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**Available online at: http://www.iajps.com** ***A Case Report***

# EPIDERMOLYSIS BULLOSA COMPLICATED BY SCC OF THE HAND

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**Abstract :**

*Epidermolysis bullosa (EB) encompasses a clinically and genetically heterogeneous group of rare inherited disorders characterized by marked mechanical fragility of epithelial tissues with blistering and erosions following even minor trauma. [1] In addition, young adults with the classic form of dystrophic epidermolysis bullosa have a very high risk of developing squamous cell carcinoma (SSC), a form of skin cancer that tends to be usually aggressive and often is life-threatening. [2] Patients with epidermolysis bullosa and SCC are uncommon and present a clinical challenge because of limited options for wound coverage and SCC's frequent recurrence. Therefore, we provide this case report to emphasize the importance of vigilance in surveying epidermolysis bullosa patients for their increased risk of developing SCC and performing a biopsy and managing the condition early.*

**Keywords:** *Epidermolysis bullosa, squamous cell carcinoma, skin flap, amputation, excision.*

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## INTRODUCTION:

Epidermolysis bullosa (EB) encompasses a clinically and genetically heterogeneous group of rare inherited disorders characterized by marked mechanical fragility of epithelial tissues with blistering and erosions following even minor trauma. EB is caused by mutations that involve at least 18 genes. [1] It is also a rare disease, with an estimated prevalence approximately 8 per million and an incidence in approximately 19 per million live births. [3,4] Based primarily upon the level of skin cleavage, EB is classified into four major groups: Epidermolysis bullosa simplex (EBS), Junctional epidermolysis bullosa (JEB), Dystrophic epidermolysis bullosa (DEB), and Kindler syndrome. [5] This group of autosomal recessive diseases is particularly prevalent in regions in which consanguinity is common, such as the Middle East. Three mutations have been found to be recurrent: Q46X in LAMC2 and Q1083X in LAMB3 were described previously in an Arab-Israeli family, and R1226X in COL17A1 also has been reported in a previous study. [2,6,7] Most often, blisters are present over the whole body and affect mucous membranes, such as the moist lining of the mouth and digestive tract. As the blisters heal, they produce severe scarring, and such scarring in the mouth and esophagus can make it difficult to chew and swallow food, leading to chronic malnutrition and slow growth. Additional complications of progressive scarring can include fusion of the fingers and toes, loss of fingernails and toenails, joint deformities (contractures) that restrict movement, and eye inflammation that leads to vision loss. Skin biopsy for immunofluorescence microscopy (IFM) typically is the first step in the diagnosis of newly-developed epidermolysis bullosa (EB). If IFM is normal or fails to demonstrate the level of cleavage and/or subtype, the diagnosis can be confirmed either with transmission electron microscopy (TEM) or mutational analysis. [8,9,10] Further, young adults with the classic form of dystrophic epidermolysis bullosa have a very high risk of developing skin cancer mainly squamous cell carcinoma (SCC), which tends to be usually aggressive and is often life-threatening. [2] Venugopol mentioned that RDEB patients' cumulative risk of developing SCC is 90.1% by age 55; the most common site of involvement is chronic wounds, followed by long term cutaneous scars. Metastatic SCC is the leading cause of death in RDEB-GS patients, with a staggering 87.3% cumulative risk of death by age 45. [11]

This case report describes SCC detection, clinical manifestation, and progression in a patient with epidermolysis bullosa, its investigation and management, as well as diagnostic modalities and genetic analysis for the patient. This case will aid in better understanding of the disease and confirm the genetic abnormality, and to present our experience when SCC develops.

## CASE REPORT:

A 24-year-old Bangladeshi male was born of an un-consanguineous marriage with blister over his extremities. He's known in our department since he was 9 years old in 2002 when he was first presented with such skin features as spontaneous blistering, poor wound healing, pseudosyndactyly of all four extremities, skin fragility, anemia, and retarded growth. The second admission was on 2004, when he was complaining of second degree burn in his both hands to level of wrist, epidermal loss and blisters. The previous admission was due to SCC in his right hand that was presented early two years ago and was treated by excision with free margins

Now he presented to our clinic most recently Now he presented to our clinic at the age of 24-year-old complaining of fungating mass in his left hand it was progressively growing for the last 6 months. The patient had systemic manifestations including iris lesions, scarring in the mouth and esophagus associated with dysphagia. His brother died from the sequelae of his disease and his aunt had a similar condition.

