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Case Report

CASE REPORT

Squamous cell carcinoma in a pregnant woman with recessive dystrophic epidermolysis bullosa

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Abstract

We report the case of a pregnant woman with recessive dystrophic epidermolysis bullosa. During pregnancy, she presents with a large, rapidly growing, tumor on her right forearm, whose biopsy revealed an invasive squamous cell carcinoma. Amputation by the middle third of the forearm was performed at 21 weeks of pregnancy, without intra- or post-operative complications. The remainder of pregnancy was unremarkable and, at 36 weeks, she gave birth to a healthy baby. One month after delivery, a large lymph node conglomerate was detected in the right axilla, highly suggestive of metastatic disease and complete lymph node dissection was then performed. Despite the prompt institution of chemotherapy, the patient died a few months later due to metastatic disease.

INTRODUCTION

Epidermolysis bullosa (EB) comprises a group of disorders characterized by skin fragility and bulla formation in areas of minor mechanical trauma. It is caused by mutations in genes that encode structural proteins of epidermis, dermal-epidermal junction or papillary dermis. Recessive dystrophic epidermolysis bullosa (RDEB) is one of its most severe subtypes. It is a rare disorder, with an incidence of 3 per 1 million live births [1]. A major complication of this condition is the development of aggressive squamous cell carcinoma (SCC), which is frequently the cause of death in these patients. Considering patients with severe generalized RDEB, the cumulative risk of death from SCC at age 45 is around 70% [2]. The etiology of these tumors is still unclear but appears to be related with repetitive tissue ulceration leading to a loss of cellular differentiation, as well as decreased immunosurveillance. The risk of developing SCC seems to be proportional to the severity and extent of ulceration in the skin [3].

Despite the vast literature on the incidence of SCC in patients with RDEB, its management during pregnancy is a challenging topic that has not been described to date.

CASE REPORT

We present the case of a caucasian 25-year-old female diagnosed at birth with RDEB. She had a history of recurrent esophageal strictures (subjected to multiple endoscopic balloon dilations) and a miscarriage 2 years earlier. As for family history, she had two healthy parents and one sister also affected by the disease. There was no history of consanguinity in the family or with her current partner.

Fourteen weeks pregnant (G2P0), she presents to the Dermatology Department with a 6-month history of a rapidly growing, painful lesion in her right hand and forearm. The lesion started before pregnancy as a small painful papule on the wrist which rapidly grew and ulcerate. She denied any other risk factors for

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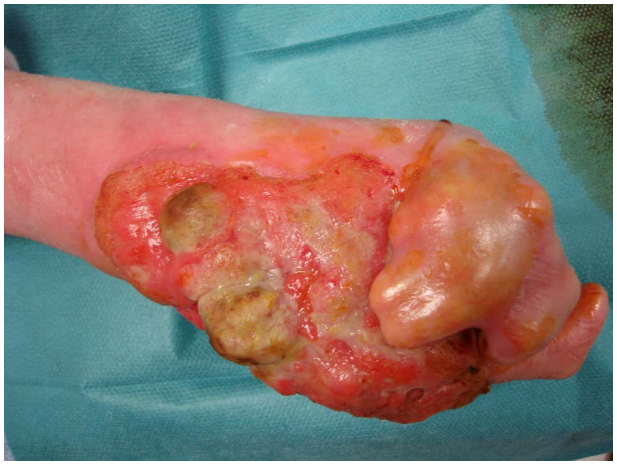

Figure 1: Ulcerated, bleeding tumor on the right hand and forearm with abundant foci of keratinization.

cutaneous neoplasia, such as excessive solar exposure, radiotherapy or the use of immunosuppressive medication.

On examination, she had an exophytic, ulcerated, hemorrhagic tumor involving almost the entire palmar surface, extending from the base of the digits to the distal third of the forearm and lateral border of the thumb, measuring about 11 cm (Fig. 1). Additionally, enlarged, hard lymph nodes were palpable in the right axilla, with 3 cm in diameter. Stigmas of its underlying pathology were also present, such as fusion of the fingers (pseudosyndactyly), extensive scarring and milia on trauma prone areas.

