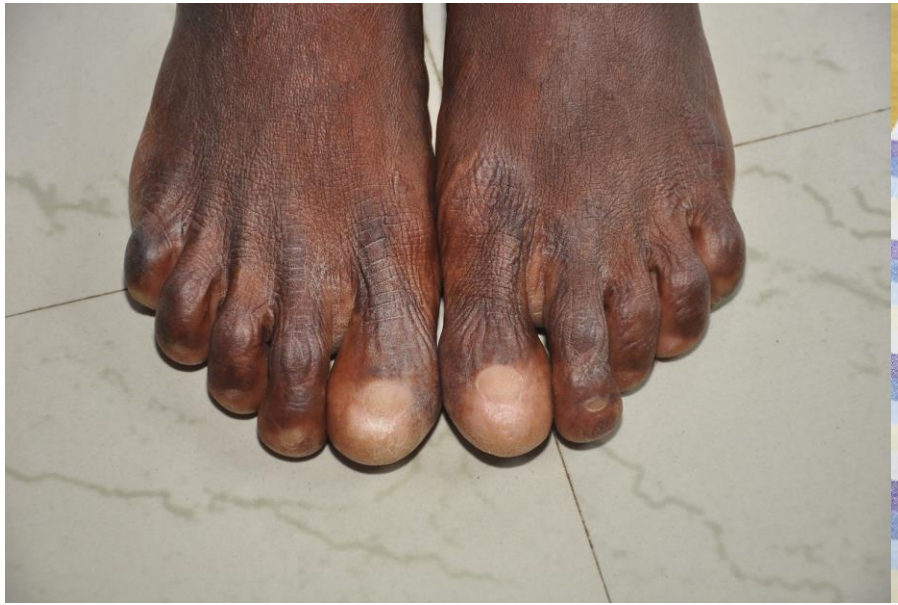
Flexion deformities are noted in the little fingers of both hands

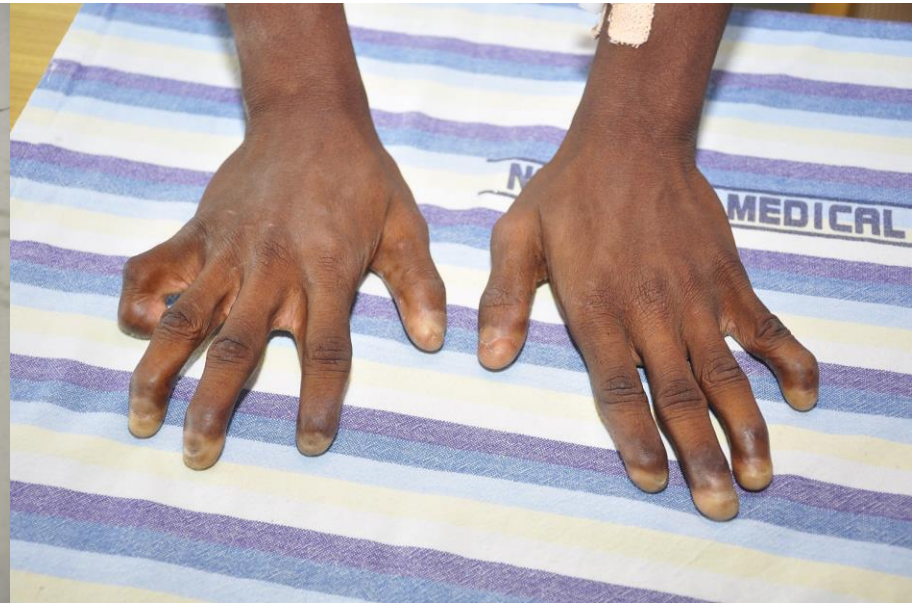
Genitals were found to be normal.










MEDICAL

Vitals:

PR: 81 bpm

RR : 18 cpm

BP: 140/90 mm of hg

SPo2 : 98% @ RA

Temperature : 98.9 F

Systemic examination:

CVS : S1, S2 + , no murmurs

RS : BAE + , no added sounds

P/A : soft, no tenderness / organomegaly.

CNS : no focal neurological deficits

INVESTIGATIONS:

On the day of presentation :

CBP (HB,TC,DC,PLATELETS COUNT)

Slno	Test	Result	Units
1	HAEMOGLOBIN	9.7	gm/dl
2	TOTAL COUNT WBC	23,200	Cells/cumm
3	DIFFERENTIAL COUNT		
4	NEUTROPHILS	87	%
5	LYMPHOCYTES	06	%
6	EOSINOPHILS	02	%
7	MONOCYTES	05	%
8	BASOPHILS	00	%
9	PLATELET COUNT	3,16,000	Per cumm
10	RBC COUNT	3.8	mill/cumm
11	PCV	31	vol%
12	MCV	80	Fl

COMPLETE URINE EXAMINATION

Slno	Test	Result	Units
1	COMPLETE URINE EXAMINATION		
2	COLOUR	PALE YELLOW	
3	APPEARANCE	CLOUDY	
4	PH	5.5	
5	SPECIFIC GRAVITY	1.020	
6	ALBUMIN	+++	
7	SUGAR	NIL	
8	KETONE BODIES	NEGATIVE	
9	MICROSCOPIC EXAMINATION		
10	PUS CELLS	PLENTY	/ HPF
11	EP CELLS	10-15	/ HPF
12	R.B.C	PLENTY	/HPF
13	CRYSTALS	NIL	/ HPF
14	CASTS	NIL	/ HPF
15	YEAST	NIL	/ HPF
16	BACTERIA	NIL	/ HPF
17	OTHERS	NIL	/ HPF

ELECTROLYTES SERUM

Slno	Test	Result	Units
1	SODIUM	142	meq/L.
2	POTASSIUM	5.7	meq/L
3	CHLORIDE	109	meq/L.

PROTEINS 24HRS URINR

Slno	Test	Result	Units
1	24 HOURS URINE PROTEINS	3.96	g/24hrs Urine
2	UrineVolume	0.9	lit

UREA SERUM

Slno	Test	Result	Units
1	SERUM UREA	128	mg/dl.

CREATININE SERUM

Slno	Test	Result	Units
1	CREATININE	1.84	mg/dl.

