

Dyskeratosis congenita: a rare congenital pancytopenia

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Abstract

Dyskeratosis congenita (DC) is a rare congenital disease involving integumentary system. It usually presents with classic triad of skin pigmentation of the upper chest and/or neck, nail dystrophy, and oral leukoplakia. Bone marrow failure (BMF) is a common complication of this disease and is an important cause of mortality in these patients. Here, we report a case of DC with BMF in a 13-year-old boy who was admitted for fever with pancytopenia with hypo- and hyperpigmented skin lesions. He was subsequently treated with blood component transfusion followed by hematopoietic bone marrow transplantation. DC must be suspected in a case of pancytopenia with skin lesions.

KEY WORDS: fever, pancytopenia, dyskeratosis congenita

Introduction

Dyskeratosis congenita (DC) is a rare congenital disease involving integumentary system. It is a male-predominant disease, and clinical manifestation occurs generally between 5 and 12 years. In complete expression of this syndrome, there is classic triad of skin pigmentation of the upper chest and/or neck, nail dystrophy, and oral leukoplakia. At least two features of the triad are required for the clinical diagnosis of classical DC. In this case report, we describe the case of a 13-year-old boy who presented with classic symptoms and signs of DC along with bone marrow failure (BMF). The boy was subsequently treated with blood component transfusion for acute management, followed by hematopoietic bone marrow transplantation (HSCT) for long-term purpose. It is quite pertinent to say that a high degree of suspicion is required for the diagnosis and consequent treatment of this rare case.

Case Report

A 13-yr-old nondiabetic nonhypertensive Hindu boy born out of nonconsanguineous marriage presented with recurrent episodes of fever for the past 6 months and decreased

appetite. He also showed skin lesions in chest. There was no history of seizure, vomiting, cough, chronic diarrhea, dysuria, and joint pain. There was exertional dyspnea (NYHA class 2). He had received blood transfusion three times in the past. There was no family history of any chronic illness. Examination revealed poor nutrition with a body mass index of 16.3 kg/m² (height, 4'8"; weight, 33 kg), pallor, hypo-hyperpigmented macular and patchy skin lesions involving chest with reticulated pigmentation in body [Figure 1], and ridging, splitting and atrophy of nails in all four limbs [Figure 2]. There was no icterus, edema, clubbing, or enlarged lymph nodes. Pulse was 120/min; blood pressure, 100/60 mm Hg right arm supine position; and



Figure 1: Hypo- and hyperpigmented skin lesions on chest.

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Figure 2: Splitting and atrophy of nails in hand.

temperature, 102 F. Leukoplakia was present in the oral cavity involving buccal mucosa and tongue [Figure 3]. Cardiovascular system examination revealed tachycardia with accentuated heart sounds and a systolic murmur (grade 2) in the pulmonary region. Sternal tenderness was present. Other systemic examinations were noncontributory.

Blood examination showed hemoglobin (Hb) of 1.7 g/dL; red blood cells, $0.5 \times 10^6/\mu\text{L}$; white blood cells (WBC) total count (TC), $1500/\mu\text{L}$; differential count, N75, L22, E2, M1, B0; erythrocyte sedimentation rate (ESR), 180 mm (first hour); platelet, $90,000/\mu\text{L}$; packed cell volume, 5.9%; mean corpuscular volume, 90.5 fL; mean corpuscular hemoglobin, 32.7 pg; mean corpuscular hemoglobin concentration, 28.8 g/dL; reticulocyte count, 1.5%; and creatinine, 0.7 mg/dL. The results of liver function tests were normal. Blood culture revealed colonies of *Klebsiella pneumoniae* sensitive to piperacillin. HBsAg, anti-HCV, and HIV 1 and 2 were nonreactive; malaria parasite dual antigen test result was negative. No evidence of tuberculosis was found. (Mantoux test and sputum test for tubercle bacilli were negative.) Vitamin B12 was 554 pg/mL and folate 7 ng/mL; ANA test was negative, and thyroid hormone profile and cortisol showed normal levels. Serum ferritin was a bit higher but other parameters of iron profile were at normal levels. Ultrasonography of the abdomen was within normal limits. A bone marrow analysis of this patient revealed hypoplastic marrow without any granuloma. Echocardiography showed normal results. Skin biopsy showed lack of melanin in the dermis along with atrophy of the epidermis. The patient was advised a genetic testing for telomere length detection, but his family could not afford that. He was treated with parenteral antibiotics, blood component transfusion, and subsequently transferred to the hematology ward for bone marrow transplantation. At discharge, his hemogram report was Hb, 9.5 g/dL; WBC TC, $2500/\mu\text{L}$; differential count, N70, L25, E4, M1, B0; ESR, 40 mm (first hour); and platelet, $100,000/\mu\text{L}$.

Three months after discharge, he was found to be doing fine. He had also gained some weight and confirmed to attend follow-ups on a regular basis.



Figure 3: Oral leukoplakia in the same patient.

