Clinical and Epidemiological Features of 19 Cases of Congenital Icthyosiform Erythroderma in Northern Nigeria: A case series

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ABSTRACT

Congenital Icthyosiform Erythroderma (CIE) is a rare genetically related skin disease (genodermatosis) that is characterized by abnormal keratinization of the skin. The disease is a variant of autosomal recessive congenital icthyosis that presents with collodion membrane at birth, generalized erythroderma and fine white scaling of the skin. It is a lifelong disease that is associated with psychological, physical, emotional and financial burden to the patients and their families. It is a rare disease with a prevalence of 1/200000 to 1/1000000 million birth. High incidence of consanguinity has been reported in pedigrees of CIE and this may play a role in transmission of the recessive defective genes causing the disease. We present a case of 19 family members with CIE associated with high rate of consanguineous marriage among the family members.

INTRODUCTION

Congenital Icthyosiform Erythroderma (CIE) is a non-syndromic disorder of keratinization that is limited to the skin[1]. The condition was described by Broq in 1902 although Sangster had earlier reported it in 1885[2]. Most patients with NBCIE are born with a collodian membrane which cracks after few weeks to reveal diffuse erythroderma and generalized fine, white, semi adherent scales. Additional features may include palmoplantar hyperkeratosis, ectropion, eclabium, alopecia, nail dystrophy or ridging[3]. Mutation of ABCA12, ALOX 12B, ALOX E3, TGT1, CYP4F22 and NIPAL4 are responsible for most of the cases of CIE. These genes are primarily concerned with transcription of proteins that maintain skin barrier function[1,3].

CIE is one of the autosomal recessive conditions termed "Autosomal recessive congenital icthyosis"[1]. It is a rare disease worldwide with a prevalence of 1/200000 – 1/1000000 birth[3]. However, consanguineous marriage may increase the risk of inheriting identical copies of recessive detrimental genes there by leading to expression of rare diseases[4,5]. Consanguineous marriage is practiced by 20% of worlds' population depending on their cultural, traditional, religious and socioeconomic status[5]. Northern Nigeria is a predominantly Moslem society with most of its inhabitants being the Hausas and the Fulanis and consanguineous marriage is quite common in this part of Nigeria[6,7]. There are reports of CIE associated with consanguinity from different parts of the world[8,9,10], but to the best of our knowledge such reports are rare from West Africa, Nigeria inclusive. We did not also come across any report of CIE affecting such large number of people from the same family anywhere in the world.

CASE REPORT

Nineteen members of an extended family (11 males and 8 females) between the ages of 1-49 years were been born encased in a tough shiny membrane that cracked and peeled off few weeks after birth. Shedding of the membrane was followed by generalized redness, dryness and fine white skin of the whole skin and scalp. No outward turning of the eyes (ectropion) or mouth (eclabium), absence of hair or nails. No hearing, visual problem or delay in developmental milestones and no short stature. Six of the affected family members (5 males and 1 female) died early in life before the age of five, cause of death could not be ascertained. However, one of them died as an adult following a road traffic

accident. There is high rate of consanguineous marriages among the family members, all parents of affected family members are first or second cousins and are phenotypically normal.

On examination, there was generalized xerosis and fine white scaling of the skin and scalp in all the patients. Palmoplantar hyperkeratosis is present in 11 of the patients. Erythroderma was however not pronounced in most of the patients at presentation although there was history of such at birth. Seven of the patients had wrinkling of the hands and feet while 5 have large plate-like icthyosis on their shins. Two of the patients have palmar hyperlinearity and transverse ridging of the nails. No alopecia or madarosis.