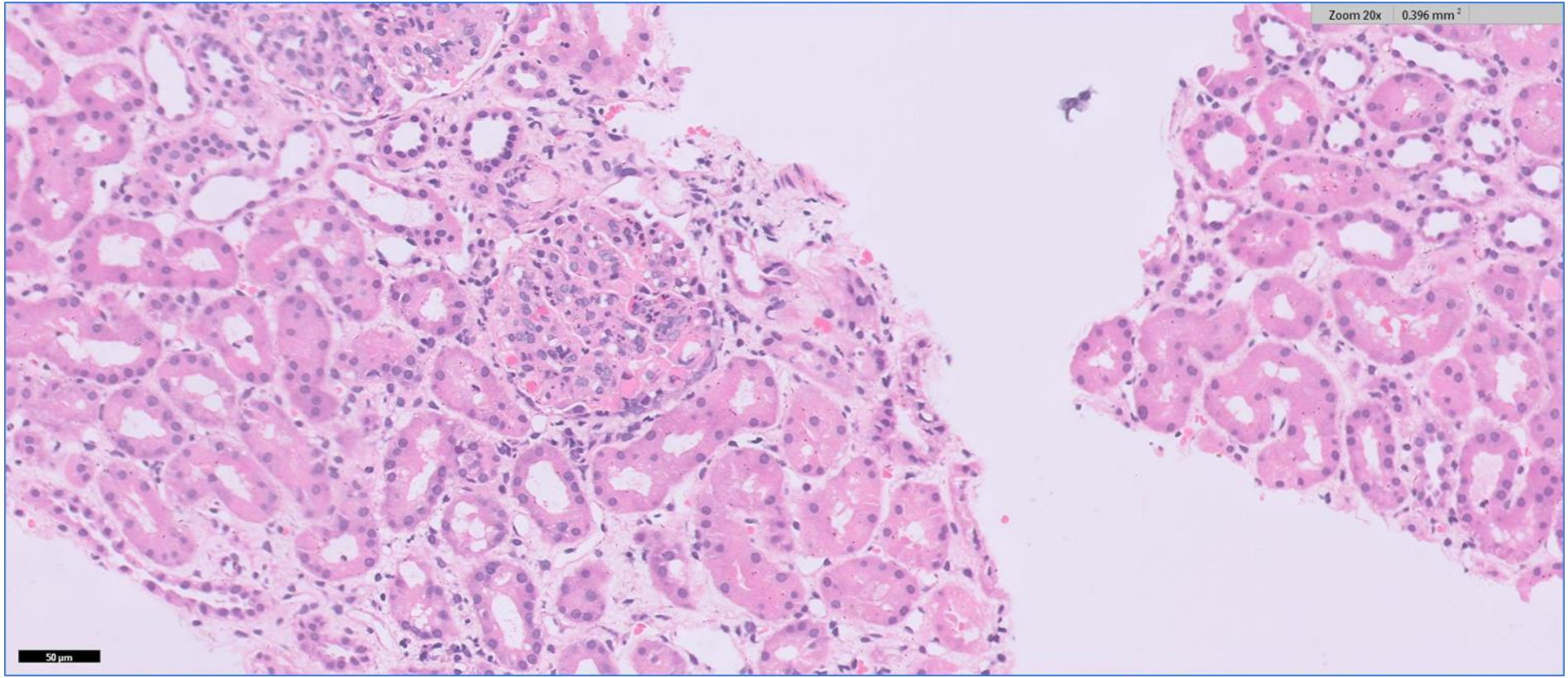
Treatment :