On examination, the patient appeared to be built poorly and undernourished. Multiple clear to hemorrhagic blisters were present over the dorsum of the hands and legs (Fig.1). Areas of active and healed erosions, scarring, and milia were seen over the upper and lower limbs. Loss of the fingernails and toenails, together with pseudosyndactyly of both feet, as well his right hand was evident (Fig. 2). On his left hand, there is an ulcerative fungating growth mainly over the dorsal side measuring 6 x10 cm (Fig.3). Lymphadenopathy was palpable in the right axilla but no palpable Lymph nodes in the left axilla.

Laboratory investigations demonstrated only hypochromic anemia ferritin, 22.4 serum iron, 3.1 low creatinine, 45 low BUN, 2.4 low albumin, and 17 high alkaline phosphatase 215. A skin biopsy taken from the tumor revealed a fragment of skin with invasive malignant neoplastic growth arranged in whorls of malignant squamous cells with frequent keratinization. The malignant cells showed a high N\c ratio, hyperchromasia, prominent nucleoli, and

pleomorphism with infrequent mitotic figures. MRI was performed and showed that the lesion involved the entire left hand up to the distal end of the radius and ulna. A chest CT showed diffused enlargement of the bilateral axillary lymph nodes and sub-pectoral groups, while a CT of the abdomen showed no evidence of intra-abdominal metastases

The entire lesion was amputated above the level of wrist with a 2cm margin proximal to the lesion (Fig. 4) on the dorsum leaving a 2.5cm skin flap on the volar uninvolved skin, the veins and arteries were devided and tied and bone was cut short just proximal to the dorsal skin .Frozen section pathology of tissues taken from the proximal end of the enblock amputated spacemen showed negative margins for malignant cells. Then the volar skin flap was used to cover the amputation stump (Fig. 5).

Dressing was done using Vaseline impregnated gauze and soft bandages

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## DISCUSSION:

Based on studies, the cumulative risk of developing SCC in EB increases with age: for patients with RDEB-SG, the cumulative risk of having at least one SCC is 7.5% at age 20 years, 67.8% at 35 years and 90.1% by 55 years. The risks for patients with other forms of EB prone to SCC are lower, with tumors occurring later in life and tending to be less aggressive. It is also important to acknowledge that many EB subtypes, especially EB simplex, are not associated with an increased SCC risk. [12,13]

Patients and family members are also encouraged to keep a personal account of ulcers that have become symptomatic or are long standing, associated with either poor or no healing.[11] In patients with RDEB should have a full skin examination every 3–6 months from age 10 years for their risk of developing aggressive SCCs in early age. For other groups such as junctional EB, EB simplex and Kindler syndrome the risk of malignancy is not as high, and it does not usually occur as early. Clinical screening for these lower-risk groups should usually commence from age 20 years and take place every 6–12 months, although if an SCC is diagnosed, 3 monthly screening should be undertaken subsequently. Areas of skin clinically suspicious for SCC should be biopsied under sub-local anesthesia for histological evaluation. Once the diagnosis has been confirmed on biopsy, the patient should be managed quickly.

We present this case report because patients with RDEB with associated SCC are uncommon and present a clinical challenge, as there are limited options for wound coverage. We have developed a strategy for these patients and hope that our experience may provide other practitioners guidance on the way to approach SCC tumors in patients with EB who have insufficient or unsuitable donor skin.

Surgical excision is the standard treatment for EB SCCs, although the techniques used vary depending on the site and size of the primary tumor. A number of approaches, including wide local excision, Mohs micrographic surgery, and amputation have been described, although there is no evidence of one modality's superiority over another.[12]

In this patient, the SCC was involved aggressively and deeply in the left hand, and therefore, amputation was the best choice, as the local recurrence of SCCs may render further local excision impossible and leave amputation the treatment of choice. In some cases, amputation also may be favored over wide excision. Ideally, there should be a 2cm excision margin around the tumor as assessed.

