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Research Article

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Pregnancy And Delivery in Late Diagnosed Kindler Syndrome: A Case Report And Review of The Literature

Malihe Ghasemi[1], Mohammad Javad Najafi[2], Atousa Mortazavi Milani[3*], Ghasem Rahmatpour Rokni[4] and Amin Ghanbarpour[5]

[1]*Assistant Professor, Department of Obstetrics & Gynecology, Faculty of Medicine, Mazandaran university of medical sciences*

[2]*Clinical Research Development Unit of Imam Khomeini Hospital, Mazandaran university of Medical Science, Sari, Iran*

[3]*Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran*

[4]*Associate Professor of Dermatology, Department of Dermatology, Mazandaran University of Medical Sciences, Sari, Iran*

[5]*Department of Anesthesiology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran*

[*]Corresponding Author
Atousa Mortazavi Milani, Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

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Abstract

Epidermolysis bullosa is a collection of infrequent, diverse, and genetic disorders with four primary classifications, identified by the skin's vulnerability and, in some cases, mucosal fragility. The skin and mucosal layers separate when subjected to friction or mechanical stress, leading to blisters and erosions within these tissues. A woman aged 29, afflicted with Kindler syndrome, presented at our hospital experiencing labor contractions. Her skin condition remained unaltered throughout her pregnancy and post-childbirth period. A cesarean section was carried out at the 38-week gestation mark due to an unplanned membrane rupture and dense meconium presence. The healing of the surgical wound proceeded without complications. In this instance, the patient's pregnancy did not intensify the skin-related symptoms of Kindler syndrome. It is critical to manage perioperative care to safeguard susceptible skin and mucosa carefully. The patient's journey throughout pregnancy and the postnatal period proceeded without notable incidents. Individuals with EB giving birth often require substantial assistance due to their condition.

Key Words: Epidermolysis Bullosa, Kindler Syndrome, Pregnancy

1. Introduction

Today, improving outcomes for pregnant women with rare diseases such as genetic defects has received increasing attention [1]. Accurate screening for early diagnosis and management of genetic diseases once a diagnosis is confirmed, along with access to prenatal diagnosis, means that more women reach reproductive age and can make informed choices about pregnancy and childbirth [2]. Despite all the advances in this field, managing pregnant women suffering from some genetic diseases, such as epidermolysis bullosa (EB), still requires more extensive studies and investigations due to infrequent evaluation in the literature.

Epidermolysis bullosa (EB) is a cluster of uncommon, diverse, and hereditary disorders marked by the frailty of the skin and sometimes the mucosa. Friction or mechanical injury prompts the separation of skin layers, leading to the development of blisters and erosions in the skin and mucosal tissues. There are four main subtypes of EB, each classified according to the depth of the ultrastructural separation within the skin: epidermolysis bullosa Simplex (EBS), Junctional epidermolysis bullosa (JEB), Dystrophic epidermolysis bullosa (DEB), and Kindler epidermolysis bullosa (KEB) (Table 1).

Type	Involved skin area	Inheritance pattern
EB Simplex	Epidermis layer	AD, AR
Dystrophic EB	Dermo-epidermal interface within basement membrane	AD, AR
Junctional EB	Dermis layer	AR
Kindler syndrome[a]	Multiple levels within the basement membrane	AR

EB- Epidermolysis bullosa; AD-Autosomal dominant; AR- autosomal recessive.
[a]Our patient had Kindler syndrome.

Table 1: Inherited epidermolysis bullosa Classification.

The severity of the disease in EB patients varies, both within each subtype and among different subtypes. For instance, patients with milder forms of EBS may face minimal disruption in their daily activities and maintain a regular life expectancy. Conversely, those with severe recessive DEB (RDEB) encounter substantial illness and potentially life-restricting complications associated with their condition [3,4].

Kindler syndrome (KS) is a rare genetic skin disorder with autosomal recessive inheritance, initially identified by Theresa Kindler in 1954 [5]. Since then, more than 250 cases have been reported worldwide [6]. The disease is associated with mutations in the FERMT1 (KIND1) gene, located on the short arm of chromosome 20 (20p12.3) that characterized by skin blistering and poikiloderma combination [7].

Since 2007, KS has been classified in the Epidermolysis bullosa (EB) group, with variable levels of skin separation and trauma-induced skin fragility [7]. In this study, we present here a pregnant woman and her labour course with KS in Iran, diagnosed at late age.