Patient was started on I.V. antibiotics and diuretics

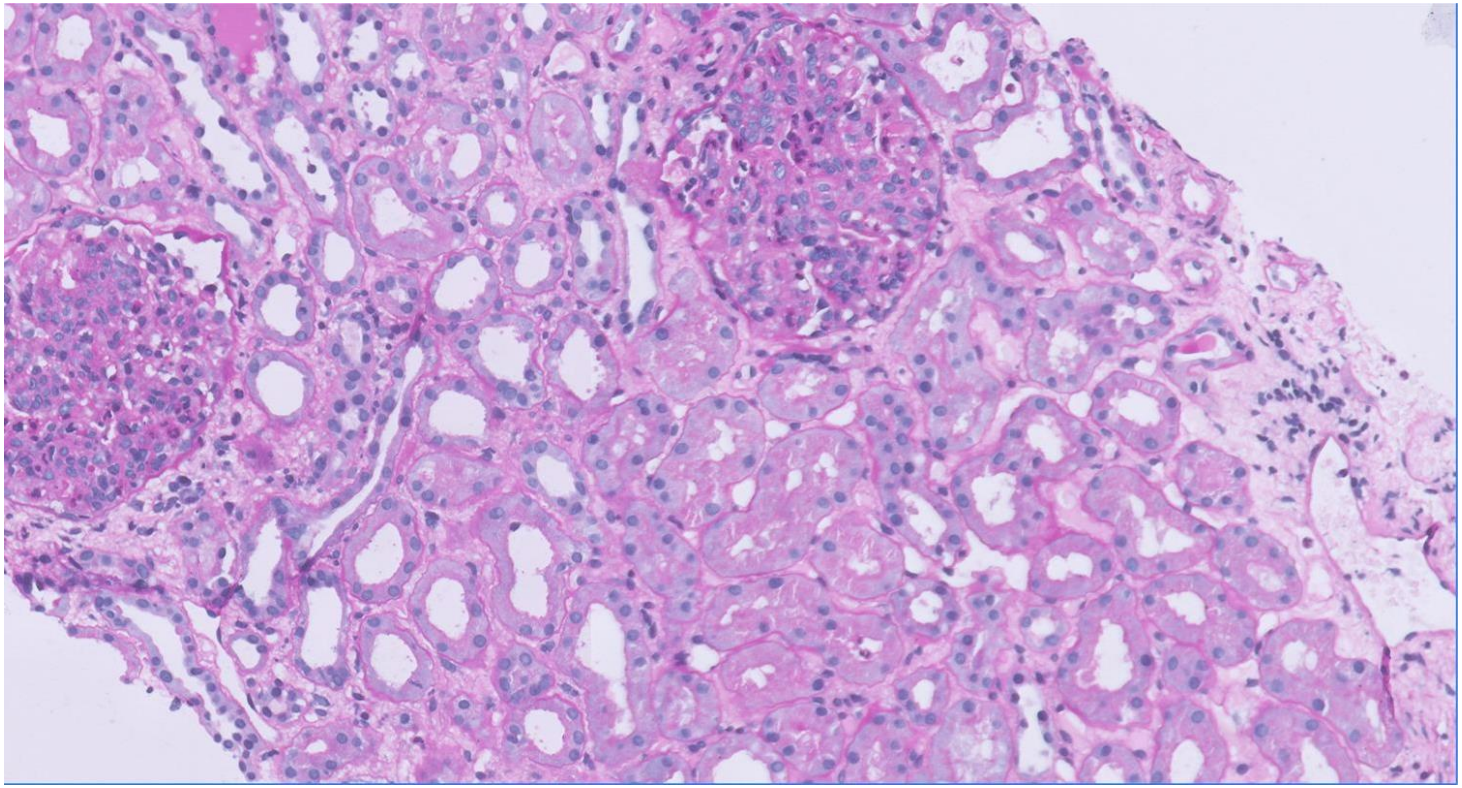
Potassium correction was given

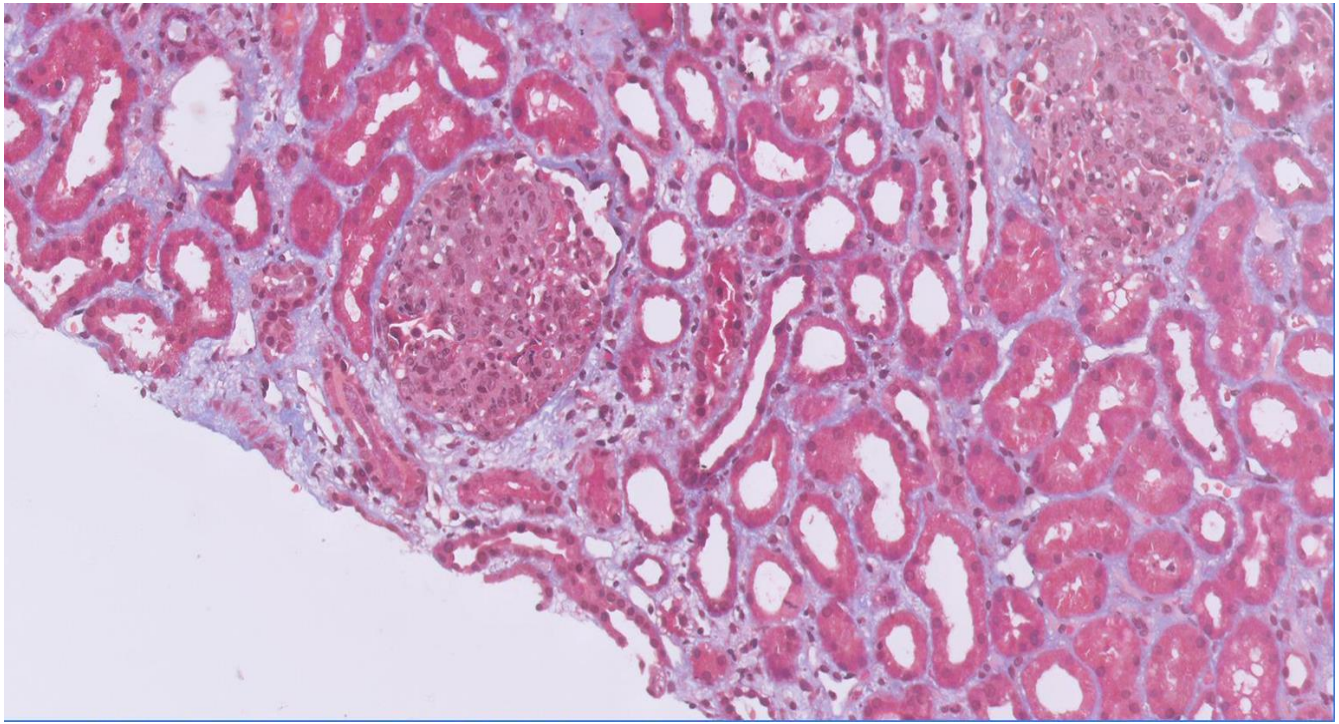
Daily dressings for the ulcers are done

After controlling hypertension and edema patient has undergone left kidney biopsy on 5th day of hospital stay.

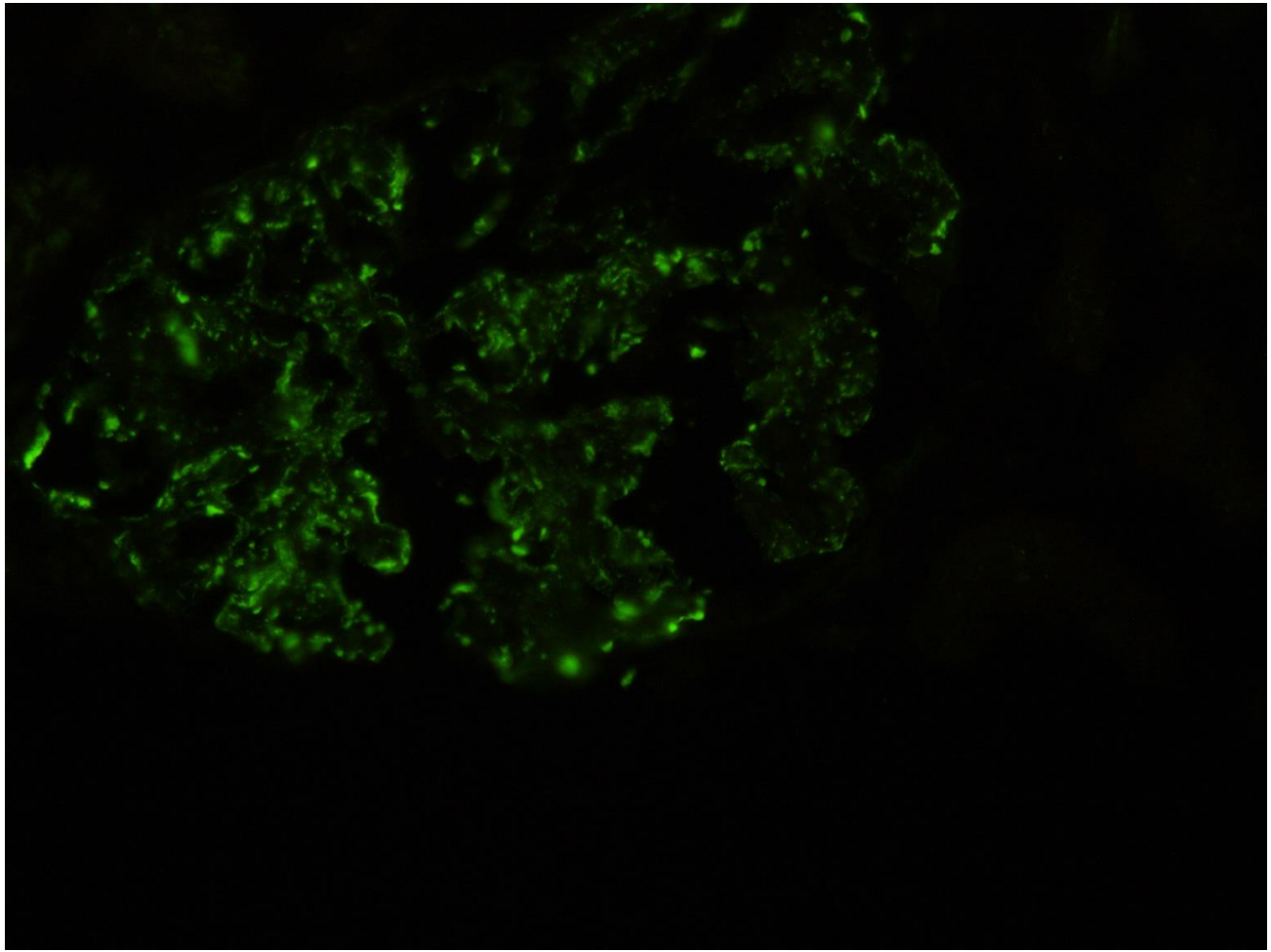


Glomeruli are enlarged and hypercellular with diffuse mesangial and endocapillary hypercellularity and neutrophils obliterating many of the capillary lumina.

