

A REPORT OF TWO CASES OF SQUAMOUS CELL CARCINOMA OF THE HAND IN PATIENTS WITH EPIDERMOLYSIS BULLOSA DYSTROPHICA

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Abstract

This is a report of two patients (brothers) with unusual generalized skin disorder, a recessive dystrophic epidermolysis bullosa (RDEB) that appeared at childhood, who developed a progressive squamous cell carcinoma (SCC) in their right hands. Later both patients underwent wide local tumor excision, and during the follow-up after surgery, axillary lymph node metastasis observed in the first case, and local recurrence in the second. Therefore early recognition of EBD is important to assist in the diagnosis and treatment of malignant lesions at an early stage in these patients to prevent the subsequent complications.

Introduction

Epidermolysis bullosa (EB) is a heterogeneous group of rare inherited skin and connective tissue diseases, characterized by fragility of the epidermis, with destabilization at the dermo-epidermal junction. EB is classified into 3 main categories, the epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa (JEB) and the dystrophic epidermolysis bullosa (DEB)¹⁻³.

The DEB may be transmitted as an autosomal dominant or recessive (RDEB) subtype².

The RDRB or scarring type is the most severe, which produce blistering, ulcerations, fibrinous adhesions, with slow or non-healing chronic lesions, also creates severe hand deformities^{1,2,4-6}, and it is not uncommon for SCC to develop at the site of chronic hand lesions in patients with severe RDEB who survive to childhood^{2,5,6}.

This study presents a case of secondary

SCC localized in the hands of two patients in whom REDB was confirmed, and although this is unusual occurrence, delay diagnosis and treatment often resulting in advanced malignant lesion at presentation and with worse prognosis.

Case 1

A 35 year old man with generalized EBD was referred from the dermatology clinic to the orthopedic department, with ulcerated fungating lesion in the right hand since 5 years, with a biopsy proven SCC. He stated that the lesion appeared as a small papule, which gradually grow in size over the last 12 months and associated with recurrent bleeding and infection.

On clinical examination at the time of presentation, a grey hair patient, with a tiny white skin spots mostly in the limbs, and with generalized decrease in the skin elasticity (Figure I).



Figure 1: Skin in the patient affected by the REBD.

The lesion was extensive and fungating with irregular margins, measured approximately 8x10 cm in size, covering the ulnar portion of the dorsum of the right hand, extending to the proximal phalanges of the ring and little fingers

and into the 3rd and 4th web spaces (Figure 2), and with associated palpable axillary lymphadenopathy.

The plain radiographs revealed no involvement of osseous structures, and no other imaging measures were performed.



Figure 2: Fungating extensive ulcerated SCC involving the hand and web spaces.

Wide local excision with ray amputation of the 3 ulnar fingers was performed, with preservation of the thumb and index finger, and the defect was covered by local flap (Figure 3). The excised tumor send for histopathology, and regional lymph node dissection was not undertaken.



Figure 3: Defect on dorsum of hand has been treated with local flap after resection of SCC

After more than 8 months of follow up, there was complete wound healing with no evidence of local recurrence in the hand (Figure 4), but a fungating axillary lymphadenopathy developed at the same side (Figure 5), and was subjected later to lymphadenectomy.



Figure 4: Complete healing at excision site



Figure 5: Fungating axillary lymphadenopathy

Case 2

The younger brother of the first case, he is 32 years of age with the same medical history of generalized EBD who presented at that time with small scaly skin lesion on the dorsum of the right hand gradually progressed into small skin ulcer within a few months, and also already diagnosed as squamous cell carcinoma by the dermatologist on histopathological study, and then referred to our department.

On physical examination, also he had grey hair, with a face appeared older than his age. Locally the ulcerated lesion measured about 2.5x5 cm on the dorsum of the right hand toward the ulnar side at the metacarpal area, with infected bleeding granulation tissue surrounded by crusts

(Figure 6), and with associated palpable antecubital and axillary lymph nodes. The radiographs revealed no bony erosion. A few months later, the lesion became deeper and extensive because of delay in surgery.

Local lesion excision with ray amputation of the ring and little fingers was performed, and after 7 to 8 months postoperatively the patient returned with locally recurrent fungating infected lesion at the previous surgical site involving the dorsal and volar portions ulnarly extending to the proximal part of the middle finger (Figure 7). Later, surgical amputation of the right hand was performed.



Figure 6: An ulcerated SCC involving the dorsum of the hand initially.



Figure 7: Local recurrence of SCC at the previous surgical site.

Discussion

Epidermolysis bullosa dystrophica is a rare hereditary disease, with an estimated incidence of approximately 1 in 300,000 live births, and the disease affects mostly the stratified squamous epithelium^{4,7,8}. The dystrophic scarring in RDEB is the most prominent and often leads to the development of hand deformities, and has the greatest degree of blistering and ulceration^{1,2,5,9}. All the hand structures may be affected, cutaneous involvement results in fibrosis, contractures, and atrophic finger tips. In response to each episode of relatively minor trauma or mechanical stresses to the hand with recurrent tissue damage, ulceration produces fibrinous adhesions and scarring, and subsequent healing cause dermal and subdermal fibrosis^{1,2,5}.

Patients with severe recessive DEB who survive to childhood are at significant risk of developing SCC at the site of chronic lesions, and may begin as early as the teenage years^{3,5}. Many series found that more than 40% of patients with RDEB develops carcinomas by 30 years of age, and many cases die of metastatic SCC^{3,5,7}. The pathway for SCC development in these cases may be attributed to the

frequent malignant degeneration of the stratified squamous epithelium in the adulthood. Also, repeated injury and healing of damaged skin, scarring, and chronic wounds such as nonhealing ulcers may play a role in the development^{4,7,10,11}.

