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Case Report **Open Access**

Suspected epidermolysis bullosa simplex with anonychia and sepsis in a malnourished 7-month-old infant in Katsina, northwest Nigeria: A case report.

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Abstract:

Epidermolysis bullosa (EB) is an uncommon hereditary cutaneous disorder inherited largely in an autosomal dominant manner. Epidermolysis bullosa simplex (EBS) typically presents at birth or early childhood, and common presenting complaints include blistering, skin fragility, and non-healing wounds inconsistent with mechanical trauma. It is associated with several complications such as sepsis, malnutrition, malignancy, and so on. The management of EBS is mainly supportive. The prognosis is good with early detection, wound care, infection control, nutritional support, and counseling. We present a case of suspected EBS-Dowling Meara type with acquired anonychia and sepsis in a malnourished 7-month-old infant in Katsina, and to the best of our knowledge the first reported case in northwest Nigeria.

Keywords: Epidermolysis bullosa simplex; Anonychia; Sepsis; Malnutrition; Infant

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Épidermolyse bulleuse simplex suspectée avec anonychie et septicémie chez un nourrisson de 7 mois souffrant de malnutrition à Katsina, dans le nord-ouest du Nigéria: à propos d'un cas

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Résumé:

L'épidermolyse bulleuse (EB) est une maladie cutanée héréditaire rare, héritée en grande partie de manière autosomique dominante. L'épidermolyse bulleuse simple (EBS) se présente généralement à la naissance ou dans la petite enfance, et les plaintes courantes comprennent des cloques, une fragilité cutanée et des plaies non cicatrisantes incompatibles avec un traumatisme mécanique. Elle est associée à plusieurs complications telles que la septicémie, la malnutrition, la malignité, etc. La gestion d'EBS est principalement solidaire. Le pronostic est bon avec une détection précoce, des soins des plaies, un contrôle des infections, un soutien nutritionnel et des conseils. Nous présentons un cas suspect de type EBS-Dowling Meara avec anonychie acquise et septicémie chez un nourrisson de 7 mois souffrant de malnutrition à Katsina et, à notre connaissance, le premier cas signalé dans le nord-ouest du Nigeria.

Mots clés: Épidermolyse bulleuse simplex; Anonychie; État septique; Malnutrition; Nourrisson

Introduction:

Epidermolysis bullosa (EB) is a rare hereditary cutaneous condition inherited largely in an autosomal dominant manner (1). EB defines a group of rare, inherited dermatoses, characteristically featuring skin fragility secondary to structural defects in the dermo-epidermal junction. Minor mechanical trauma and shear stress can consequently aggravate skin blistering, erosions, and ulceration (2,3). This predisposes patients with certain forms of EB to a higher risk of infection, disabling deformities and aggressive cutaneous malignancy, causing early death in some cases. A wide-ranging phenotypic variety is described, from fragility and blistering confined to areas of weight-bearing or pressure to widespread generalized engrossment, together with extracutaneous disease. Hence, certain subtypes of EB confer high morbidity, with a risk of increased mortality due to multi-system pathology (4,5). EBS is reported to occur equally in males and females (2).

Mutational changes in sixteen genes have been implicated in at least 30 observed EB subtypes. Each subtype is characterized by varying phenotypic severity and influence on morbidity and mortality. These subtypes have been organized into 4 major groups based on the ultrastructural plane within the dermo-epidermal junction that the defect affects; (i) Epidermolysis bullosa simplex (EBS) comprises about 70% of all EB cases and is characterized by a fragility defect in the epidermis, typically inherited in an autosomal dominant pattern (2,6); (ii) Junctional epidermolysis bullosa (JEB) is an autosomal recessive fragility defect associated precisely with the lamina lucida and makes up about 5% of all EB cases (2,6); (iii) Dystrophic epidermolysis bullosa DEB) comprises about 25% of all EB cases and might be autosomal dominant or recessive and is a fragility defect underneath the lamina densa of the basement membrane zone (2,6); and (iv) Kindler epidermolysis bullosa (KEB) is the infrequent of the 4 major EB types inherited in an autosomal recessive pattern. The kindlin-1 protein is affected in KEB, resulting in fragility in any dermo-epidermal junction plane (2,6).