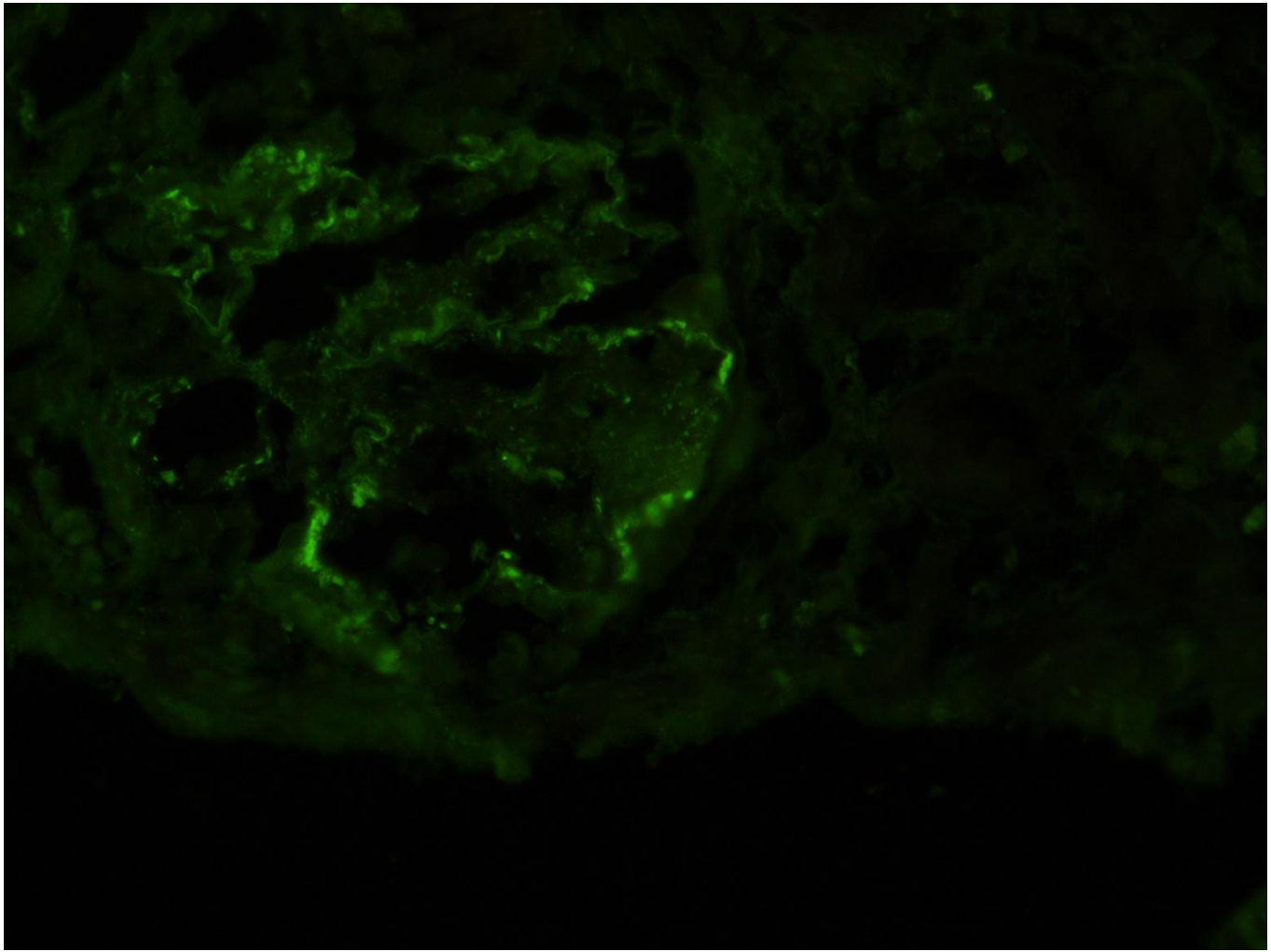




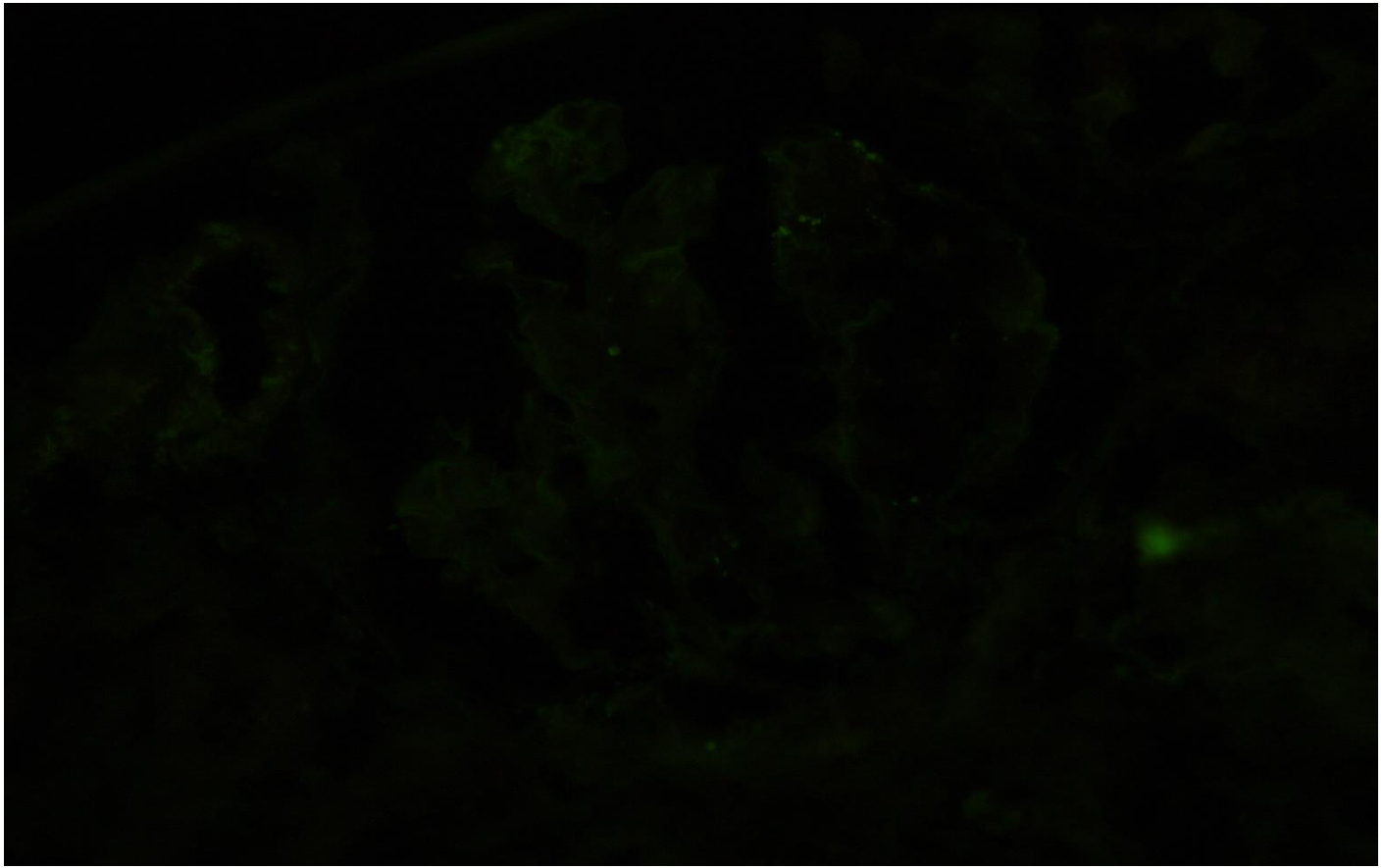
There is mild tubular injury with focal denundation & flattening of lining epithelium.
Occasional tubules show PAS positive eosinophilic casts, red cells occasional neutrophils
Interstitium is widened, edematous with infiltrates of lymphocytes and occasional neutrophils.



Significant peripheral and mesangial coarse granular deposits of C3c



Minimal IgG deposits



No deposits of IgA

Biopsy shows diffuse proliferative and exudative glomerulonephritis suggestive of infection related glomerulonephritis

I/V/O skin ulcers patient was referred to the department of Dermatology

Clinically diagnosed as Junctional epidermolysis bullosa.

referred to oral medicine , ENT and ophthalmology as well for further evaluation. The latter two evaluations came out normal.

He was diagnosed with Chronic pulpitis and fibrosis of buccal mucosa.