Serial No.	Gender	Age	Collodian Memb.	Gen. scaling/ erythroderma	Palmoplanter keratoderma	Large Plate icthyosis on the legs	Wrinklig of hands /feet	Heat intolera nce	Hyper Linear palms	Outcome
1	F	49	+	+	+	+	+	+	_	Alive
2	F	45	+	+	+	–	+	+	–	Alive
3	F	27	+	+	+	+	+	+	–	Alive
4	F	44	+	+	+	+	+	+	–	Alive
5	F	37	+	+	–	–	–	+	–	Alive
6	M	17	+	+	–	–	–	+	+	Alive
7	M	30	+	+	–	–	–	+	–	Alive
8	M	30	+	+	+	–	–	+	–	Dead (typhoid)
9	F	1	+	+	–	–	–	Not known	–	Dead (pneumonia)
10	F	19	+	+	+			+	+	Alive
11	M	1	+	+	–	–	–	Not known	–	Dead (diarrhoea)
12	F	26	+	+	+	+	_	+	_	Alive
13	M	44	+	+	–	–	+	+	–	Alive
14	M	33	+	+	+	+	–	+	–	Alive
15	M	45	+	+	+	–	+	+	–	Dead (RTA)
16	M	38	+	+	+	–	+	+	–	Dead (headache)
17	M	22	+	+	+	–	–	+	–	Alive
18	F	5/12	+	+	–	–	–	Not known	_	Alive
19	F	3/12	+	+	_	_	_	Not known	_	Dead (cause unkown)

