Case Reports in Ophthalmology

Case Rep Ophthalmol 2024;15:572–576
DOI: 10.1159/000540221
Received: May 22, 2024
Accepted: July 3, 2024
Published online: July 24, 2024

Case Report

Presumptive Cytomegalovirus Retinitis as a Complication of Dyskeratosis Congenita: A Case Report

Yuxi Du[a, b] Yalong Dang[a, b]

[a]Department of Ophthalmology, Sanmenxia Eye Hospital/Sanmenxia Central Hospital Affiliated to Henan University of Science and Technology, Sanmenxia, China; [b]Henan International Joint Laboratory of Outflow Engineering, Sanmenxia Central Hospital, School of Medicine, Henan University of Science and Technology, Sanmenxia, China

Keywords
Dyskeratosis congenita · DKC1 gene · Cytomegalovirus · Retinitis · Immunodeficiency

Abstract
Introduction: Dyskeratosis congenita is a rare genetic disorder characterized by abnormalities of the skin, nails, and oral mucosa. Retinal involvement in this condition is uncommon. Here, we present a case of a young male patient diagnosed with presumptive cytomegalovirus retinitis, ultimately found to be concomitant with dyskeratosis congenita. ***Case Presentation:*** A non-HIV-infected young male with recurrent infections, including aspergillus pneumonia and pneumocystis pneumonia, presented with presumptive cytomegalovirus retinitis in both eyes. Systemic manifestations included cutaneous hyperpigmentation, nail dystrophy, and oral mucosal leukoplakia. Genetic testing revealed a mutation in the DKC1 gene. The final diagnosis was dyskeratosis congenita complicated by presumptive cytomegalovirus retinitis. ***Conclusion:*** Cytomegalovirus retinitis can serve as an ocular complication of dyskeratosis congenita. When a patient presents with cytomegalovirus retinitis, a comprehensive systematic examination should be conducted as it indicates severe immunodeficiency.

Introduction

Cytomegalovirus (CMV) is a double-stranded DNA virus, with humans as its exclusive host, commonly affecting organs such as the eyes and lungs. Cytomegalovirus retinitis (CMVR) is an opportunistic infection that occurs in specific high-risk populations, primarily in

Correspondence to:
Yalong Dang, yalong.dang@gmail.com

Case Rep Ophthalmol 2024;15:572–576
DOI: 10.1159/000540221

immunocompromised patients, such as those with acquired immunodeficiency syndrome, those who have undergone organ transplantation, and individuals receiving immunosuppressive therapy [1]. The ultimate manifestation of the disease depends on the surveillance of CD4+/CD8+ cells. In the absence of the aforementioned common etiologies, a comprehensive systematic examination is warranted.

Dyskeratosis congenita (DKC) is a multisystem disorder characterized by bone marrow failure, rendering individuals more susceptible to infections. This condition may present with ocular manifestations, particularly affecting the retina. Herein, we present a case of CMVR, which, upon genetic testing, was confirmed to be concomitant with DKC. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000540221).

Case Description

A 24-year-old male was admitted to the respiratory department and diagnosed with pneumocystis jirovecii pneumonia and immunodeficiency. He received combined antimicrobial and anti-inflammatory therapy. Five days post-admission, the patient reported blurred vision in his right eye, leading to an ophthalmic consultation. Ocular examinations revealed the best-corrected visual acuity of 3/60 in the right eye and 20/40 in the left eye. The patient presented with entropion and trichiasis in both lower eyelids. Anterior segment examination and intraocular pressure were normal, but mild vitreous opacity was noted. Fundus examination demonstrated dense yellow-white exudates along the vascular distribution in both eyes, patchy hemorrhages and retinal necrosis (Fig. 1a, b), and macular edema (Fig. 1c, d), particularly severe in the right eye.

The patient's medical history was significant for childhood skin pigmentation (Fig. 2d), emaciation, dystrophy of the fingernails and toenails (Fig. 2a, b), and oral mucosal leukoplakia (Fig. 2c). Over the past 2 years, he had multiple admissions for recurrent aspergillus pneumonia and pneumocystis pneumonia, which resolved with regular antifungal therapy. No similar presentation was observed within the patient's family, except for his mother, who passed away more than 20 years ago due to suspected aplastic anemia.