Treatment:

Vitamin D supplementation

Advised to avoid tight clothing and to frequently change position while lying down

Extraction of teeth with caries is advised

INVESTIGATIONS :
On the day of discharge

CBP (HB,TC,DC,PLATELETS COUNT)

Slno	Test	Result	Units
1	HAEMOGLOBIN	8.2	gm/dl
2	TOTAL COUNT WBC	7,100	Cells/cumm
3	DIFFERENTIAL COUNT		
4	NEUTROPHILS	68	%
5	LYMPHOCYTES	23	%
6	EOSINOPHILS	03	%
7	MONOCYTES	06	%
8	BASOPHILS	00	%
9	PLATELET COUNT	1,99,000	Per cumm
10	RBC COUNT	3.3	mill/cumm
11	PCV	26	vol%
12	MCV	80	Fl

COMPLETE URINE EXAMINATION

Slno	Test	Result	Units
1	COMPLETE URINE EXAMINATION		
2	COLOUR	LIGHT YELLOW	
3	APPEARANCE	CLEAR	
4	PH	5.5	
5	SPECIFIC GRAVITY	1.025	
6	ALBUMIN	++	
7	SUGAR	NIL	
8	KETONE BODIES	NEGATIVE	
9	MICROSCOPIC EXAMINATION		
10	PUS CELLS	PLENTY	/ HPF
11	EP CELLS	6-8	/ HPF
12	R.B.C	20-25	/HPF
13	CRYSTALS	NIL	/ HPF
14	CASTS	NIL	/ HPF
15	YEAST	NIL	/ HPF
16	BACTERIA	NIL	/ HPF
17	OTHERS	NIL	/ HPF

ELECTROLYTES SERUM

Slno	Test	Result	Units
1	SODIUM	142	meq/L.
2	POTASSIUM	4.9	meq/L
3	CHLORIDE	105	meq/L.

UREA SERUM

Slno	Test	Result	Units
1	SERUM UREA	26	mg/dl.

CREATININE SERUM

Slno	Test	Result	Units
1	CREATININE	1.15	mg/dl.

On 7 th day after discharge :

COMPLETE URINE EXAMINATION

Slno	Test	Result	Units
1	COMPLETE URINE EXAMINATION		
2	COLOUR	PALE YELLOW	
3	APPEARANCE	CLEAR	
4	PH	5.5	
5	SPECIFIC GRAVITY	1.025	
6	ALBUMIN	++	
7	SUGAR	NIL	
8	KETONE BODIES	NEGATIVE	
9	MICROSCOPIC EXAMINATION		
10	PUS CELLS	4-6	/ HPF
11	EP CELLS	0-1	/ HPF
12	R.B.C	1-2	/HPF
13	CRYSTALS	NIL	/ HPF
14	CASTS	NIL	/ HPF
15	YEAST	NIL	/ HPF
16	BACTERIA	NIL	/ HPF
17	OTHERS	NIL	/ HPF

CREATININE SERUM

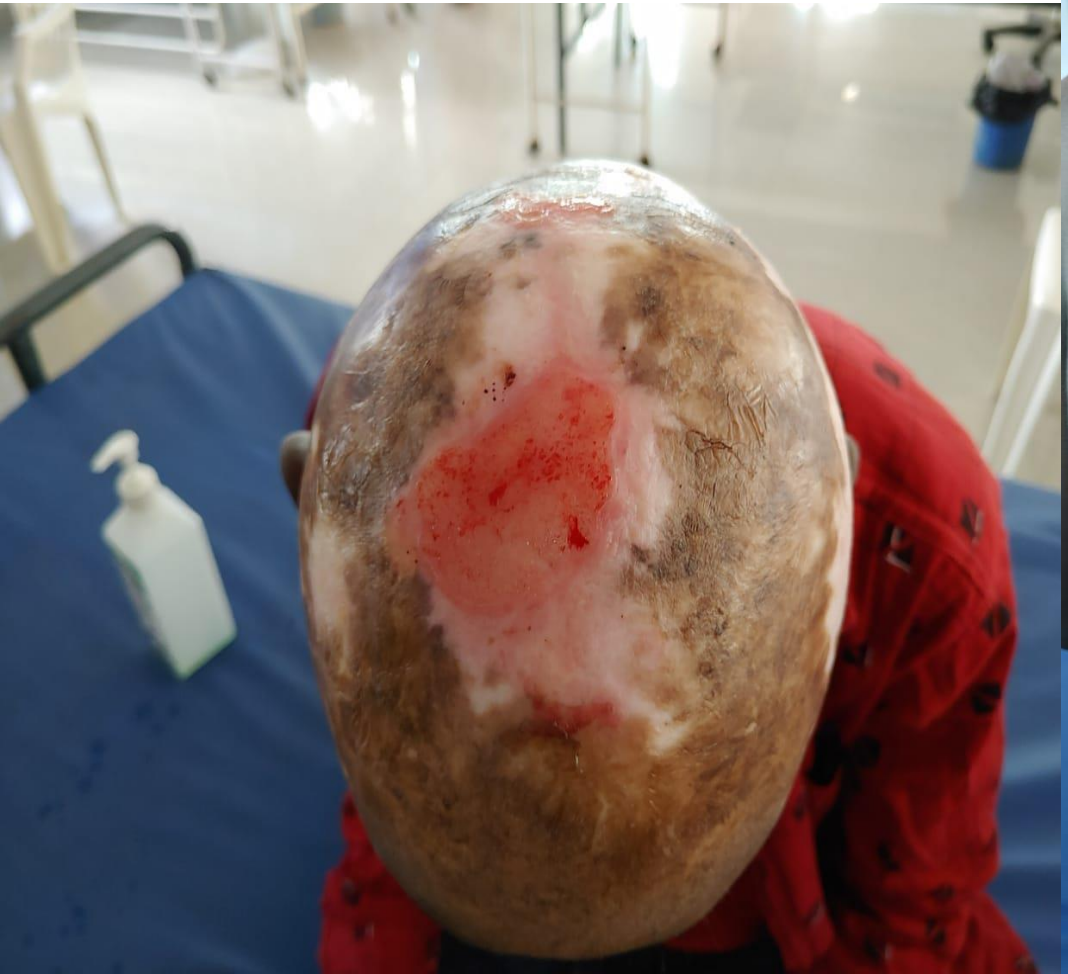
Slno	Test	Result	Units
1	CREATININE	1.33	mg/dl.