2. Presentation of Case

29 years old pregnant woman gravid 1 at gestational age 38 weeks was referred to our tertiary Hospital (Imam Khomeini Hos. Sari, Iran) (Figure 1). She was born in a rural family after 6 brothers. At birth, she had skin lesions in the form of skin blisters on the first finger of the right hand, and gradually, during infancy, more blisters were formed in different parts of the body. She also had a history of minor labia adhesions, which did not follow up. At age 2, she took a course of medical treatment due to the possibility of skin allergy, which was unsuccessful. At the age of 9, she was admitted to the hospital due to the blister's growth and infection. During the hospitalization, amputation was recommended, but due to the lack of consent of the patient's parents, it was not performed, and finally, he recovered with expectant treatment and medication after two weeks. From the age of 12, the patient's disease progressed more slowly, and the blisters did not develop spontaneously, but they continued to develop following trauma. At the age 19, they were diagnosed with Kindler syndrome by going to diagnostic centers and doing genetic tests, and it was confirmed that it was transmitted from the carrier's parents. All 6 brothers of the patient mentioned a history of similar skin lesions, and all of them were confirmed to have Kindler syndrome after a genetic exam. At the age 20, he underwent surgery due to urinary tract adhesions. She married 1.5 years ago, and her contraception was withdrawn. She mentioned that she got a vaginal lesion after coitus.

She came to our obstetric emergency with labor pain. Her primary physical exam was one finger loose, cephalic, without effacement, with 25 seconds of contractions every 4 minutes. Her prenatal screening and cell-free test were normal. During labor, routine tests were performed for her, which were normal. Dermatological consultation was requested, the route of delivery was determined based on obstetric indication, and the disease does not prevent cesarean section or natural delivery, and no need to do special action before or after delivery.

She was admitted to the maternity ward, and biophysical and Non-stress tests were performed for her. The biophysical test score documented 6 from 8, and NST was non-reactive, also she candidates for an oxytocin challenge test, but in her labor phase, she had a spontaneous rupture of the membranes, and due to thick meconium and lack of imminent delivery, according to the examination (one finger loses), she was a candidate for emergency cesarean section (CS). After being transferred to the operating room, the patient was given spinal anesthesia. The delivery result was a boy with an Apgar score of 9-10 and a weight of 31150 grams, with no apparent skin problems. She had uncomplicated postpartum course, without blister development; she discharged on second postoperative day and her pfannenstiel scar view after postpartum follow-up period was normal (Figure 2).

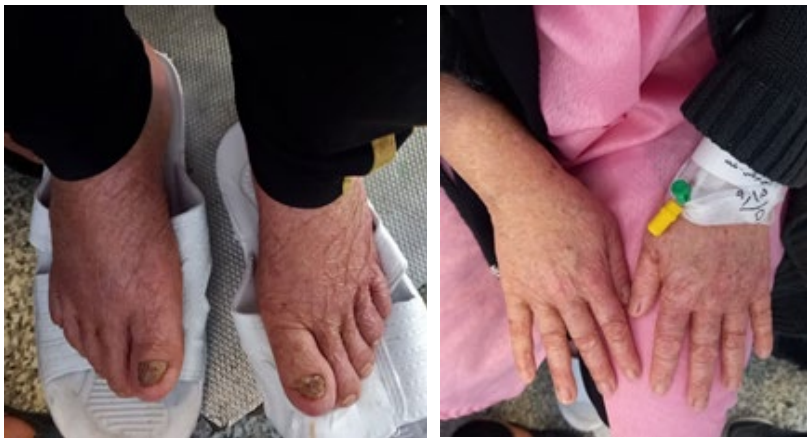

Figure 1: Appearance of the patient in admission

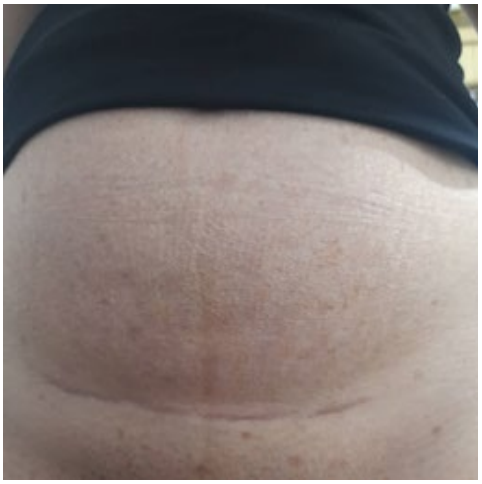

Figure 2: Pfannenstiel scar view after postpartum follow-up period

3. Discussion

Kindler syndrome is a rare skin syndrome and one of the types of EB, which clinically manifests with minor blisters following trauma at birth or in the first days of life, which regress with age. Photosensitivity, poikiloderma, skin fragility, and diffuse skin atrophy occur in infancy or early childhood, especially in areas of skin exposed to sunlight. Photosensitivity usually decreases with age, while poikiloderma and atrophy are progressive throughout life [8].

Kindler Syndrome can be confirmed through immunofluorescence mapping and/or by identifying mutations in the FERMT1 gene [9]. This particular gene is responsible for the production of kindlin-1 protein in keratinocytes, and its absence results in reduced adhesion between the dermis and epidermis. Up until now, over 70 distinct pathogenic variants have been detected in the FERMT1 gene [6].