Table showing clinical and demographic characteristics of the patients

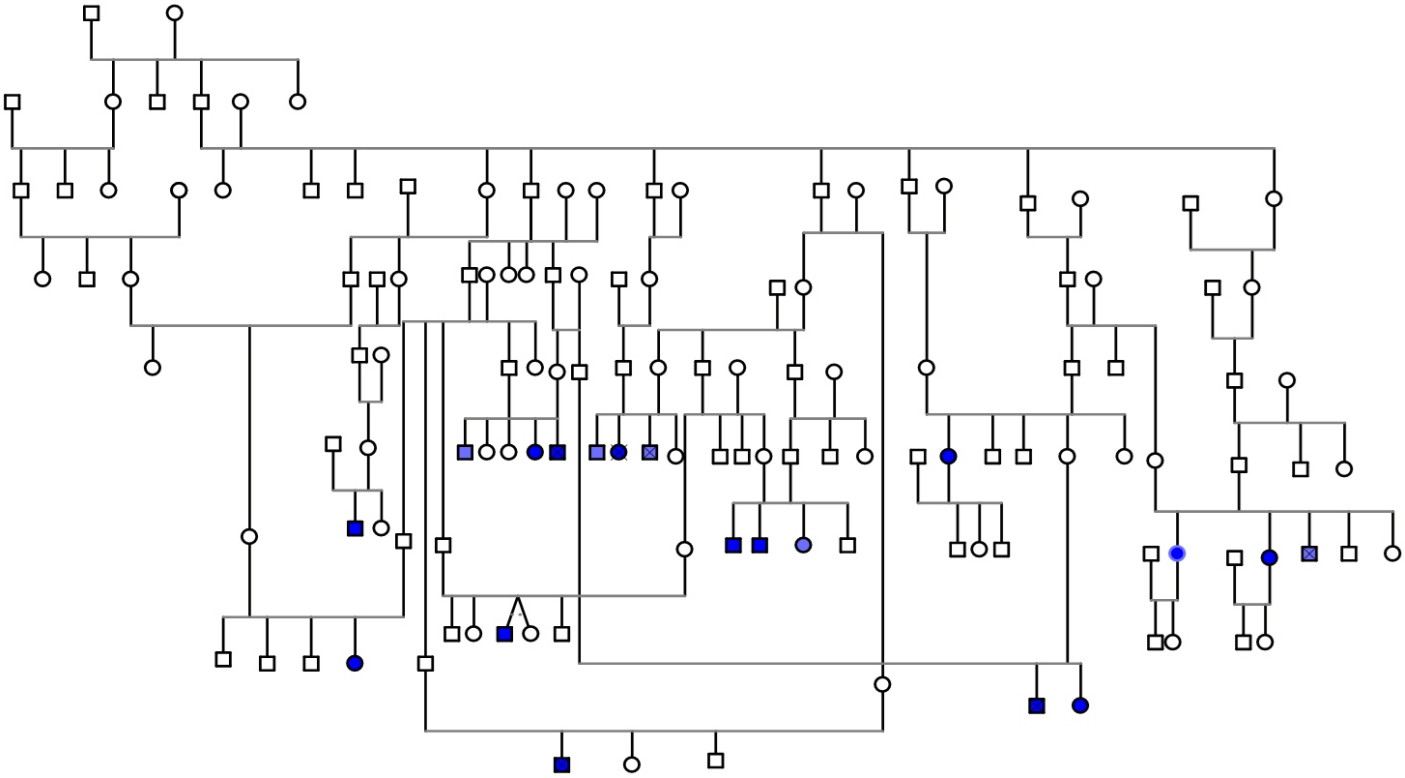

Fig 1: family pedigree showing the high rate of consanguinity among the family members and affected members with NBCIE

Fig 2: picture of some of the patients showing xerosis and fine white scaling of the skin.