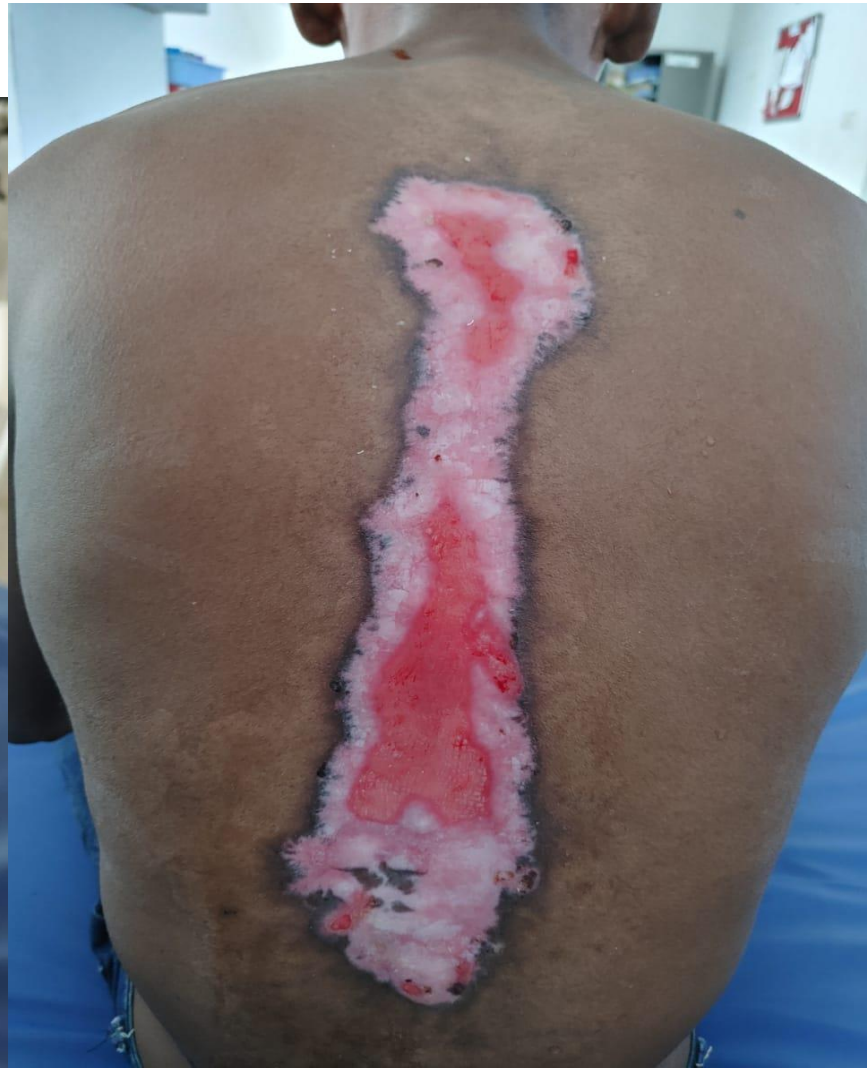
SODIUM(NA) SERUM

Slno	Test	Result	Units	Range
1	SODIUM	143	meq/L.	130-143 mEq/L

POTASSIUM SERUM

Slno	Test	Result	Units	Range
1	SERUM POTASSIUM	4.2	meq/L	3.50-5 meq/L





Patient’s samples are being sent for genetic testing to CCMB for confirmation of diagnosis

Epidermolysis bullosa gene panel

CD151, COL17A1, COL7A1, DSP, DST, EXPH5, FERMT1, ITGA3, ITGA6, ITGB4, KRT14, KRT5, LAMA3, LAMB3, LAMC2, MMP1, PKP1, PLEC, TGM5

THANK YOU

EPIDERMOLYSIS BULLOSA

Presenter : Dr. P. Hareesh

EPIDERMOLYSIS BULLOSA DEFINITION

- Epidermolysis Bullosa is a heterogeneous group of inherited mechanobullous disorders, which is clinically characterised by the development of blisters over the skin and mucous membrane following minor functional trauma.

- Blisters result from frictional forces that mechanically seperate the epidermal cells. Hydrostatic pressure causes the area of the separation to fill with a fluid that is similar in composition to plasma but has a lower protein.
- Magnitude of frictional forces determine the possibility in the development of blisters.

TYPES OF EPIDERMOLYSIS BULLOSA

Criteria for the types

Based on the level of cleavage at the dermoepidermal basement membrane, these are classified into 4 types.

1. Epidermolysis bullosa simplex (EBS)
2. Junctional epidermolysis bullosa
3. Dystrophic epidermolysis bullosa
4. Mixed epidermolysis bullosa

EB Classification

eb Research Network

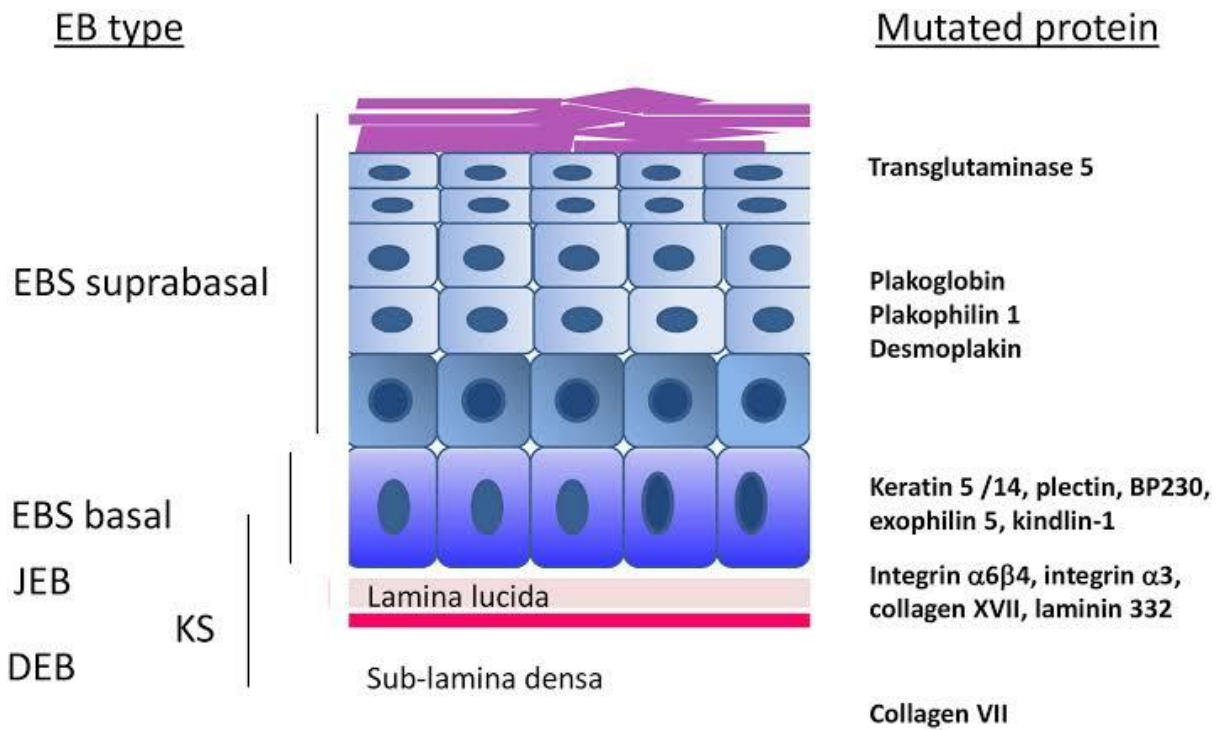
Dystrophic EB (DEB)	Junctional EB (JEB)	EB simplex (EBS)	Kindler Syndrome
Mutations in: COL7A1 (100 % of all DEB cases)	**Mutations in:** LAMA3, LAMB3 and LAMC2 COL17A1 ITGA6, ITGB4, ITGA3	**Mutations in:** KRT5 and KRT14 (75 %) PLEC KLHL24 DST EXPH5 CD151	**Mutations in:** FERMT1
Recessive or dominant	Recessive	Mostly dominant but can be also recessive	Recessive
Blisters in the dermis (lower-most skin layer)	Severe blistering in the basement membrane	Blistering in the epidermis	Blisters across different skin layers
About 11 clinical subtypes	About 8 clinical subtypes	About 14 clinical subtypes	
In RDEB (recessive DEB): • Severe blistering • Mitten deformities and fusion of digits • Mouth and gastrointestinal mucosae are compromised • Chronic wounding with scarring and hyperfibrosis • High risk of developing SCC	**Depending on the type:** • Death in early infancy • Chronic ulceration, nail dystrophy and loss • Scarring • Alopecia • Mucosal involvement	• 70 % of all EB cases • Lack of adhesion above the basement membrane (outer-most skin layer)	• Mucosal involvement • Photosensitivity • Very rare

Pathophysiology of EB Simplex

• In epidermolysis bullosa simplex , the level of separation is within in the epidermis.