A lesion biopsy and additional imaging studies were performed. Skin biopsy revealed an invasive SCC (Fig. 2). Hand and forearm magnetic resonance imaging showed a heterogeneous soft tissue mass invading the muscular plane, without apparent bone invasion. A thoraco-abdominopelvic computerized tomography showed the absence of systemic metastasis. Axillary ultrasound showed a 32 mm long lymph node conglomerate with suspect ultrasonographic features. Fine-needle biopsy of this mass revealed the absence of epithelial cells and the presence of small lymphocytes and histiocytes, suggestive of reactive lymphadenopathy.

The case was discussed at the oncology multidisciplinary group, whose decision was amputation by the middle third of the forearm. The surgery was performed at 21 weeks of pregnancy and underwent without intra- or post-operative complications, with no signs of fetal distress. The histopathological examination of the surgical specimen showed a moderately differentiated SCC with invasion of muscle and tendon sheaths and signs of perineural invasion. The excision was complete.

The next few weeks were uneventful. Prenatal testing was performed and no genetic anomalies were found. At 36 weeks of gestation (only 15 weeks after surgery), the patient gave birth by cesarean delivery to a healthy baby with no signs of skin pathology.

One month after delivery and with no signs of recurrence of the primary lesion, the physical examination revealed the growth of the previously detected axillary mass. The positron emission tomography–computed tomography (PET–CT) demonstrated a hypercaptant lymph node conglomerate highly suggestive of metastatic disease (Fig. 3). Thus, 7 weeks after delivery the patient underwent complete right axillary lymph node dissection without intercurrences. Pathological examination of the specimen revealed metastases of SCC in four of the excised lymph nodes, with evidence of perineural invasion.

Despite the prompt institution of chemotherapy, the patient died 6 months after delivery due to neoplastic progression.

DISCUSSION

EB is a heterogeneous group of rare disorders characterized by epithelial fragility with blistering, erosions and ulcers after minimal trauma. Based on the skin cleavage plane, it can be classified into four major groups: EB simplex, junctional, dystrophic, and Kindler syndrome [4]. Dystrophic EB is caused by mutations in the COL7A1 gene that encodes collagen VII [5], and it can be transmitted in an autosomal recessive or dominant fashion.

The management of pregnancy in patients with RDEB can be challenging particularly during delivery, as it can be associated with anesthetic complications and genital ulceration, scarring and stenosis [6]. A correlation between EB and intrauterine growth restriction has also been suggested [7]. Nevertheless, the evidence suggests that RDEB does not contraindicate pregnancy, although the risk of complications may be higher [8].

SCC is the leading cause of death in patients with RDEB [2]. It shows an aggressive behavior, with high recurrence and metastization rates [3]. Its management in pregnancy in patients with EB is a highly complex topic. Given the initial presentation of the tumor and the patient's good general condition, the radical excision of the lesion with limb amputation by the distal third seemed the most sensible attitude, combining the curative potential of the surgery with poor fetal morbidity, enabling the

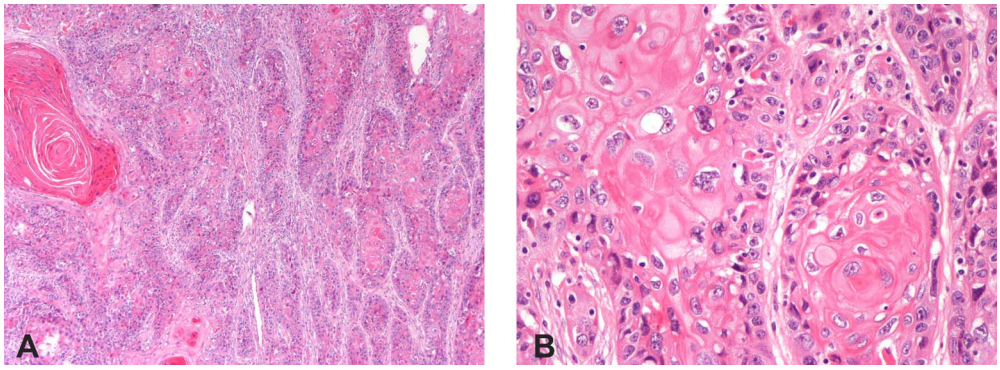

Figure 2: (**a**) Invasive SCC with abundant keratinization (hematoxylin and eosin, ×100); (**b**) squamous epithelium with visible intercellular bridges (hematoxylin and eosin, ×400).