Laboratory findings revealed pancytopenia with decreased counts across all three blood cell lines (white blood cell count: 3.17×10^9/L, red blood cell count: 2.67×10^{12}/L, platelet count: 106×10^9/L). Notably, there was a reduction in the absolute number of total T lymphocytes, especially CD3–CD4+ lymphocytes, with levels at only 75×10^6/L. This severe immunodeficiency and recurrent opportunistic infections suggested an underlying undiagnosed immunosuppressive disorder. HIV testing was negative, while serum CMV IgG antibody was positive. Though viral testing of the patient's aqueous humor was initially planned, it was not pursued due to the patient's extremely poor overall condition.

Peripheral blood samples were collected from the patient, his father, son, aunt, and two uncles. Using second-generation sequencing, nearly 20,000 functional genes were analyzed. The sequencing data were compared to the human reference genome sequence GRCh37/hg19 to identify genetic variants. Exome sequencing revealed that only the patient (without his families) carried the DKC1 c.1058C>T mutation, a hemizygous pathogenic variant. Mutations in the DKC1 gene are known to cause X-linked DKC, which is inherited in an X-linked recessive manner.

Based on the laboratory and fundus findings, which included perivascular yellow-white retinal lesions associated with retinal hemorrhage and focal white granular infiltrates, we diagnosed the patient with presumptive CMVR. Due to his compromised immunity, he declined intravitreal injection of ganciclovir. Consequently, intravenous ganciclovir was

Case Rep Ophthalmol 2024;15:572–576
DOI: 10.1159/000540221

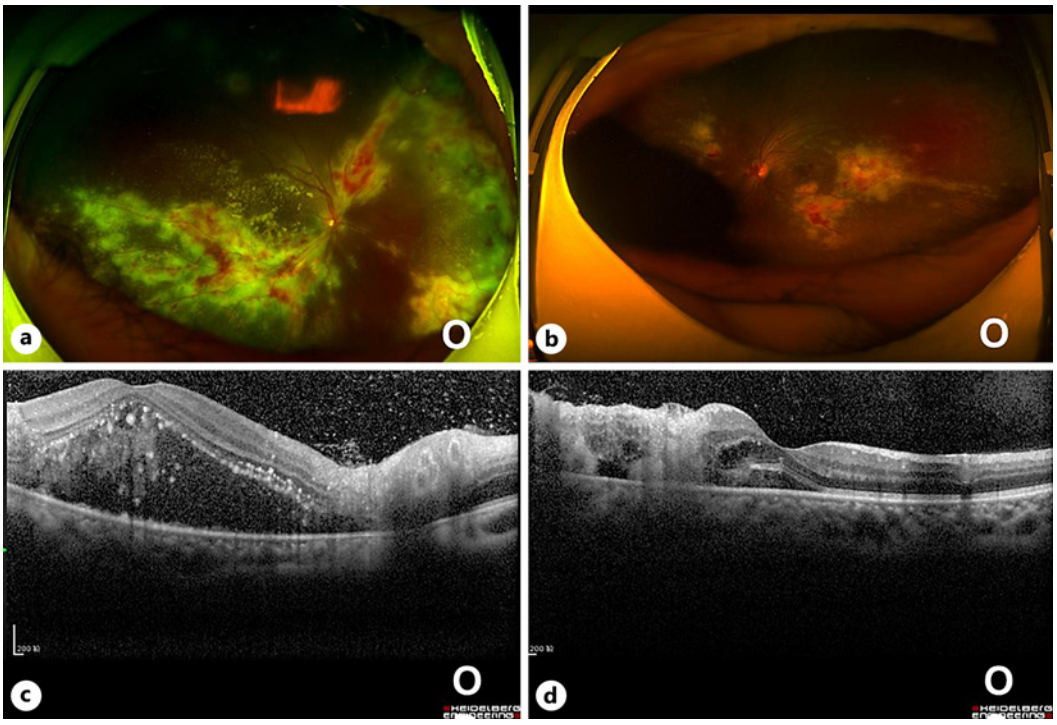

Fig. 1. Ocular fundus examinations. Dense yellow-white exudates along the vascular distribution in both eyes, patchy hemorrhages and retinal necrosis (**a**, **b**), and macular edema (**c**, **d**), particularly severe in the right eye.

administered. However, there was no significant improvement in his best-corrected visual acuity or fundus condition. Two months later, the patient succumbed to a mixed pulmonary infection.