Discussion

DC, first described by Zinsser in 1906 (also known as Zinsser–Cole–Engman syndrome), is a rare, hereditary disease. DC is a male-predominant disease (M:F = 3:1), and clinical manifestation occurs between 5 and 12 years. In complete expression of this syndrome, there is classic triad of skin pigmentation of the upper chest and/or neck, nail dystrophy, and oral leukoplakia.^[1–3] At least two features of the triad are required for the clinical diagnosis of classical DC.^[4] Additional features present are BMF, epithelial cancers, myelodysplastic syndrome, leukemia, epiphora, blepharitis, prematurely gray hair, alopecia, developmental delay, short stature, cerebellar hypoplasia, microcephaly, esophageal stenosis, urethral stenosis, pulmonary fibrosis, liver disease, and avascular necrosis of hips or shoulders.^[5] DC involves X-linked transmission in most cases. The responsible gene encodes for a protein “dyskerin” that is essential for ribosomal biosynthesis and telomerase RNP assembly. Autosomal dominant form is also reported and has mutations in the human telomerase RNA component (hTERC). These defects lead to diminished telomere length.^[6] There are two major and severe subtypes of DC: first, Hoyeraal–Hreidarsson (HH) syndrome, a severe form of DC characterized by cerebellar hypoplasia, microcephaly, developmental delay, immunodeficiency, intrauterine growth retardation (IUGR), and BMF. The original descriptions of HH also included cerebellar hypoplasia.^[7–9] Second, Revesz syndrome (RS) presents with BMF and exudative retinopathy, IUGR, sparse fine hair, and central nervous system calcifications; some patients also show nail dystrophy and oral leukoplakia.^[10,11]

As per clinical presentation, our patient belongs to classic DC with BMF. He did not reveal any malignancy on presentation. In DC, HSCT is the best treatment for hematologic problems such as BMF if there is a matched-related donor. Unrelated donors can also be considered for HSCT. A trial of androgen therapy (e.g., oxymetholone) may also improve the

pancytopenia.^[12] G-CSF with erythropoietin has occasionally been used but perhaps should not be used in combination with androgens.^[13]

Our patient was subsequently treated with HSCT, and on follow-up, after 3 months, he was doing fine. His hematologic parameters also showed improvement.

Conclusion

DC must be kept in mind when dealing with a case of BMF with skin lesions, and these patients must also be screened for any presence of malignancies. However rare it may seem, it is frequently encountered in varied situations and is likely to be missed if a high degree of suspicion is not maintained.

References

1. Tanaka A, Kumagai S, Nakagawa K, Yamamoto E. Cole-Engman syndrome associated with leukoplakia of the tongue: a case report. *J Oral Maxillofac Surg* 1999;57(9):1138–41.
2. De Boeck K, Degreef H, Verwilghen R, Corbeel L, Casteels-Van Daele M. Thrombocytopenia: First symptom in a patient with dyskeratosis congenita. *Pediatrics* 1981;67(6):898–903.
3. Shetty S, Gokul S. Keratinization and its disorders. *Oman Med J* 2012;27(5):348–57.
4. Dokal I. Dyskeratosis congenita in all its forms. *Br J Haematol* 2000;110(4):768–79.
5. Young NS, Alter BP. *Aplastic Anemia Acquired and Inherited*. Philadelphia, PA: WB Saunders Company, 1994.
6. Bessler M, Wilson DB, Mason PJ. Dyskeratosis congenita and telomerase. *Curr Opin Pediatr* 2004;16:23–8.
7. Hoyeraal HM, Lamvik J, Moe PJ. Congenital hypoplastic thrombocytopenia and cerebral malformations in two brothers. *Acta Paediatr Scand* 1970;59:185–91.
8. Hreidarsson S, Kristjansson K, Johannesson G, Johannsson JH. A syndrome of progressive pancytopenia with microcephaly, cerebellar hypoplasia and growth failure. *Acta Paediatr Scand* 1988;77(5):773–5.
9. Aalfs CM, van den BH, Barth PG, Hennekam RC. The Hoyeraal-Hreidarsson syndrome: the fourth case of a separate entity with prenatal growth retardation, progressive pancytopenia and cerebellar hypoplasia. *Eur J Pediatr* 1995;154(4):304–8.
10. Revesz T, Fletcher S, al Gazali LI, DeBuse P. Bilateral retinopathy, aplastic anaemia, and central nervous system abnormalities: a new syndrome? *J Med Genet* 1992;29(9):673–5.
11. Kajtar P, Mehes K. Bilateral coats retinopathy associated with aplastic anaemia and mild dyskeratotic signs. *Am J Med Genet* 1994;49(4):374–7.
12. Sharon A. Savage, Blanche P. Alter, dyskeratosis congenita. *Hematol Oncol Clin North Am* 2009;23(2):215–31.
13. Alter BP, Gardner FH, Hall RE. Treatment of dyskeratosis congenita with granulocyte colony-stimulating factor and erythropoietin. *Br J Haematol* 1997;97(2):309–11.

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