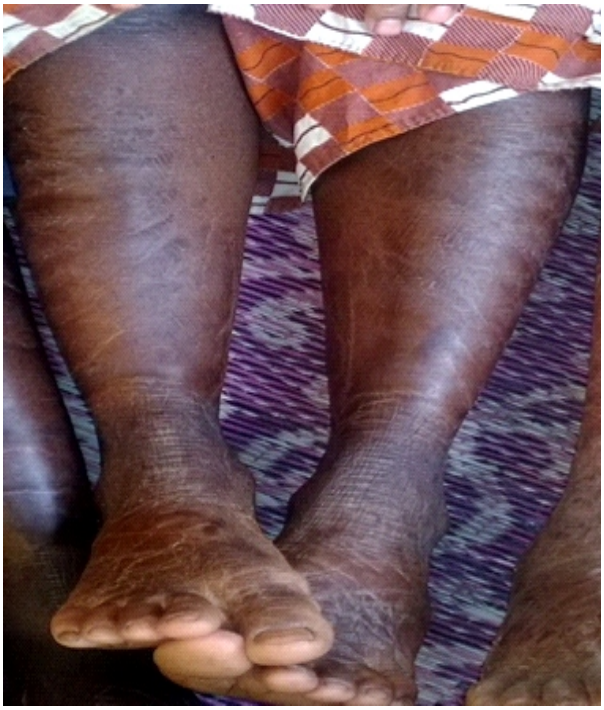

Fig 3: Picture showing large brownish scales on the legs

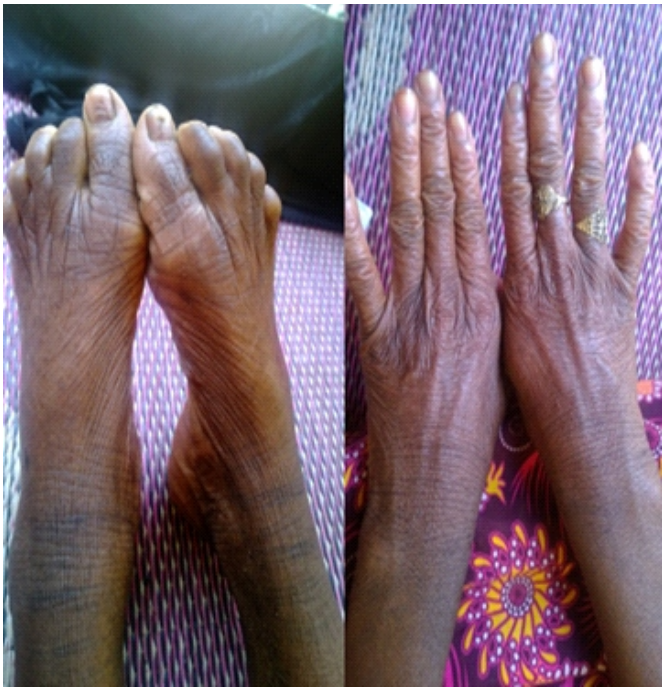

Fig 4: Wrinkling of the hands and feet, transverse ridging of the toe nails

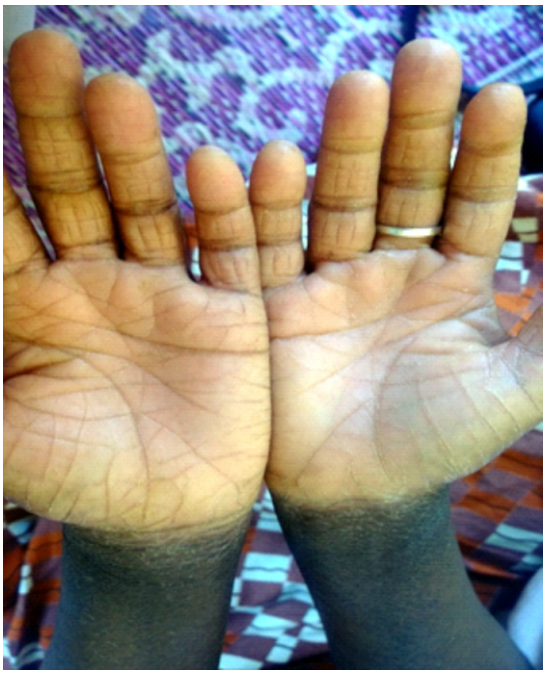

Fig 5: palmar hyperlinearity

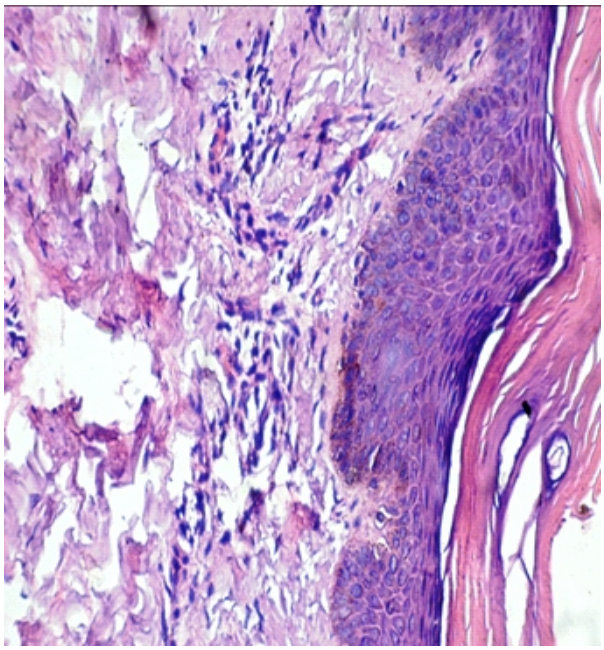

Fig 6: hyperkeratosis, hypergranulosis, acanthosis and superficial dermal infiltrates

Skin biopsy was performed on one of the patients. The result showed hyperkeratosis, mild hypergranulosis, acanthosis and superficial dermal infiltrates. Patients were counseled on the mode of inheritance of this condition and the effect of consanguinity on recessively inherited genetic diseases like NBCIE. They were then placed on 20% salicylic acid ointment for the palmoplantar hyperkeratosis and 8% urea lotion to be applied to the body, moisturizing soaps and to avoid long hot bath. Two of the patients with more severe symptoms were prescribed tabs acitretin 30mg daily for 2months.

DISCUSSION

Congenital Icthyosiform Erythroderma is a rare and severe form of Autosomal Recessive Congenital Icthyosis (ARCI) that is characterized