Four clinical forms of EBS are known, ranging from mild blistering of the hands and feet (EBS, Weber-Cockayne type) to a generalized blistering EBS (Kobner type), EBS with mottled pigmentation, and the deadly Dowling Maera type EBS (7). The defect in all types of EBS is in the central á-helical coil of keratin 5 and 14 which makes up intermediate filaments of the basal keratinocytes. Keratin 5 and 14 genes are located on chromosome 17q and 12q respectively. The intraepidermal bullae result from cytolysis of the basal cell (2).

EBS initially presents at birth or early childhood, and common presenting complaints include blistering, skin fragility, and non-healing wounds disproportionate to mechanical trauma. A family history of similar complaints may be present. Additionally, pain and pruritus are common concerns. Blistering is distributed with bias for sites prone to pressure and friction, with the hands, feet, buttocks, and knees most susceptible. The diaper region is also susceptible in neonates, infants, or children (8).

Several complications have been associated with EBS due to the fragile nature of the skin, and they include chronic blisters, scarring, infection, pain and discomfort, malnutrition, esophageal strictures, anemia, heat intolerance, psychosocial impact, and eye involvement (2,8). Early diagnosis, expert medical care, and a multidisciplinary approach are essential for managing EBS and minimizing complications (2,8). Management and prevention usually include counselling, wound care, pain management, avoidance of trauma, nutritional and psychosocial support (2,8). The aim of this case report is to raise awareness about the existence of EB in Katsina and northern Nigeria.

Case presentation:

We present a 7-month-old male child who was referred from a primary healthcare centre, and initially managed at Turai Umaru Yar'adua Maternal and Children Hospital Katsina (TUYMCH) but later referred to the Federal Teaching Hospital (FTH), Katsina, on account of the detachment of the fingernails and toenails since birth. The first nail removal was noticed 6 hours after delivery involving the fingernails of the thumb. This progressively continued to involve the removal of all the nails in the fingers within 40 days of life. Fingernail removal was preceded by swelling of the proximal part of the nail bed (cuticle and lunula) of the fingers and toes extending to the lateral part of the nail bed after which the nail fell off spontaneously. The detachment of the nails was associated with pain and bleeding which subsequently involved the toenails, there was complete removal of all the toenails by the second month of life. There is no history of such in the family or other siblings.

Bullous blister swelling was noticed around the perineum one week after birth which ruptured, formed ulcers, and healed afterward without scarring. Similar bullous blisters were seen over the scalp, face, trunk, and upper and lower extremities, rupturing after pressure application, and becoming ulcerated. Some of the ulcers healed without scarring while new ones emerged. There was associated pain and itching. The recurrent skin blis-

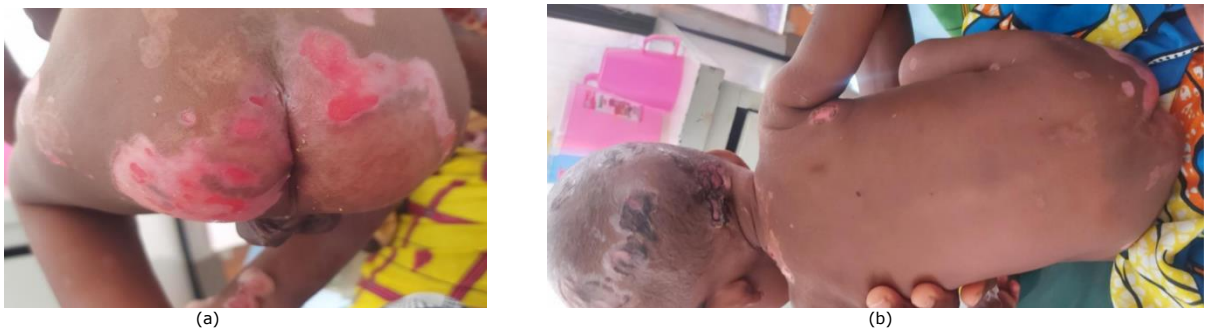
ters and ulceration persisted till presentation. There was a history of easy denudation of the skin after applying pressure such as tourniquet and plaster during admission.

Fever was noticed 2 weeks before presentation and was high-grade intermittent. Child also passed watery stool 5-6 bouts per day, mucoid and non-bloody and had some oral medications at several health centres including herbal medicines with no improvement. Mother is para 7, the pregnancy was unbooked and delivery was at home through spontaneous vaginal delivery (SVD). The child was not exclusively breastfed and complementary diet was commenced at 4 months of life. He was fully immunized for age according to the National Programme on Immunization (NPI) schedule.