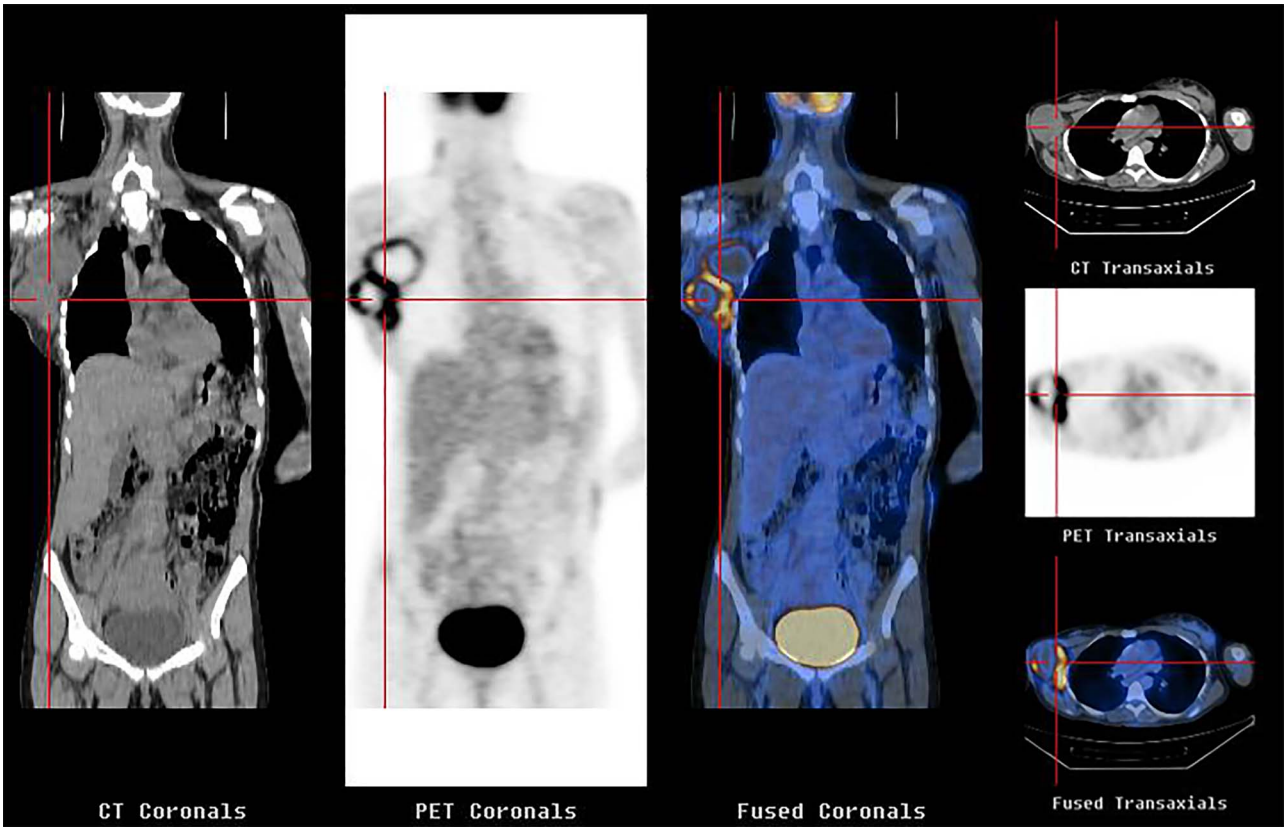

Figure 3: PET–CT with fluorodeoxyglucose showing a large hypercaptant lymph node conglomerate on the right axilla.

normal course of pregnancy. Despite our best efforts, the condition would eventually result in the patient's death, a frequent scenario given the general behavior of these tumors.

This case depicts the aggressive behavior SCC in patients with RDEB. Its management during pregnancy is a highly sensitive topic, for which there are no reports in the literature. Overall, this case brings a new perspective on the management of the disease and its complications during a delicate period of life. With this case we hope that we have demonstrated the therapeutic challenges this rare condition imposes during pregnancy.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

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ETHICAL APPROVAL

The case is exempt from ethical approval in this institution.

INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review on request.

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