CASE REPORT

Dyskeratosis congenita in a Nigerian boy

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ABSTRACT

Dyskeratosis congenita is a rare hereditary disease. It mainly affects males and manifest between 5 years and 12 years. Its classic manifestation consists of skin pigmentary changes, nail dystrophy, oral leukoplakia, bone marrow failure and predisposition to malignany. We report the case of a 9-year-old boy who presented with hyperpigmentation of the skin, palms and soles, leukoplakia of the tongue, dystrophy of the nails, epiphoria and recurrent epistaxis with gum bleeding. Full blood count showed pancytopenia and bone marrow biopsy showed hypocellular marrow with no abnormal cells. He was transfused with pack red blood cells, platelets concentrate and was commenced on co-trimoxazole prophylaxis and anabolic steroid. He is currently on follow-up in the paediatric clinic.

Key words: Dyskeratosis congenita, nail dystrophy, oral leukoplakia, pancytopenia, skin pigmentation

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INTRODUCTION

Dyskeratosis congenita (DC) is a rare multisystem disorder first described in the early 20th century (1906); it is also known as Zinsser-Engman-Cole syndrome.[1] It is characterised by the classic triad of mococutaneous pigmentary disorder, nail dystrophy and oral leukoplakia seen in 89%, 80% and 45% of cases respectively.[2] However abnormalities involving the digestive system (oesophageal stricture, liver cirrhosis), ocular (corneal ulcers, conjunctivitis, blepharitis, lacrimal duct stenosis with epiphoria), neurologic (mental retardation, delayed developmental milestones) have also been reported,[3] and bone marrow failure occurs in about 75% of cases with X-linked form.[4] Bone marrow failure is the major cause of death, while other causes of mortality are pulmonary fibrosis and malignancy.

There is scarcity of information on this disorder among Nigerians to the best of our knowledge. Therefore, the case of a 9-year-old boy who presented with recurrent febrile illness, repeated blood transfusion with dystrophic nails and hyperpigmentation of the skin in whom a diagnosis of DC was made is reported.

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CASE REPORT

A 9-year-old boy presented with complaints of easy fatigability, recurrent nose and gum bleeding with recurrent blood transfusion of 2 months duration; he had four blood transfusions in the past 2 months. There was history of easy bruisability, but no history of prolonged bleeding following circumcision which he had at the age of 7 years. There was history of generalised darkening of the body, palms and soles with some whitish and dark patches on the tongue noticed around the age of 5 years. The patient had normal delivery and developmental milestones. He was the 2nd child in a monogamous non-consanguineous marriage setting of six children. There was no history of similar illness in other family members. The mother was a 30-year-old stay-at-home mother while the father was a 35-year-old self-employed trader. An initial diagnosis of acute leukaemia was entertained by the referring physician. The patient had epistaxis from both nostrils; he was pale with hyperpigmentation of the skin of the neck, chest [Figure 1], arms and palms of the hands [Figure 2]; and soles of the feet with scattered areas of hypopigmentation. He had some white and black plaques [Figure 3] on the tongue which were non-scrapable. There were dental caries, gum bleeds [Figure 4], while the other mucosal surfaces of the oral cavity were normal. Both eyes had epiphoria [Figure 5], but more on the right eye. The nails of both fingers and toes were cracked, ridged and atrophic [Figures 6 and 7]. The anthropometry, cardiovascular and respiratory system examinations were not remarkable. He had a normal renal function test with no skeletal anomaly.

The full blood count showed haemoglobin of 56 g/L white blood cells count of 2.0×10^9 /L (normal = 4 – 11 × 10^9 /L),

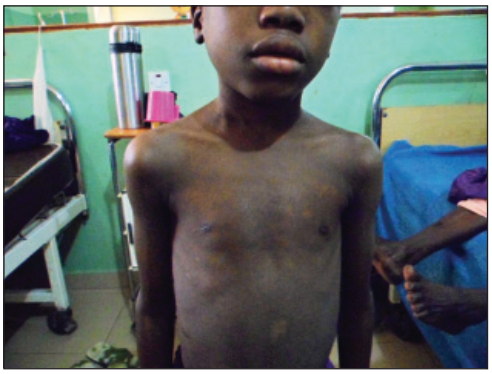

Figure 1: Hyperpigmentation of the skin of the neck, chest with areas of hypopigmentation