On examination, the child was lethargic, febrile (39.8^{o}C), and malnourished, with erosion of the skin and ulcerations over the elbows, right pinna, trunk, perineum, ankles, and both feet (Fig 1). There was also swelling and ulceration of the fingers and toes (Fig 2). Weight for length z-score was less than 3 (weight 4.5 kg, length 59.5 cm), mid-upper arm circumference (MUAC) was 106 mm, haemoglobin concentration was 9.9g/dl, and random blood sugar was 9.5mmol/l.

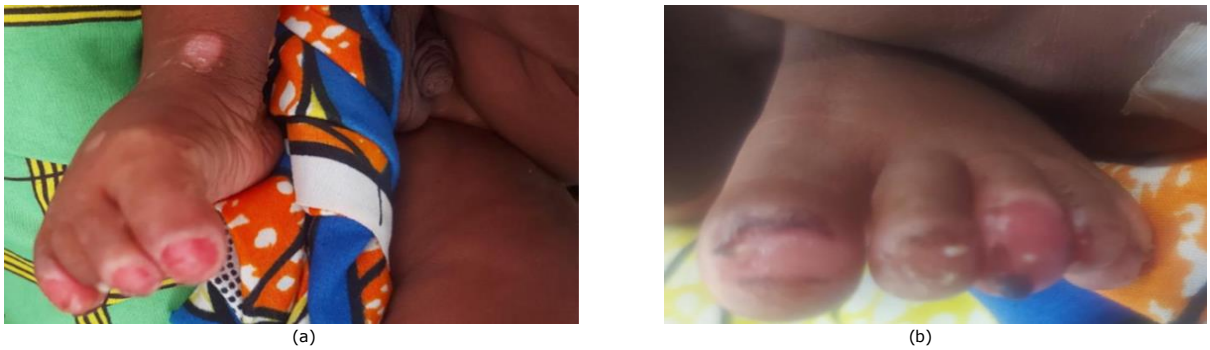
Initial diagnoses of severe acute malnutrition (SAM) with suspected sepsis, epidermolysis bullosa simplex and acquired anonychia, were made. Features suggestive of sepsis were lethargy, inability to feed, fever, and diarrhea. About 2 milliliters of blood was aseptically collected from the peripheral vein into an appropriately labeled Bact/Alert pediatric bottle, which was then moved into a closed flask and instantly transported to the laboratory for analysis, using BacT/Alert Blood culture and VITEK-2 compact system for bacterial identification and antibiotic susceptibility test.

The infant was placed on empirical antimicrobial combination of intravenous ceftriaxone and clindamycin, and received intramuscular 750 i.u. of anti-tetanus serum (ATS), F-75 milk and Ready-to-Use Therapeutic (RUTF) nutrition, and daily wound dressing with soft-ratulle after saline bath. Dermazin cream and gentamicin cream were also topically applied. Other supportive management in line with the hospital pediatric unit protocol were given pending the outcome of blood culture. Blood culture results after about 20 hours with the VITEK-2 compact system detected *Staphylococcus aureus* sensitive to cefuroxime, ceftriaxone, cloxacillin, and vancomycin. Patient completed the course of antimicrobial therapy and was discharged 10 days after admission to commence follow-up care. However, he was lost to follow-up.



(a) (b)

Fig 1: Erosion of the skin with ulcers over: (a) perineum, ankles, and feet; and (b) elbows, right pinna, and trunk



(a) (b)

Fig 2: Swelling and ulceration of: (a) fingers and (b) toes

Discussion:

Epidermolysis bullosa (EB) is a group of inherited bullous disorders characterized by blisters formation in response to mechanical trauma (9). EBS initially presents at birth or early childhood. Common presenting complaints include blistering, skin fragility, and non-healing wounds inconsistent with mechanical trauma (9). Our diagnosis was based on history and physical examination, and the infant presented with the typical pattern of developing blisters on the hands and feet from birth with detachment of the nails, with associated complications such as sepsis and malnutrition.