Different approaches to wound closure following excision of EB SCCs have been employed, including healing with secondary intention autologous split skin, epidermal or full-thickness grafting, allogeneic or cadaveric skin grafting, artificial skin equivalents, flaps, application of autologous or allogeneic keratinocyte suspensions, or combinations of the above. Among these techniques, split-skin grafting has been employed most frequently. [12]

In our patient, we covered the amputation stump with skin flap on the volar uninvolved skin then we use vaseline impregnated gauze and soft bandages to prevent blistering and irritation during dressing changes. Further, it provides an even surface for re-epithelialization and healing.

Because of SCCs' very aggressive nature in RDEB, many patients with these tumors reach a stage at which their disease is no longer "curative," and efforts must focus on palliation and providing the individual with the best quality of life possible.[12]

Recently, Cetuximab, a monoclonal antibody against the epidermal growth factor receptor, has been used to treat locoregionally advanced head and neck cancers and cutaneous SCCs. It also can be used as a single agent in the first treatment stage of patients with unresectable SCCs. [11]

A possible future consideration in EB patients with SCC is the sentinel lymph node biopsy technique to detect micrometastasis. [14,15]

## CONCLUSION:

EB is a genetically inherited disease for which there is no known medical cure at present. A number of different forms of the disease occur, and are accompanied by different signs and symptoms. Because EB cannot be cured, the health

professional's objective must be to recognize the condition and its associated problems and complications as they arise, with the hope that painful and disfiguring symptoms may be reduced and such potentially life-threatening problems as SCC have better outcomes.

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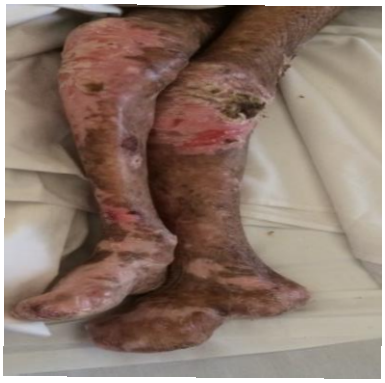

Fig 1. Multiple hemorrhagic blisters, active and healed erosions and scarring were present over the legs.

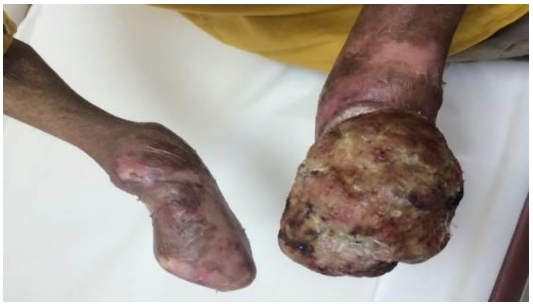

Fig.2:Loss of the fingernails with pseudosyndactyly, right hans is amputated due to prevous SCC .

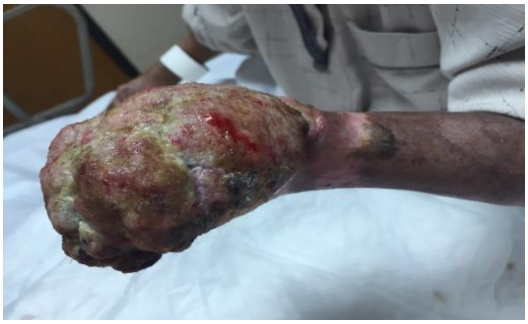

Fig. 3: ulcerative fungating growth mainly over the dorsal side measuring 6 x10 cm.

Fig. 4: The entire lesion was amputated above the level of wrist with a 2cm margin proximal to the lesion.

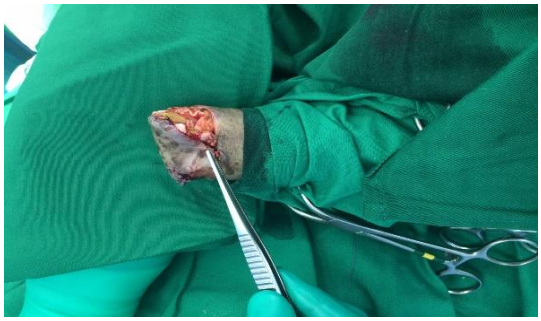

Fig. 5:The volar skin flap was used to cover the amputation stump.