Angelova-Fischer et al. in 2005 proposed five main criteria and two sub-clinical diagnostic criteria as well as some relevant clinical findings for the diagnosis of KS [10]. The main criteria suggested were acral blisters in infancy and childhood, progressive poikiloderma, skin atrophy, abnormal photosensitivity, gingival fragility and/or swelling. Partial suggested criteria are syndactyly and mucosal involvement (stenosis of the anus, esophagus, urethra, larynx). The diagnosis is "definite" in the presence of four main criteria. The presence of three main criteria and two minor criteria makes the clinical diagnosis "probable", and if there are two main criteria and two minor criteria or related findings, the diagnosis is considered "likely" [11]. The algorithm proposed above has not yet been confirmed in comparison with laboratory results, especially in relation to the investigation of mutations in the FERMT1 gene. Therefore, it can only be useful in the clinical practic when genetic tests are unavailable.

KS has been described mainly in Arab, Iranian, Pakistani, Indian, and Turkish origin. It has also been identified in European people, especially those of British Caucasian, Italian, Albanian, and Serbian descent [6,9,10].

The principles of pregnancy care in patients with all types of EB are the same regardless of the disease subtype, and pregnancy is relatively uncommon due to disability and concerns about affected children [12,13]. However, some studies have reported successful pregnancy outcomes even in affected women [13-

19]. Complications related to pregnancy in women with EB are rare and the disease does not seem to progress during pregnancy [12,13]. Pregnancy in affected individuals may be associated with malnutrition, severe anemia, and chronic infection and should be considered [15].

In 2022, experts from all over the world came together and based on previously published studies, they presented a consensus-based guideline for the management of pregnancy and delivery in patients with epidermolysis bullosa, which we used in patient management [20].

Our patient is a candidate for the oxytocin challenge test. Still, due to spontaneous rupture of the membranes, thick meconium, and lack of imminent delivery, she is a candidate for emergency cesarean section. Natural vaginal delivery is considered safe and is generally preferred over CS, even if a baby with EB is expected to delivered [12]. In theory, it is possible to create a blister in the vaginal mucosa, the possibility of shedding the epithelium of the cervix and perineum, and damage to the soft tissue of the pelvic floor [13]. Prolonged labor and immobility and related complications may be associated with the possibility of lesions in the back, hips and arms [15]. Episiotomy is an option to prevent perineal tears [12]. In addition to obstetric indications, CS may be indicated when genital tract involved to minimize perineal blisters [13]. Although there is a possibility of blistering and scarring at the incision site, cesarean wounds heal well in women with EB [13]. Intrapartum EB precautions were meticulously followed in our patient without complications (Table 2, Table 3). Rates of skin blistering in affected fetuses remain the same in both delivery modes. Although there are no differences in outcome between vaginal and cesarean deliveries, risks and benefits should be discussed in all cases.

Caution during cardiotocography due to the possibility of blisters
Minimize internal examination, only when absolutely necessary
Adequate lubrication of intrauterine pressure catheter
Avoid internal fetal monitoring
Limit insertion of hands into the vagina when patient is pushing during second stage of laborAvoid operative delivery (vacuum extraction, forceps delivery)

Table 2: Considerations during vaginal delivery.

Gel or soft foam padding for pressure areas such as trunka and extremities
Minimize handling and transfer of patients, no rolling or sliding devices, encourage auto-positioning
Adequate padding beneath intermittent pneumatic compression devices
Cut adhesive border of electrocautery pad, leaving only gel surface and secure with silicone-based tapeb
Consider bipolar diathermy instead of monopolar diathermy to avoid electrocautery pad
Non-adherent surgical field drapes
Consider bigger skin and tissue incisions to aid in the atraumatic delivery of the neonate
Subcuticular sutures can be used for the closure of skin
Avoid vigorous rubbing to stimulate the infant at the time of delivery

Table 3: Intrapartum considerations cesarean section.

After delivery, postpartum care is important. Tight pain control is important to prevent excessive movement and new skin damage [21]. In most cases, pruritus in EB is a bothersome condition, worsened by the use of narcotics for pain control and analgesia. If necessary, it is better to prescribe anti-pruritic drugs in the initial stages. While there is no contraindication for breastfeeding, the presence of blisters may make this process annoying and painful. Lubricated nipple shields may help reduce blister formation [13]. Thrombotic events do not appear to be at increased risk [15]. If necessary, it is safe to perform injections away from areas with skin lesions [14].

In this instance, the patient's pregnancy did not worsen the skin symptoms of Kindler syndrome. Vigilant perioperative care is essential to shield the susceptible skin and mucosa. Our patient's pregnancy and postpartum course remained uneventful. Parturients with EB often need considerable support due to their disability. A coordinated team approach can facilitate uneventful outcomes [22].

Patient (parent's) Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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