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Case report

Dyskeratosis congenita (DC) in a Saudi boy: an uncommon genodermatosis

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Abstract A 6-year-old Saudi boy presented to our hospital with severe thrombocytopenia. The patient was managed for a long time (6 years) as having chronic idiopathic thrombocytopenic purpura. Later on features consistent with dyskeratosis congenita were recognized by the authors. The main features were: skin manifestations, nail dystrophy, alopecia totalis, microcephaly and mental retardation. The condition was associated with acute necrotizing ulcerative gingivitis. At the age of 10, he developed pancytopenia and died at the age of 14 years from acute fulminant sepsis.

Key words
Dyskeratosis congenita, acute necrotizing ulcerative gingivitis, pancytopenia.

Introduction

Dyskeratosis congenital (DC) is a rare genodermatosis and multisystem disorder, characterized by cutaneous reticulated hyperpigmentation, nail dystrophy and mucous membrane lesions (ulcers, premalignant oral leucoplakia), and progressive pancytopenia.[1] Bone marrow hypoplasia is frequent.[2] The majority of cases (90%) are males.[3] The age of presentation is between 5-15 years.[4] The most common pattern of inheritance is X-linked recessive caused by mutations in the DKC1 gene.[1] Autosomal dominant and recessive forms exist. The gene causing the X-linked recessive forms is located to Xq 28 and codes dyskerin, a 514 amino acid protein.[5] 80% of patients with DC have progressive bone marrow (BM) failure, which is the major cause of death.[6] Few of the patients die from pulmonary complications (e.g. fibrosis), and malignancy (acute myeloid leukemia and Hodgkin disease).[7]

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Case report

At the age of 6 years a Saudi boy presented to our hospital complaining of the following since the age of 6 months: chronic recurrent bleeding from gums, easy bruising following minor injuries, epistaxis and excessive tearing. During pregnancy his mother developed chicken pox. Delivery was normal with no problems. Developmental history revealed delayed speech and also other milestones. Parents were first degree cousins. There were nine siblings (7 males and 2 females) all were normal except one brother who died at the age of 3 years with similar complaint and physical picture as our patient and another 17-year-old brother with cutaneous hyperpigmentation, nail dystrophy and alopecia totalis but no

hematological manifestations. There were seven maternal uncles who died in early childhood (the cause not known).

Physical examination Our patient was pale, microcephalic, with alopecia totalis and sparse hair of eyebrows and eye lashes (**Figure 1**), dystrophic nails of the hands (**Figure 2**) and feet, reticular skin with hyperpigmentation of the neck (**Figure 3**), upper chest and lower limbs, multiple purpuric spots with ecchymosis over the neck and bleeding spots in the gums, throat and uvula. The skin on extensor surfaces of upper and lower limbs and soles was hyperkeratotic. There were also subconjunctival haemorrhages (**Figure 4**). Dental caries with enamel hypoplasia was evident. Mouth examination showed: acute necrotizing ulcerative gingivitis (ANUG) with focal acute pseudomembranous candidiasis. No hepatosplenomegaly or lymphadenopathy detected, with normal joints and genitalia. Vital signs were normal. The weight, height and head circumference were all below the 3rd centile. Retinal hemorrhages in both eyes revealed by fundoscopy.

Investigations done on admission: 1. CBC: WBC: 8.6x10^9/l, HB: 7.2 g/dl, MCV: 100.0 fl, MCH: 31.2 pg, MCHC: 31.2 g/dl, RDW: 17.9 between 2-17x10^9/l, reticulocyte count of 1.6%. 2. Peripheral smear: macrocytic anemia with severe thrombocytopenia. 3. Prothrombin time (PT) and activated partial thromboplastin time (APTT): normal. 4. Chemistry was normal.

Later on the patient had frequent admissions in the pediatric department with severe anemia, severe thrombocytopenia and bleeding, mainly from gums. Lastly he presented in August, 2000 (at the age of 12 years) with high

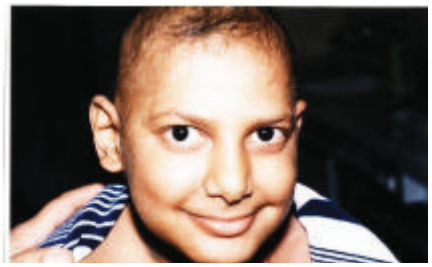

Figure 1 Pale, microcephalic child with diffuse alopecia over scalp and sparse eyebrows and eye lashes

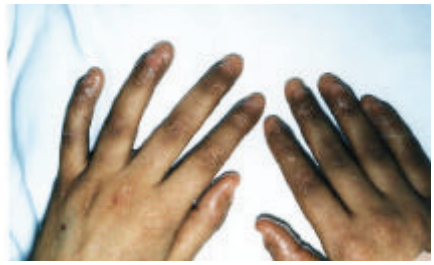

Figure 2 Dystrophic fingernails

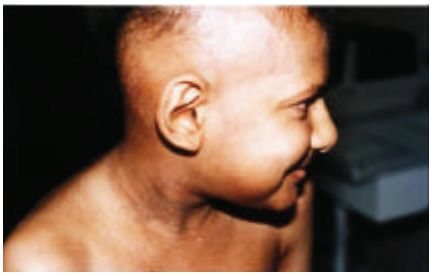

Figure 3 Reticulate hyperpigmentation affecting the sides of neck.