Discussion

Mutations in the DKC1 gene, situated in the q28 region of the X chromosome, are linked to X-linked DKC, a rare and progressive bone marrow disorder. Characteristic features of this disease include reticular skin hyperpigmentation, nail hypoplasia, and oral leukoplakia. Early mortality is frequently associated with bone marrow failure, infections, pulmonary complications, or malignancies. According to the "ACMG Classification Criteria and Guidelines for Genetic Variations" of the Chinese Genetics Society, the DKC1:c.1058C>T variant is classified as "pathogenic."

The majority of these patients die due to bone marrow failure resulting from progressive cytopenias [2]. DKC can also lead to aplastic anemia. Considering the X-linked recessive inheritance pattern of DKC, it is highly likely that the patient's mother also has DKC.

Eighty percent of patients with DKC present with ocular complications [3]. Common ocular abnormalities include eyelid eversion, inversion, trichiasis, and blepharitis [4]. However, retinal lesions are rare, primarily presenting as hemorrhages and infarctions of the nerve fiber layer [5]. Parchand et al. [6] reported a case of a 45-year-old male patient diagnosed with CMVR concomitant with DKC, who also had gastric cancer. Arora et al. [7] reported a 25-year-old male patient with bilateral CMVR concomitant with DKC, who later developed retinal detachment. Our patient shares similarities with the cases reported by Parchand and Arora, exhibiting the classic triad of DKC. What distinguishes our patient is the

Case Rep Ophthalmol 2024;15:572–576
DOI: 10.1159/000540221

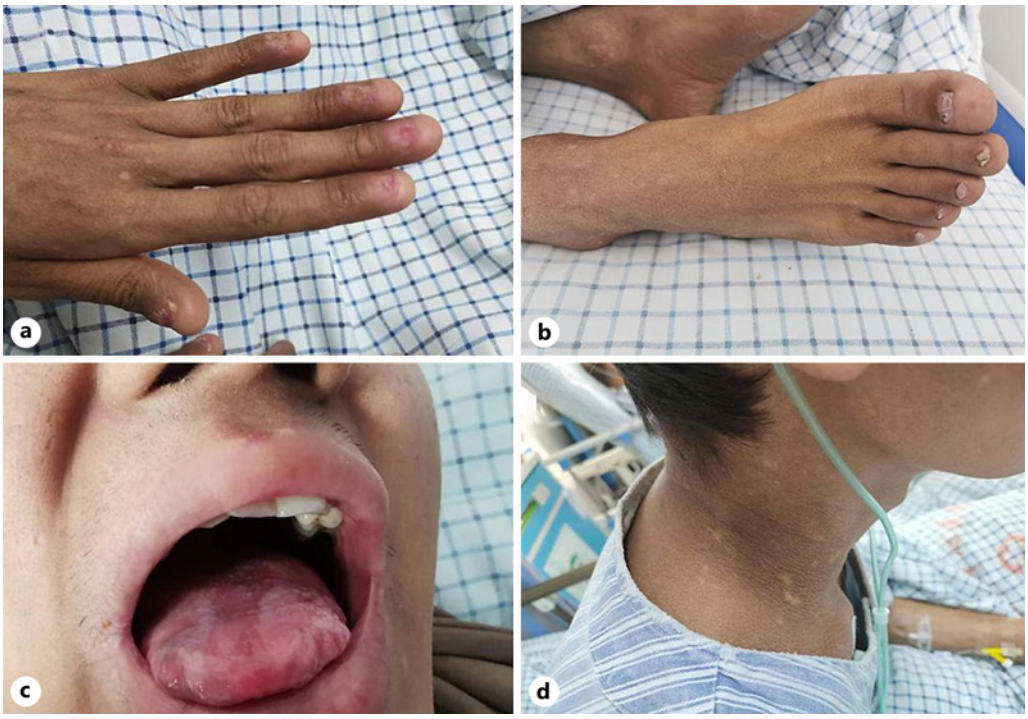

Fig. 2. Systemic manifestation. Dystrophy of the fingernails and toenails (**a**, **b**), oral mucosal leukoplakia (**c**), and skin pigmentation (**d**).