Just as symptoms of generalized severe EBS were earliest seen at birth, our patient also had swelling and redness of the nailbeds which subsequently led to the detachment of all the nails with ulcers over the nail bed of the fingers in the hands and toes of the feet within 6 hours of birth to 40 days of life. The patient presented with the characteristic pattern of development of blisters over the face, trunk, perineum, scalp, and extremities with detachment and removal of the nails. Blisters usually occur as a sequel to minor pressures or trauma. In our patient, the blisters on the skin were more on the perineum, extremities, and scalp which may have been triggered by friction during the changing of diapers, changing of clothes, and shaving of hair.

The generalized severe EBS subtype (Dowling Meara type) was found in our patient. In this subtype, blisters occur at birth, nails are usually affected. Blisters often occur anywhere on the body. Though they improve as they grow older, widespread skin involvement and thickened skin which may interfere with movement can also occur, but this could not be ascertained in our patient who was lost to follow-up care after discharge. Peterside et al., (10) in Yenagoa, Nigeria reported similar conditions in their patient, an infant, who was also born with blisters formation peeling of the skin, and detachment of the nails from birth and associated sepsis. Their diagnosis was also made based on history and physical examination. Similar to our patient, Oseni et al., (11) in Owo, Nigeria reported three patients with similar skin presentation, even though they faced diagnostic difficulty and mortality. However, their patients had skin biopsy done for histology to confirm the diagnosis and were neonates as against ours. In Benin City, Nigeria, Kubeyinje et al., (12) reported an 8-year-old boy with recurrent blistering skin disorder since birth with associated destruction and loss of nails like our patient.

A similar condition like our patient was reported by Amal et al, (13) in Russia in a 23-year-old Caucasian with severe EB but no family history of similar skin disorder. Although the patient's mode of inheritance of EB was autosomal recessive, which was confirmed by indirect immunofluorescence (IF) using antibodies to various skin proteins (that was not done in our patient), there was no history of similar skin lesions in the parents, family, and seven other children. There is a likelihood of this condition not being recessive but a sporadic *de novo* genetic mutation in the patient as reported by Wakiguchi et al., (14) in Japan and Ferreira et al., (15) in Brazil. In addition, the patient reported by Amal et al., (13) developed pyoderma and increased frequency of allergy to food. This could not be assessed in our patient who was an infant and lost to follow-up, as against theirs who was an adult.

EBS is associated with several complications due to the fragile nature of the skin, which includes, infection, malnutrition, anae mia, and others. Our patient presented with features of sepsis and malnutrition. Blood culture results using the VITEK-2 compact system detected *S. aureus*, sensitive to cefuroxime, ceftriaxone, cloxacillin, and vancomycin. In the EBS case reported by Otaigbe et al., (15), heavy growth of *Klebsiella* spp from blood culture was seen while wound swabs yielded heavy growth of both *Pseudomonas aeruginosa* and *S. aureus* sensitive to ceftriaxone and gentamicin. Frank and Kern (16) reported malnutrition associated with EBS in a 60-year-old man who developed skin ulcers since birth and also developed large squamous cell carcinoma, that was not seen in our patient who presented at infancy and lost to follow-up.

The management of EBS is mainly supportive. While a high index of suspicion must be raised among clinicians when a child is seen with blistering skin lesions and ulcers, infection is a major complication which is due to extensive loss of protective skin. Hence, there is a need for urgent empirical antibiotic coverage. Other supportive care such as proper wound and skin care, pain relief, nutritional support, and counseling are important. Epidermolysis bullosa is rare in Nigeria with few reported cases (7,10,11,12,17). This is the first reported case in Katsina in Northern Nigeria.

Conclusion:

EBS is a rare condition that is associated with several complications such as sepsis and malnutrition. The diagnosis of this condition in resource-poor settings like ours is hampered by the non-availability of immunofluorescent antibody/antigen mapping and transmission electron microscopy of skin biopsy, hence diagnosis can easily be missed. The management of EBS is mainly supportive. The prognosis is good with a high index of suspicion, early detection, wound care, infection control,

nutritional support, and counseling. This case was reported with the aim of raising awareness about the existence of such conditions in Katsina and Northern Nigeria.

Contribution of authors:

AOB, MK, ONAE, OM, MAL, UA, ABT and OHK conceived and developed the idea of the case report; AOB, MAL, and UA managed the patient; and OHK performed the laboratory work. All authors contributed and approved the final manuscript submitted for publication.

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Conflict of interest:

No conflict of interest is declared.

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