• The localized, generalized, and Dowling–Meara variants of EBS are caused by missense mutations in keratin 5 and 14 gene.

• The degree of impairment of structural integrity is determined by the site and nature of the mutation which in turn influences the phenotype.


EB type
Mutated protein
EBS suprabasal
EBS basal
JEB
KS
DEB
Lamina lucida
Sub-lamina densa
Transglutaminase 5
Plakoglobin
Plakophilin 1
Desmoplakin
Keratin 5 /14, plectin, BP230, exophilin 5, kindlin-1
Integrin α6β4, integrin α3, collagen XVII, laminin 332
Collagen VII

Supra basal forms of EBS

Blisters appear by the cytololysis of keratinocytes in the suprabasal epidermis.

Basal forms of EBS

Blisters form by cytolysis of the infranuclear portion of basal keratinocyte.

Major EBS types	EBS subtypes*	Pattern of inheritance	Targeted proteins
Suprabasal	*Lethal acantholytic EB*	AR	Desmoplakin
	Plakophilin deficiency	AR	Plakophilin-1
	EBSS	AD	?
Basal	EBS-loc	AD	K5, K14
	EBS-DM	AD	K5, K14
	EBS, other generalized (EBS, gen-non DM, EBS, gen-nDM)	AD	K5, K14

Among Epidermolysis Bullosa Simplex, the important ones are

1. EBS localised (Most common)
2. EBS – Dowling Meara syndrome (very rare) (fatal)
3. EBS – Non Dowling Meara syndrome

Clinical feautures of EBS Localised

Onset : It occurs in the early childhood

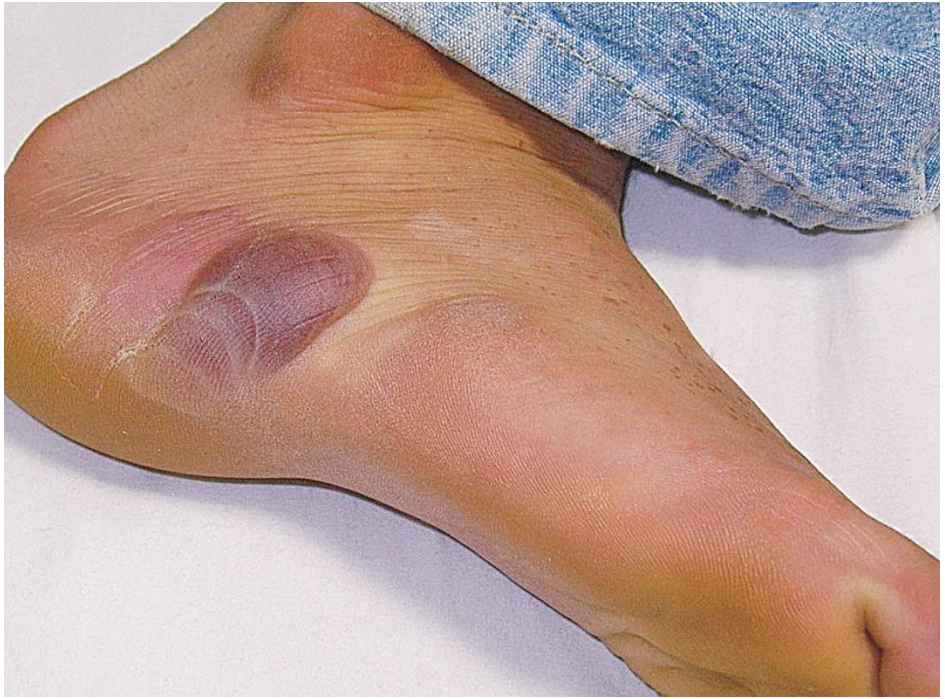
Skin distribution : Mainly seen in the palms and soles

Atrophy /Scarring – Not seen

Oral Involvement – Erosions are seen in 25% of patients

Precipitating factors – Heat and friction

Associated feautures – Localised congenital absence of skin on the Legs



EBS localised showing hemorhagic bullae on the feet

Clinical feautures of EBS Dowling Meara Syndrome

Onset : It occurs usually at birth

Skin distribution : Generalized herpetiform blistering seen

Atrophy /Scarring – Yes

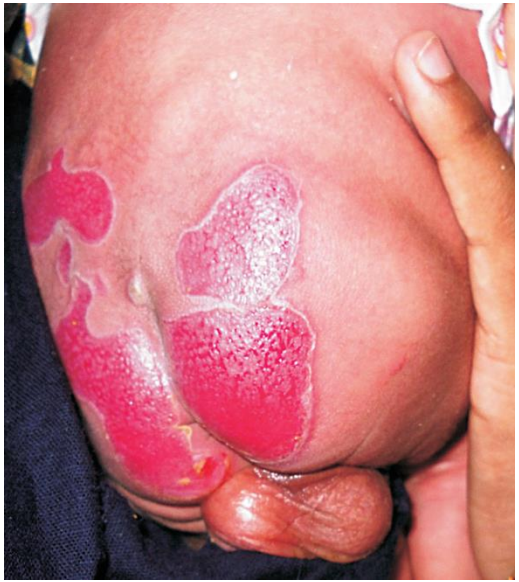
Oral Involvement – Erosions are seen in 80% of patients

Precipitating factors – spontaneous

Associated features – Growth retardation, hoarseness of voice, Gastro oesophageal reflex

Junctional Epidermolysis Bullosa

• Cleavage occurs in the Lamina Lucida layer of the skin, hence the name Junctional as it is between epidermis and dermis.



Junctional epidermolysis bullosa showing excessive erosions

Pathophysiology of Junctional Epidermolysis Bullosa

- JEB is associated with premature termination codons in both alleles of anyone of the three genes—LAMA3, LAMB3, and LAMC2, encoding, respectively, the three constituent polypeptide chains (α3, β3, γ2) of Laminin 332 gene.
- This is a major component of anchoring filaments that cross the lamina lucida

• Patients with Junctional epidermolysis bullosa also have anemia, and failure to thrive and death is often due to septicemia.