presence of entropion and trichiasis, common ocular symptoms, in addition to CMVR and pulmonary opportunistic infections.

CMVR is an opportunistic infection, and its occurrence in non-HIV patients is a major concern as it often indicates severe immunodeficiency in the patient. If the patient presents with opportunistic infections in other parts of the body, a comprehensive systematic examination is warranted. The treatment of CMV retinitis necessitates a comprehensive evaluation of the patient's immune status and precise classification of the retinal lesions. Once retinitis is diagnosed, anti-CMV therapy with oral valganciclovir, intravenous ganciclovir, foscarnet, or cidofovir should be administered [8].

In conclusion, CMVR may serve as an ocular complication of DKC. When a patient presents with the classic triad of DKC – reticular skin pigmentation, nail dystrophy, and oral leukoplakia – suspicion for this condition should be high. Furthermore, when CMVR is detected in a patient, efforts should be made to investigate immunologically related diseases to promptly diagnose and treat the underlying condition.

Statement of Ethics

This study protocol was reviewed and approved by Sanmenxia Eye Hospital, Approval No. 20230282. Written informed consent was obtained from the patient and his families for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was supported by the Central Guidance Project of China for Developing Local Science and Technology (Z20221341047), the International Science and Technology Cooperation Program of Henan (232102521033), and the Medical Education Research Project of Henan (WJLX2022165).

Author Contributions

Y. Du collected the samples and drafted the manuscript. Y. Dang supervised and approved the study, revised the manuscript, prepared the figures, and provided the funds for this research.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author upon reasonable request.

References

1 Port AD, Orlin A, Kiss S, Patel S, D'Amico DJ, Gupta MP. Cytomegalovirus retinitis: a review. J Ocul Pharmacol Ther. 2017;33(4):224–34. https://doi.org/10.1089/jop.2016.0140
2 Abdel-Karim A, Frezzini C, Viggor S, Davidson LE, Thornhill MH, Yeoman CM. Dyskeratosis congenita: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(2):e20–24. https://doi.org/10.1016/j.tripleo.2009.03.042
3 AlSabbagh MM. Dyskeratosis congenita: a literature review. J Dtsch Dermatol Ges. 2020;18(9):943–67. https://doi.org/10.1111/ddg.14268
4 Li F, Li W, Qiao X, Xie X. Clinical features of dyskeratosis congenita in mainland China: case reports and literature review. Int J Hematol. 2019;109(3):328–35. https://doi.org/10.1007/s12185-018-02582-x
5 Callea M, Martinelli D, Cammarata-Scalisi F, Grimaldi C, Jilani H, Grimaldi P, et al. Multisystemic manifestations in rare diseases: the experience of dyskeratosis congenita. Genes. 2022;13(3):496. https://doi.org/10.3390/genes13030496
6 Parchand S, Barwad A. Cytomegalovirus retinitis as a presenting feature of multisystem disorder: dyskeratosis congenita. Middle East Afr J Ophthalmol. 2017;24(4):219–21. https://doi.org/10.4103/meajo.MEAJO_230_15
7 Arora A, Singh R, Dogra M. Bilateral cytomegalovirus retinitis as the presenting feature of dyskeratosis congenita. Eur J Ophthalmol. 2023;33(3):Np122–5. https://doi.org/10.1177/11206721221086154
8 Stewart MW. Optimal management of cytomegalovirus retinitis in patients with AIDS. Clin Ophthalmol. 2010;4:285–99. https://doi.org/10.2147/opth.s6700