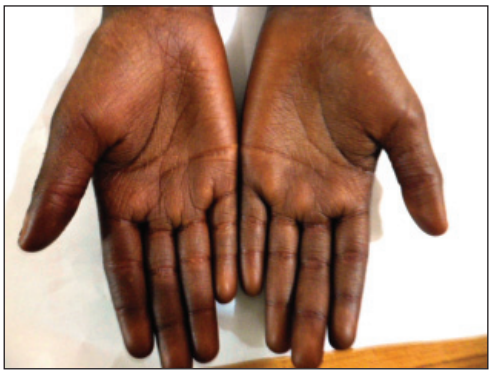

Figure 2: Hyperpigmentation of the palms

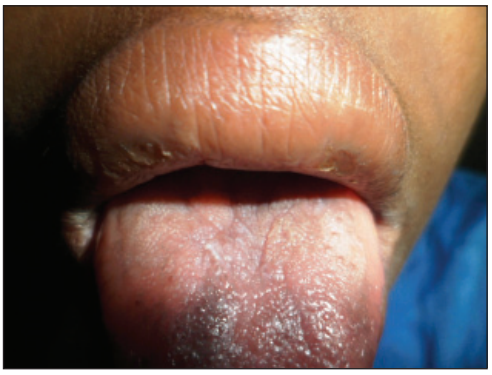

Figure 3: White and black plaques on the tongue

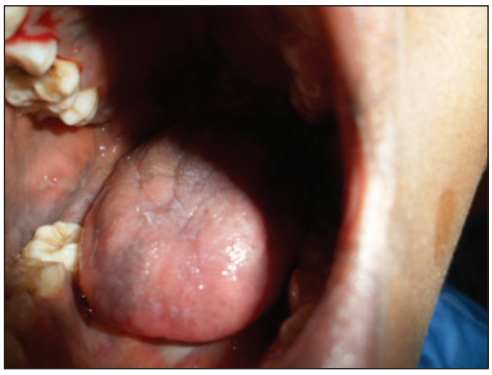

Figure 4: Dental caries with gum bleeds

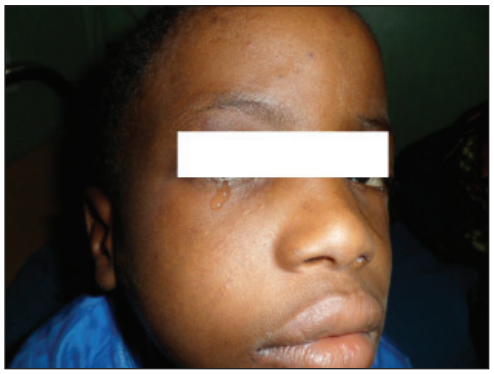

Figure 5: Epiphoria from both eyes

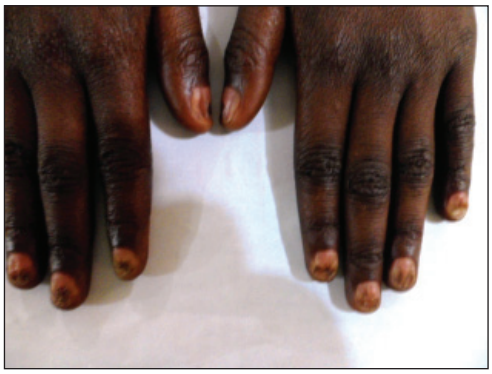

Figure 6: Dystrophic finger nails

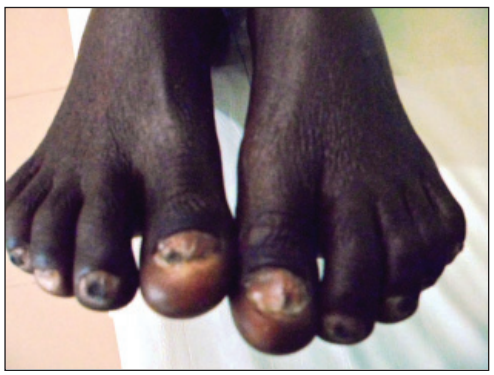

Figure 7: Dystrophic toe nails

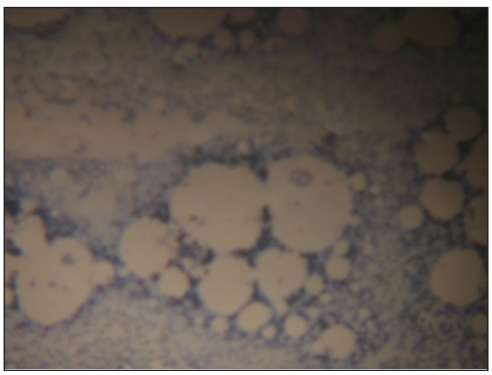

Figure 8: Hypocellular bone marrow

with an absolute neutrophil count of 1.0 × 10^9 /L, platelet count of 23 × 10^9 /L (normal = 150-450 × 10^9 /L), clotting profile was normal and bone marrow biopsy revealed a hypocellular marrow [Figure 8]; therefore, he had a pancytopenia. Based on the clinical and laboratory findings the diagnosis was DC. He was transfused with pack red blood cells and platelets concentrate twice. Epistaxis subsided and patient was stable. He was placed on co-trimoxazole prophylaxis and discharged home on oxymetholone. He was also referred for ophthalmologic evaluation which revealed lacrimal duct stenosis. Despite being on anabolic steroid for 12 weeks the bone marrow failure persisted and due to financial constraints he could not afford haematopoietic cell transplantation; he is currently on supportive care and is being followed up in the paediatric clinic.

DISCUSSION

DC occurs worldwide with very few cases reported so far.[5,6] Although X-linked, autosomal recessive and dominant modes of inheritance have been reported, our case had no family history of same disease and was a product of a non-consanguineous marriage, which makes a sporadic relationship most likely. DC is a disease with multisystemic manifestations. It is more common in males,[6] but the onset and progression varies. Those with mild manifestations may have minimal physical features with normal bone marrow function, while those with severe manifestation may present with serve multisystemic disorders like Revesz syndrome and Hoyeraal Hreidarsson syndrome[7] presenting early in childhood. In classical DC, most of the somatic abnormalities are often absent at birth, but develops with increasing age; therefore, the diagnosis of DC is often delayed until adulthood, but our patient had all the major clinical features which made the diagnosis easy even in the absence of genetic analysis. Our patient had the classic triad