Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18877
DOI URL: http://dx.doi.org/10.21474/IJAR01/18877

RESEARCH ARTICLE

DISCOVERY OF DYSKERATOSISCONGENITA BY APLASTICHEMORRHAGE: A REVEALINGCLINICAL CASE

C. Salhi, A. Ghanam, M. Azizi, H. Zahiri, A. Elouali, A. Babakhouya and M. Rkain

Manuscript Info

Manuscript History
Received: 12 April 2024
Final Accepted: 15 May 2024
Published: June 2024

Key words:
Dyskeratosiscongenita, Bone MarrowfailureSyndrome, Leukoplakia, Hyperpigmentation, Nail Dystrophy, Pancytopenia

Abstract

Dyskeratosiscongenita (DC) is a rare geneticdisordercharacterized by a distinctive clinicaltriadaffecting the skin, mucous membranes and bonemarrow. Although the condition has been described for over a century, itoftenremainsunrecognized and under-diagnosed due to its variable clinicalpresentation. Typicalclinical manifestations of DC includereticular skin pigmentation, naildystrophy and mucosallesionssuch as oral leukoplakia. However, the clinicalpresentation can beheterogeneous, sometimescomplicating the diagnosis. In addition to cutaneous and mucosalsymptoms, DC can also lead to serious complications such as bonemarrowfailure, increasing the risk of anemia, thrombocytopenia and neutropenia. In addition, patients with DC have an increasedrisk of neoplastic complications.Wepresent the case of a 7-year-old childfrom a first-degreeconsanguineousmarriage, whoconsulted for the first time with an anemic syndrome. Afterdetailedevaluation, the diagnosis of bonemarrowaplasia syndrome on a background of dyskeratosiscongenitawasestablished. This observation highlights the diagnostic challenges encountered in DC and underscores the importance of early recognition and appropriate management to improve patient prognosis.

Introduction

Dyskeratosiscongenita (DC) is a rare geneticdisordercharacterized by a distinctive clinicaltriadaffecting the skin, mucous membranes, and bonemarrow [1,2]. The condition iscaused by genetic mutations that affect the function of telomerase, an enzyme thatiscritical for chromosome stability and stem cellintegrity [2]. Despitebeingdescribed over a century ago, DC oftenremains unrecognized and underdiagnosed, partly due to its variable clinicalpresentation and insidious course [3]. This lack of recognition often leads to delays in implementingappropriate management, exposing patients to serious complications such as bonemarrowfailure, severe infections, and neoplastic complications [3,4]. Therefore, cliniciansneed to be more aware of thispathology and itsatypical manifestations to ensureearlydiagnosis and optimal management of patients with DC.

Wepresent the case of a 7-year-old childfrom a first-degreeconsanguineousmarriagewhoconsulted for the first time with an anemic syndrome. Afterdetailedevaluation, the diagnosis of medullaryaplasia syndrome on a background of dyskeratosiscongenitawasestablished.

Corresponding Author: C. Salhi

Case presentation

A seven-year-oldchild, from a 1st degreeconsanguineousmarriage, lives in a rural area and is the onlymember of hisfamily. He consultshisdoctor for the first time becausehisgeneral condition has been deteriorating for a year. During the medicalhistorytaking, itwasnotedthatsince the age of 5, the childhad been experiencing progressive pallor, moderategingivorrhagia, and recurrentepistaxis.

Clinicalexaminationrevealedmucocutaneouspallorwithtachycardia at 142 bpm, reticular hyperpigmentation of the face and neck (figure1), nailinvolvement of all nails, withonychodystrophy and xantonichia (figure2).Mucosalexaminationrevealed a leukoplakia and depilatedtongue (figure3). The rest of the clinicalexaminationwasunremarkable, includingassessments of weight, height, pleuropulmonary, and abdominal regions. The haemogramshowedthrombocytopeniawithplatelets at 44,000/mm³, anaemiawithhaemoglobin at 7g/dLnormochromicnormocyticaregenerative, leukopeniawith white bloodcells at 2,995/mm³ and neutropeniawithneutrophilpolynuclearcells (PNN) at 1,155/mm³. The haemostasis and infectiouswork-up was normal. Myelogram of the iliaccrest and bonemarrowbiopsyrevealedbonemarrowhypoplasia, in favor of bonemarrowaplasia on a background of congenitaldyskeratosis. This diagnosiswassupported by the presenceof theabnormalreticular pigmentation, depilatedtongue, naildysplasia and medullaryaplasia. Geneticstudieswere not performed due to financialconstraints. Initial management includedblood and platelet transfusion, antibioticprophylaxis and regularhaematological monitoring. The patient is a candidate for hematopoietic stem cell transplantation.