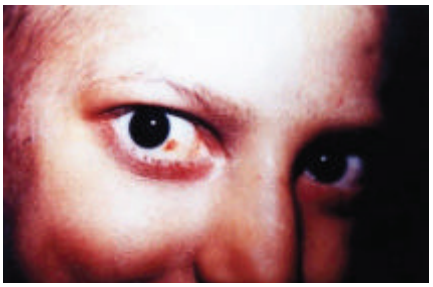

Figure 3 Subconjunctival hemorrhage in the right eye.

fever, multiple oral ulceration and same previous physical changes. Investigations at this time revealed: 1. CBC: severe pancytopenia, ESR: 122mm/hr. 2. Peripheral smear: anisocytosis, normochromia, some macrocytes and few spherocytes. There was severe leucopenia

with 51% lymphocytes and very low platelets count. 3. PT and APTT: still normal4. Chemistry, urea and electrolytes and hepatitis panel were normal 5. Hb electrophoresis: HbA-97.9%, HbA2-2.1% 6. Chest X-ray and X-ray of limbs were normal. 7. Ultrasound (U/S) abdomen showed: coarse echo pattern of the liver. 8. Liver function tests were mildly disturbed. 9. High serum ferritin of 3216 ng/ml. 10. Bone marrow aspirate: showed a picture of aplastic anemia. 11. Septic screening was done many times, showed no bacterial growth. CT brain: showed mild cerebral atrophy.

Management The patient received many courses of prednisolone tablets since the age of 6 years in different hospitals before he was seen by the authors. He received also short courses of androgens: oxymethalone 60mg OD and androlone 25mg intramuscular every 2 weeks. During the last 8 years, our patient received many packed red blood cells and platelets transfusions due to severe anemia and thrombocytopenia, and many courses of parenteral and oral antibiotics, due to repeated systemic infections of the lower respiratory tract. Bone marrow transplantation was planned, but at the age of 14 years (in 2002) our patient presented with severe fulminant sepsis and in spite of extensive and aggressive management in our pediatric intensive care unit he expired after two days.

Discussion

Since the age of 6 years our patient had been admitted in the hospital due to bleeding per gums and skin and found to have severe thrombocytopenia. He was diagnosed and managed as having idiopathic thrombocytopenic purpura. This attracts the attention to physicians and pediatricians of the importance of knowing such a rare condition like DC. We saw the patient for the first time when he was referred to our hospital at the age of 10 years, due to pancytopenia. At that time the following features were recognized: microcephaly, alopecia totalis with sparse hair of eye lashes and brows, dystrophic nails of the hands and feet, dermatologic features such as reticular hyperkeratotic skin and hyperpigmentation, which is the usual presentation in DC.[1] He also presented with mucous membrane changes in the form of acute necrotizing ulcerative gingivitis (ANUG), which from literature review is found to be common in patients with immunodeficiency and HIV infection.[8] ANUG is rare in DC. The patient was found to have bone marrow failure, which is considered to be a late manifestation of DC.[2,9,10] Differential diagnosis to be considered is Hoyeraal-Hreidarsson syndrome, a severe infantile variant of DC, inherited as X-linked manner, in which there may be overlap with DC.[1,11,12] The features of this syndrome include: intrauterine growth retardation, microcephaly, mental retardation, cerebral malformation, immunodeficiency and progressive bone marrow failure.[1] Our patient presented with microcephaly, mental retardation and brain atrophy, which is not the usual presentation of classical DC.[12]

Other differential diagnoses are Rothmund-Thomson syndrome (short stature, skin telangiectasias, small hands and feet, hypoplastic thumbs with a high risk of osteosarcoma) and graft versus host disease.[4] Our patient died at the age of 14 years with fulminant sepsis which is one of the leading causes of death in DC.[13] Other causes of death include bone marrow failure[6] and the development of malignancies, especially acute myeloid

leukemia[14] and squamous cell carcinoma,[2] which can occur on leucoplakia or normal mucous membranes and skin.[7] As mentioned, there was one brother, who died at the age of 3 years, another 17 year-old brother, who is still living, both with similar features and 7 maternal uncles who died undiagnosed, in early childhood, suggesting an X-linked mode of inheritance. The patient received androgens for the bone marrow failure as there is about 50% response15 in many cases, but in our patient there was no improvement.

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