of the disease, namely skin hyperpigmentation, nail dystrophy and oral leukoplakia which fulfilled the clinical diagnostic criteria. He also had a severe manifestation of the disease, with early onset of bone marrow failure. Bone marrow failure is often delayed until the second decade of life, but our case presented early-at the age of 9-years-involving all the three major blood cell lines (pancytopenia).[5]

Dermatologic manifestation of DC can be reticular hyperpigmentation or hypopigmentation of the skin, especially affecting the neck and chest. The patient had hyperpigmentation of the skin of the neck, chest, arms and the palms and soles of the feet. White patches may affect the tongue, buccal mucosa or the palate, but the tongue is mostly affected. In our patient, the white patches were limited to the tongue. The epiphoria was attributed to lacrimal stenosis, while the dental caries and repeated gum bleeds are due to deficiencies in the neutrophils and platelets respectively.

The cause of DC has been linked to mutations in genes related to telomere maintenance (telomerase) and to date, eight genes have been implicated.[8,9] Mutations in a component of the shelterin complex are involved in autosomal dominant DC. The shelterin complex determines the structure of the telomeric terminus; it also controls the synthesis of telomeric DNA. Therefore, without the shelterin complex telomeres are exposed to the DNA damage-repair mechanisms, which may result in the ends of chromosome being incorrectly processed by the DNA-repair pathways predisposing to fusion of chromosomal ends during replication.[7]

The fact that pancytopenia did not respond to oral androgen and the non-availability of facilities for haematopoietic stem cell transplant, which is the main stay of treatment,[10] represent a big challenge in the management of this patient. Moreover, even if the patient had responded to steroids, a long-term anabolic steroid regimen may be complicated by side effects considering the age of this patient. Furthermore, oral anabolic steroid does not often cure pancytopenia.

CONCLUSION

DC is a rare genetic disorder with variable clinical expressivity. The case of a 9-year-old boy, who had all the major clinical features-hypo-/hyperpigmentation of the skin, nail dystrophy, leukoplakia and early bone marrow failure- which before now had not been documented in Nigeria, is reported.

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