Discussion

DC is an inherited syndrome, first described by Zinsserin 1910 [1]. Alsoknown as Zinsser-Engman-Cole syndrome [3], DC is a diseaseprimarilyaffecting the mucocutaneous and hematopoieticsystems, and associatedwithvarious somatic abnormalities[2]. The main proteinaffectedisdyskerin, and mutations affect telomeraseactivity [2]. DC can beinheritedthroughthreemodes: autosomal dominant, autosomal recessive, and X-linked[5].

The estimatedprevalence of DC in childrenis 4 in 1 million [5], withapproximately 200 cases reported in the literature [3]. The main causes of death are bonemarrowfailure, immunosuppression, pulmonary complications and malignancies [1,3].

Clinically, DC ischaracterized by a diagnostic triad of reticularlacy skin pigmentation, naildystrophy and oral leukoplakia [6]. However, thistriadis not alwaysobserved, and the diseasemaypresent as aplasticanemia in itsoccultform [3]. Sun-exposed areas, such as the uppertrunk, neck and face, are mostaffected. Otherectodermalabnormalitiessuch as alopecia of the scalp, eyebrows and eyelashes, prematuregraying of the hair, hyperhidrosis, hyperkeratosis of the palms and soles, and adermatoglyphia (loss of dermalridges on fingers and toes) are alsoobserved [7]. Mucosalleukoplakia, a pathognomonicfeature, affects around 80% of patients, typicallyinvolving the buccal mucosa, tongue and oropharynx, with an increasedrisk of malignant transformation requiringfrequent monitoring [7]. It can alsooccur in the lacrimalduct, conjunctiva, oesophagus, urethra, glanspenis, vagina and recto-anal region, wherestrictures can occur, leading to dysphagia, dysuria, phimosis and epiphora [1,5]. Splenomegaly and/or hepatomegalymaybeobserved due to extramedullaryhematopoiesis [8].

DC patients have an 11-fold increasedrisk of developingneoplasiacompared to the healthy population [6]. They are also at increasedrisk of myeloidhemopathies, pulmonary and hepaticfibrosis, and immune deficiencies [4]. Othermalignancies, such as Hodgkin'slymphoma, gastrointestinal adenocarcinoma, and bronchial and laryngealcarcinomas, have been reported in the thirddecade of life [2]. Additionally, many patients willdeveloppancytopeniasecondary to bonemarrowaplasia [4].

Diagnosisisbased on the presence of at least twosigns of the clinical diagnostic triadinitiallydescribed, or on the existence of otherhematological or neoplasticabnormalities forming part of the picture of DC associatedwith the presence of a mutation in one of the knowngenes, or with the presence of short telomeres [4]. Frequentlyfoundgene mutations includethoseaffecting TERT (telomerase Reverse Transcriptase), TERC (Telomerase RNA Component), DKC1 (Dyskerin), TINF2 (TERF1-Interacting Nuclear Factor 2), RTEL1 (Regulator of Telomere Elongation Helicase 1), NOP10 (NucleolarProtein 10), NHP2 (NucleolarProtein H/ACA Domain 2), and NOP2 (NucleolarProtein 2) [9].

There iscurrently no consensus on treatment, withindividualized management aimed at treatingeachpatient'sspecificsymptoms. Supportive care is essential, including infection control, appropriateblood transfusion, oral care and the use of moisturizingcreams to prevent skin lesions [3]. On the hematopoietic front, maintaininghematopoieticfunctionis crucial. Treatment options include the use of oxymetholone, hematopoieticgrowthfactorssuch as erythropoietin and filgrastim, and hematopoietic stem cell transplantation [1,2]. The prognosisisthereforeparticularlypoor [4].

Conclusion

DyskeratosisCongenitaremains a complex and oftenunder-diagnosedgenetic condition, withvaried and potentiallyseriousclinical manifestations. Increasedawareness and ongoing training of clinicians are essential to enable earlydiagnosis and appropriate management, aimed at improving patients' prognosis and quality of life. Supportive care, regular monitoring and specifictreatments, such as hematopoietic stem cell transplantation, are essential to manage this rare disease.