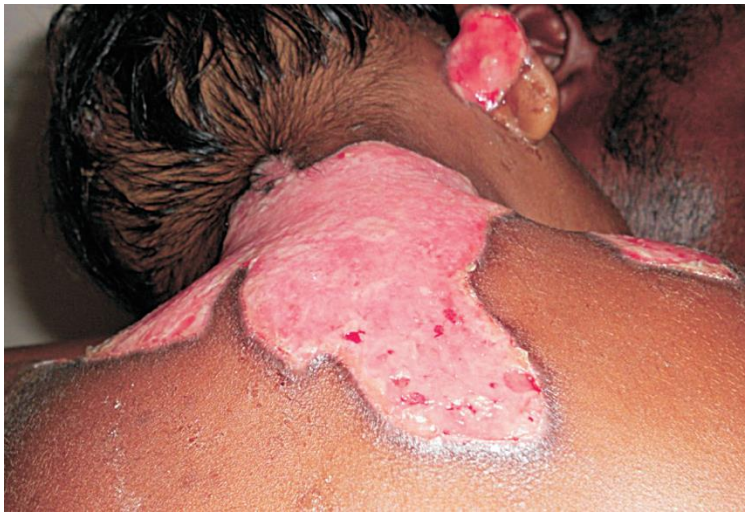
If the survival is prolonged,

• Perioral and occipital granulation tissue

• Nonscarring hair loss

• Granulation tissue of the nail beds,

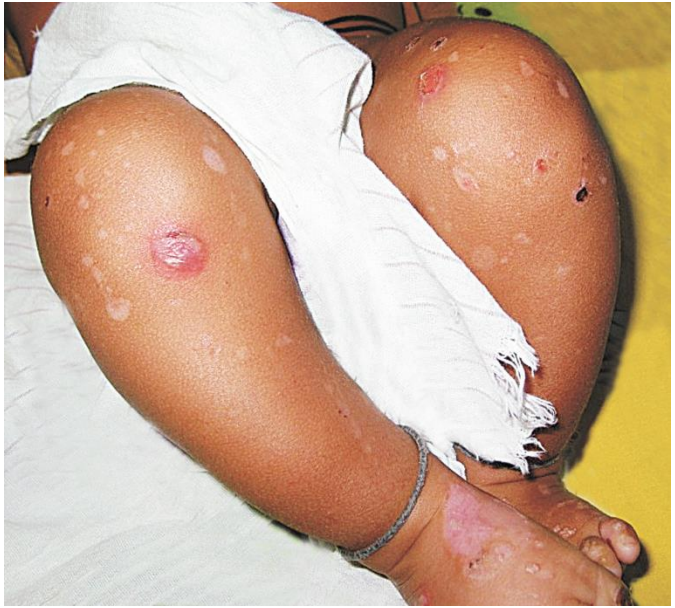
- Dental enamel hypoplasia with pitting
- Conjunctival involvement with corneal ulceration
- Pannus and symblepharon,



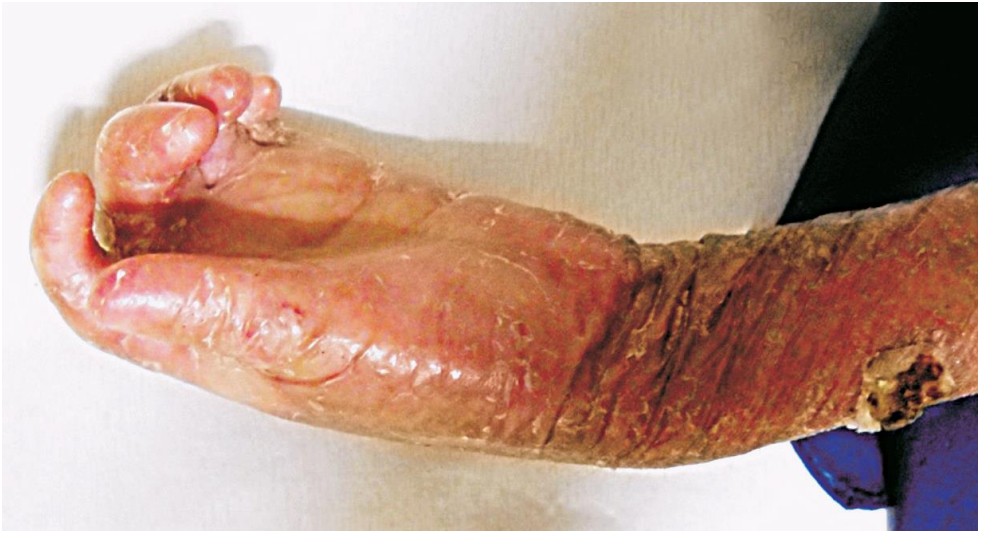
JEB showing granualtion tissue

Dystrophic Epidermolysis Bullosa

- Bullae in DEB heal with scarring and milia and are associated with varying degrees of nail dystrophy.
- Atrophic scarring and milia are prominent Nails can be thickened with discoloration of the nail plate or may be totally absent.
- Albopapuloid lesions are commonly seen on the trunk.



Generalized showing flaccid bullae, mild scarring, and extensive milia.



Severe generalized dystrophic bullosa showing fusion of the fingers.

RENAL INVOLVMENT IN EPIDERMOLYSIS BULLOSA

- Kidney injury most commonly seen in non-simplex EB type.
- It may be caused by ureter stenosis, glomeluronephritis or amyloidosis.
- Kidney got injured due to result of systemic inflammatory response.
- End stage kidney disease is the most common cause of death of Epidermolysis bullosa patients.

The Genitourinary involvement is as follows.

KIDNEY : Pyelonephritis, Post streptococcal Glomerulonephritis, Mesangial Glomerulonephritis (mainly in DEB), renal amyloidosis, recurrent urinary tract infections, recurrent urosepsis. In severe EB, renal insufficiency and renal failure occurs.

URINARY TRACT : Urinary retention, urethral fibrosis and stenosis, hydroureter, hydronephrosis, renal pelvis stenosis, stenosis or obstruction of ureterovesical junction.

- It causes dysuria
- Blisters, fibrosis and scarring of glans penis, urethral meatal stenosis are most commonly seen
- Associated abnormalities like epispadias, hypospadias, urethral diverticula, penile and bladder urethral strictures are seen in males.
- In females, erosions and ulcerations on labia, narrowing of vaginal vestibule, urinary reflux into vagina and filling of uterine cavity is seen.

GIT INVOLVMENT IN EPIDERMOLYSIS BULLOSA

- Most of the consequences such as oesophageal strictures and microstomia occured in recessive dystrophic EB.
- GERD is most common in severe forms of EB.
- Constipation, perianal blistering is commonly seen in all types of epidermolysis bullosa.
- Malabsorption, protein losing enteropathy, IBD and Irritable bowel synrome are most commonly seen

CVS INVOLVMENT IN EPIDERMOLYSIS BULLOSA

- Congestive HF and cardiomyopathy are the unknown complications in Epidermolysis bullosa simplex and Junctional epidermolysis bullosa.
- The patients with coexistent chronic renal failure had high risk of mortality.

Laboratory Approach to diagnosis

• The diagnosis of EB is mainly clinical. However, skin biopsy must be sent for ultrastructural examination to confirm the subtype of EB.

• Biopsy must be taken from the unaffected skin after inducing a blister by rubbing the skin with a fingertip.

- **Transmission Electron Microscope (TEM)** helps in direct visualization of the various components of the dermoepidermal junction (DEJ) and a semi qualitative assessment of these structures.
- **Immunoflorescence antigen mapping** utilizes monoclonal antibodies and provides a clue to the most likely mutated Protein.

Treatment

• Treatment of all forms of Epidermolysis bullosa is supportive. There is no cure for EB as for now.

a. Prevention of new blisters
b. Preventing and treating infections and enhancing wound healing
c. Nutritional support
d. Management of extracutaneous complications and preserving function
e. Providing psychological support to patients and family members.

Prevention of new blisters

1. Keeping the soles and palms cool and dry particularly in summer.
2. Well-fitting footwear, leather shoes with lining.
3. Wearing two pairs of cotton socks to minimize friction.
4. Corn flour can be sprinkled into the shoes or socks to reduce friction.

Novel therapies

Tremendous progress in the understanding of molecular basis of EB has provided the basis for the development of novel genetic and cellular therapies. Strategies include

1. Gene therapy;
2. Protein replacement therapy;
3. Cell-based therapies