by abnormal keratinization of the skin[11]. There is paucity of data on the epidermiology of this rare and important disease. The prevalence worldwide is 1/200000 to 1/1000000 birth[3]. In the USA and Norway, the prevalence is 1/200000 to 1/300000 and 1/90000 births respectively[12]. Higher prevalence in Norway is believed to be due to 'founder effect'. There are few reports of CIE from Nigeria[13,14], but its prevalence is not known. We found 19 members of an extended family from Northern Nigeria to be affected by CIE; this is likely due to the high rate of consanguineous marriage in the family. This form of marriage is very common in Northern part of Nigeria[6,7]. In a study by Olatunji A et al in Northern Nigeria, 68% of the participants were into consanguineous marriages[7]. Additionally, Hampshire KR et al found consanguinity among the Fulani to be between 65.8% to 71%[6]. Similarly, in a study in Egypt, CIE was reported among 26.5% of patients with hereditary icthyosis and consanguineous marriage was reported among the parents of 79% of the patients[9]. In a study in Saudi Arabia by Al Amro et al, CIE constituted 0.2% of dermatological cases reported and consanguinity among the parents of CIE patients was 95%[14]

At birth, most cases of CIE (about 90%) present with collodion membrane[16] (as was the case in our setting). Al-Amro et al in Saudi Arabia reported that 90% of the 21 patients with CIE were born with a collodion membrane.[15] Additionally, CIE is said to be the commonest cause of collodian baby[1], it is therefore not surprising that all our patients had history of collodian membrane at birth. After shedding of the collodian membrane, the skin becomes covered with fine white semi adherent scales. All our patients presented with the fine white scaling of the skin and scalp but in addition, 5 of our patients have large plate-like icthyosis on their shins. Although large brownish plate-like scales are features of lamellar icthyosis, sometimes they may be present in patients with CIE.[1,15] Most of our patients reported heat intolerance. This is not surprising because of the thickness of the skin and scaling which does not allow sweet to reach the surface of the skin effectively and cool them. Patients with biallelic mutation in CERS3 gene present with large brownish scales on the legs, hyperlinear and hyperkeratotic palms and soles, as well as prematurely aged appearance of the skin.[16] This may explain the palmoplantar hyperkeratosis among 11 of our patients, the aged appearance (wrinkling) of hands and feet that was seen among 7 of the patients as well as the palmar hyperlinearity that was observed in 2 patients. Two of our patients have transverse ridging of the nails. Nail abnormalities like ridging, subungual hyperkeratosis and hypoplasia have been reported in about 50% of cases of NBCIE.[12] Although generalised erythroderma was said to have been present at birth, it was not prominent in most of our patients on examination. This could be due to their racial skin colour. Erythema may also be mild or invisible in later life in patients with ARCI.[12] Alopecia, eclabium and ectropium were not present in any of our patients, they are more commonly seen in patients with lamella icthyosis and in severe cases of CIE[1,15].

Histologically, CIE is indistinguishable from lamellar icthyosis.[5] There is hyperkeratosis, a normal or thickened granular layer and acanthosis.[1,5] Dermal perivascular superficial infiltrate seen more commonly in CIE[5] as observed in our patient. Management of CIE entails genetic counseling, use of mild keratolytics like alpha hydroxyl acids and humectants like urea (10-20%) and propylene glycol (40-60%). In severe cases, oral retinoids like acitretin at a dose of 0.1 to 0.75mg/Kg/day can be used intermittently to help reduce pruritus, erythema and scaling.[5] most of our patients improved on 20% salicylic acid ointment and 10% urea lotion. Two of the patients with more severe disease (large brownish scales on the legs, wrinkling of the hands and feet) were prescribed acitretin 30mg daily for 2 months with significant improvement.

CONCLUSION

Congenital icthyosiform erythroderma is a rare chronic skin disorder that affects the quality of life of the affected individual and that of his family. However, consanguineous marriage may increase the risk of homozygosity for the recessive defective genes there by making this disease more prevalent

in societies that practice consanguinity. Therefore, there is need for increased awareness on the health implication of consanguineous marriage and need for it to be discouraged. Similarly, increased awareness of prenatal diagnosis and genetic counseling will also be beneficial in this regard

LIMITATION

Although we found clustering of CIE among family members that have high rate of consanguinity, this report is not conclusive because we could not assay for the defective gene or genes in this family. Additionally, there is need for a more robust study to determine the clinical and epidemiological features of CIE in this part of Nigeria.

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