Figure :

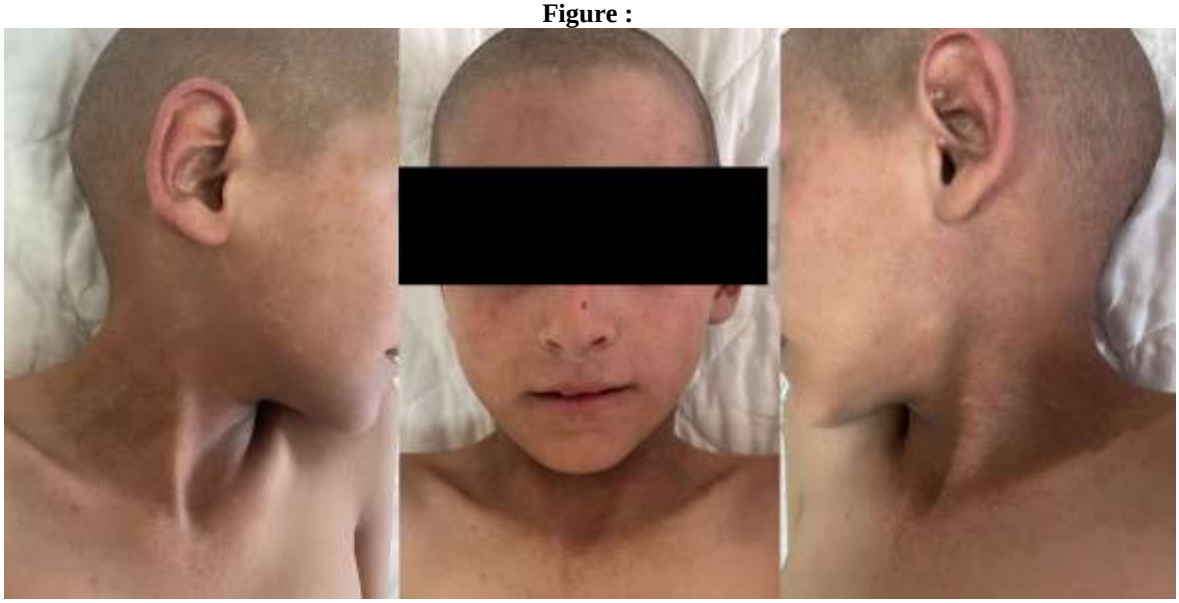

Figure 1: Photograph of patient showingreticular pigmentation on face and neck

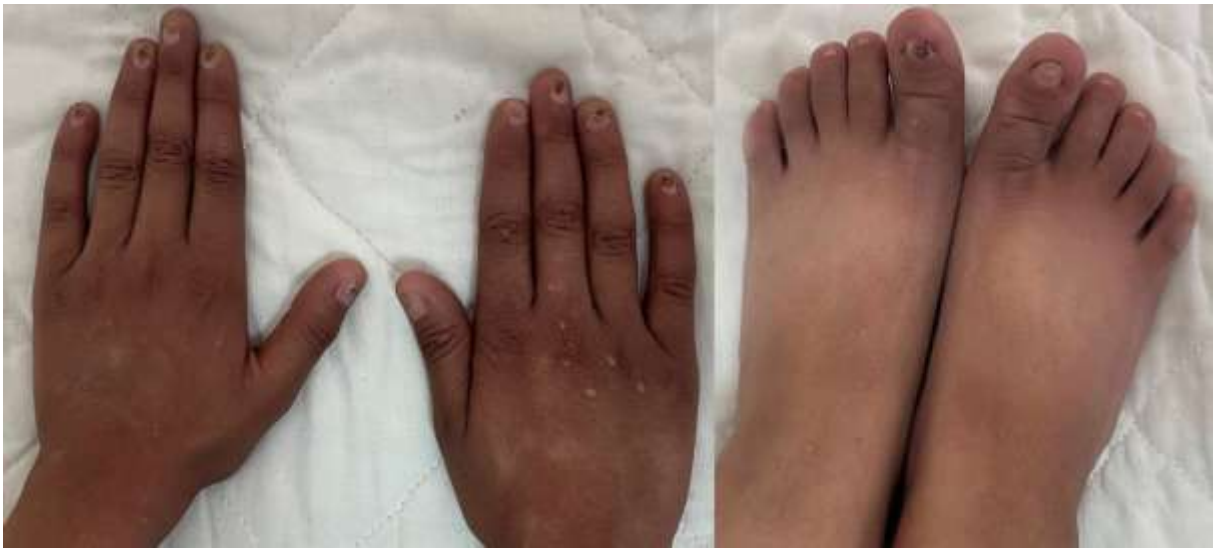

Figure 2: Photograph of patient showingonychodystrophywithxantonichia of fingernails and toenails