According to some authors, SCC tends to grow and spread faster in people with RDEB than in those without the disease^{3,5}, and may primarily occurs in the hand, often develop over the dorsum of the joints and tends to be extremely aggressive and surgical excision is the only effective therapy^{2,3,6}.

This is a report of 2 brothers from the south of Iraq (Basrah, Fao) with RDEB since childhoods who were diagnosed by the dermatologist, and during the follow up they found to have a non-healing skin lesion over the dorsum of their right hands, SCC was suspected, and confirmed with skin biopsies, they were referred to our orthopaedic department relatively late, when there was an ulcerated SCC, with no improvement following repeated local treatments.

Initially, a wide local excision and ray amputation was performed, and a few months later subsequent fungating axillary

lymph node metastasis occurred in one case, and local recurrence in the other, which necessitated axillary lymphadenectomy, and amputation of the hand for the recurrent tumor.

To our knowledge, SCC regarded as the most common malignant tumor of the hand, approximately 15% of all SCCs arise in the hand, and the dorsal surface is the most common location and are locally aggressive¹²⁻¹⁵. A higher rate of metastasis has been reported for tumors occurring in the hand (6% to 30%), usually to the regional lymph nodes^{14,15}.

The local recurrence rates following surgical excision of SCCs of the hand in several series range from 5%–28%^{11,14,16}, and the risk of recurrence has been linked to the initial diameter and depth of the tumor, with rate of 15% in larger lesions (>2 cm), or due to failure to excise the primary tumour with the positive margins^{15,17,18}.

The SCC presenting on the dorsal skin of the hand had a high risk for recurrence

and metastasis, and most metastases are found within the first 2 years, with 95% evident within the first 5 years, and SCCs arising in areas of previous injury have a poor prognosis because they tend to metastasize early^{15,19}.

Finally, RDEB is a rare inherited skin disorder, and SCC is not uncommon in this disease characteristically develop in the hands, which have potential for aggressive local growth and metastasis, and the metastatic SCC is one of the important causes of death when the diagnosis of the disease or its complications failed. Therefore this reinforces the importance of recognition of RDEB with close follow up, to facilitate the early identification of malignant lesions in suspected cases, and treatment to prevent severe complications, because in late cases the surgical excision of extensive lesions may be challenging and becomes increasingly difficult, also there will be a higher rates of metastasis and local recurrence.

References

1. Fiona Mullet. A review of the management of the hand in Dystrophic epidermolysis bullosa. *J Hand Ther* 1998; 11:261- 265.
2. Catina Bernardis, Rachel B. Surgery of the hand in recessive dystrophic epidermolysis bullosa. *Dermatol Clin* 2010; 28:335–341.
3. Kam L. Ellis, Joshua J. Age and etiology of childhood epidermolysis bullosa mortality. *J Dermatolog Treat* 2015; 26(2):178–182
4. Campiglio G.L, Pajardi G. A new protocol for treatment of hand deformities in recessive dystrophic epidermolysis bullosa. *Ann Hand Surg* 1997; 16(2): 91- 101.
5. Shan Pai, Peter M. Marinkovich. Epidermolysis Bullosa: New and emerging trends. *Am J Clin Dermatol* 2002;3(6): 371- 378.
6. Van Rengen A, Degreef H. Epidermolysis bullosa dystrophica of Hallopeau-Siemens and squamous cell carcinoma. *Dermatology* 1996;192(4):418-420
7. A Chaves, S Carvalho. Epidermolysis bullosa dystrophica and anesthesia. *Internet J Anesthesiology* 2008;22(1):1-4.
8. Amy L. Ladd, Alice K. Surgical treatment and postoperative splinting of recessive dystrophic Epidermolysis bullosa. *J Hand Surg* 1996; 21A (5): 888- 897.
9. Robert L. Horner. Involvement of the hand in Epidermolysis bullosa. *J Bone Joint Surg* 1971;53A (7): 1347- 1356.
10. Donna M. Hepper, Clifford T. Hepper. Treatment options of squamous cell carcinoma of the dorsal hand. *JHS* 2009; 34A:1337- 1339.
11. Ross Rudolph, Daniel E. Zelac. Squamous cell carcinoma of the skin. *Plast Reconstr Surg* 2004; 11(6): 82- 94.
12. Jennifer A. Wilson, Alan T. Evans. Pathology of malignant tumours of the skin. *Surgery* 2010; 28(10):473- 477.
13. Patrick J. O'Neill, Christopher Litts. Hand and forearm reconstruction after skin cancer ablation. *Clin Plastic Surg* 2004; 31:113– 119.
14. Sarvam P. TerKonda, Galen P. Non-melanotic skin tumors of the upper extremity. *Hand Clin* 2004; 20:293–301.
15. Morad Askari, Sanjeev Kakar. Squamous cell carcinoma of the hand: A 20- year review. *J Hand Surg* 2013; 38A:2124-2133
16. Erum N. Ilyas, Charles F. Skin cancers of the hand and upper extremity. *J Hand Surg* 2012; 37A:171–178
17. Christopher English, Warren C. Hammert. Cutaneous malignancies of the upper extremity. *J Hand Surg* 2012; 37A:367–377
18. R. Motley, P. Kersey. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. *British J Plastic Surg* 2003; 56: 85–91
19. Ann-Marie Plate, German S. Malignant tumors of the hand and wrist. *J Am Acad Orthop Surg* 2006; 14: 680-692.