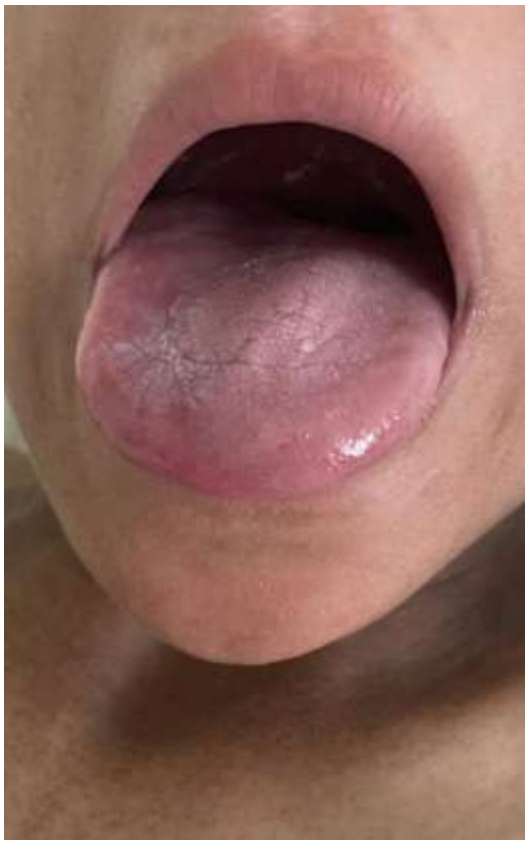

Figure 3: Photograph of the patient showing a whitish non-detachablelesion on the tongue in favour of leucodysplasiawith a tonguedepapillated at the periphery

References

1. Ghanekar J, Chopra R, Thakkar M: Dyskeratosis Congenita: A Rare Case. MGM Journal of Medical Sciences. 2016, 3:42–4. 10.5005/jp-journals-10036-1085
2. Roy B, Mondal G, Paul DK, Kalam A, Basu K: Dyskeratosis congenita: a rare case report. Journal of Nepal Paediatric Society. 2013, 33:223–6. 10.3126/jnps.v33i3.8166
3. Karim MA, Jamal CY, Kaes MI, Ahmed KM: A Case Report on a Rare Inherited Bone Marrow Failure Syndrome: Dyskeratosis Congenita. Bangladesh J Child Health. 2020, 44:122–5. 10.3329/bjch.v44i2.51139
4. Mialou V, Leblanc T, Latour RPD, Dalle J-H, Socié G: Dyskeratosis congenita: an update. Archives of Paediatrics. 2013, 20:299–306. 10.1016/j.arcped.2012.12.003
5. Bagchi B: Dyskeratosis congenita: a case report. International Journal of Contemporary Pediatrics. 2022, 9:1204. 10.18203/2349-3291.ijcp20223069
6. Shiyi Chen, Chenbin Xu, Yizhen Wu, Wei Liu, Xi Yang: Oral leukoplakia in adolescents: Attention to differential diagnosis of inherited genetic syndromes with emphasis on dyskeratosis congenita and Fanconi anemia. Oral Oncology Reports. 2023, 6:. https://doi.org/10.1016/j.oor.2023.100043
7. Karunakaran A, Ravindran R, Arshad M, Ram MK, Laxmi MKS: Dyskeratosis Congenita: A Report of Two Cases. 2013. 10.1155/2013/845125
8. Owlia MB, Arjmandzadeh E, Setayesh S: Dyskeratosis congenita; a case with a favorable outcome. https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=e1fa0cc69825fd8275e84882af5974f131aa47b7
9. Savage SA: Dyskeratosis congenita and telomere biology disorders. Hematology. 2022, 2022:637–48. 10.1182/hematology.2022000394.