Acta Scientific Clinical Case Reports

Volume 4 Issue 2 February 2023

Case Report

A Case Report to Describe Peculiar Ocular Lesions at Today Not Well Characterized in the Spectrum of this Disease

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Received: December 20, 2022

Published: January 10, 2023

Abstract

Background: To describe the ocular findings in a 44-year-old white female in whom a diagnosis of Gorlin Syndrome was confirmed by genetic testing, which identified a homozygous mutation in PTCH-1 gene.

Methods: Observational case report of a 44-year-old female who presented with multiple cutaneous basal cell carcinoma, nystagmus, myelinated nerve fiber layer, iris leiomyoma, ovarian leiomyoma and skeletal abnormalities such as prominent frontal bone.

Results: Clinical examination and multimodal imaging documented presence of myelinated nerve fiber layer and whitish nodular iris lesion with leiomyomatous appearance.

Conclusion: Recognition that ocular abnormalities in Gorlin syndrome are frequent with a various range of prevalence. To the best of our knowledge, the following is the first report in the ophthalmic literature of iris and retinal lesion in a patient with a genetically confirmed Gorlin syndrome.

Keywords: Gorlin; Gorlin Syndrome; Gorlin-Goltz Syndrome; Genetics; Ocular Syndrome; Leiomyoma; Myelinated Nerve Fiber; Cancer; Basal Naevus Syndrome; Basal Cells Carcinoma; Erivedge; Ocular Oncology

Introduction

Gorlin syndrome, also known as nevoid basal cell carcinoma syndrome, is an autosomal dominant inherited condition that increases the risk of developing several tumors.

The estimated prevalence ranges between 1/30827 and 1/256,000 [1].

The most frequent diagnosis in Gorlin's syndrome patients is the basal cell carcinoma, which is the most ordinary form of skin cancer [2].

Ocular findings in Gorlin syndrome are various: nystagmus, myelinated nerve fiber layer, hyperterolism, strabismus, epiretinal membrane. Infrequent are solid nodular lesions [3].

Material and Methods

A 44-year-old Caucasian female presented with a history of multiple nevoid basal cell carcinoma which lead the dermatologist to evaluate the genetical pattern in a highly suspected inherited syndrome. The genetic test confirmed the mutation in PTCH1 gene, with a 9q22.3 microdeletion. Genetical examination showed other suggestive findings such as high stature, hyperthelorism, "palmar pits" in the hands, multiple cutaneous keratocystic lesions. At the gynecological consultation was founded bilaterally nine ovarian round shaped solid lesion at the ultrasound, hystopatologically identified as multiple ovarian leiomyomas.

A treatment with Erivedge (Vismodegib) was started after genetically confirmation of syndrome in reason of a multiple basal cell carcinoma [4].

Ocular examinations identified bilateral nystagmus, hypertelorism, corneal basal membrane dystrophy with a "railway appearance" (Figure 1) and a solid white lesion in the anterior chamber in the left eye (Figure 1). This lesion, whitish, poorly vascularized and exophytic which rise from the iris surface, near the angle structure taking contact with the overlaying corneal endothelium. At the ultrasound examination of the anterior segment, this lesion showed a solid and homogeneous eco-structure, but no tractional or invasive appearance was identified. The anterior-segment OCT (Figure 2) showed the same characteristic founded at ultrasound examination, on the other hand this permitting to better estimate the volume and the extension of the lesion, taking into account the involvement of other ocular structures, such as the underling iris plate and the overlying corneal endothelium. No angular structure involvement was identified. The clinical diagnosis of iris leiomyoma was made. At today the surgical removing of the lesion is not considered due to the clinical and instrumental stability at follow-up examination.

At the funduscopic evaluation of the same eye, a wide triangle shaped tuft of myelinated fibers in the superior branch of retinal nerve fiber layer was seen (Figure 2).

Non other ocular lesion was founded. The examination of the right eye was unremarkable exception only for the corneal basal membrane dystrophy.

Figure 1: (a) corneal basal membrane dystrophy with a "railway appearance"; (b) iris leiomyoma, exophytic lesion which rise from the iris surface, near the angle structure taking contact with the overlaying corneal endothelium.

Figure 2: (a) The anterior-segment OCT shows the extension of leiomyoma which grow up from the iris body taking contact with the corneal endothelium. Hypereflectivity of the muscle fiber of the iris stroma may indicate the leyomiomatous transformation; (b) Myelinated tuft on nerve fiber layer (Multicolor image - Heidelberg SD- OCT).

Discussion

The cutaneous, ocular, gynecological and genetic findings in our case are compatible with Gorlin Syndrome.

Basal cell carcinoma typically start to appear during adolescence or early adulthood. The most frequent locations are the face, chest, and back. The number of lesions that develop during lifetime varies among affected individuals.

Individuals with Gorlin syndrome have an elevated risk to develop other type of tumors, as brain tumors [5] (most frequent is medulloblastoma in childhood which may lead to early onset of strabismus and congenital blindness), and ovarian tumors, most frequently represented by fibromatous and leiomyomatous lesions.

Keratocystic odontogenic tumor is a frequent manifestation of this syndrome. These lesions arise in the adolescent individual.

Facial abnormalities such as prominent frontal bone and macrocephalia are frequent findings.

The genetic mutations incriminated in Gorlin Syndrome involve the PTCH1 [6] gene which in turn code for a receptor protein called "Patched-1" in Sonic Hedgehog's pathway. This is a pathway involved in a cell proliferation regulation, for this reason a mutation at this level deregulates the cell proliferation checkpoints, lead to characteristic neoplastic manifestation of this syndrome.

The Hedgehog signalling pathway is crucial for a proper development of embrions and cell mitosis and its deregulation is implicated in several congenital defects and malignancies. This signalling pathway is inhibited by the tumor suppressor membrane protein (Patched-1) in the unstimulated cells.

The secretion of Hedgehog ligand bind, and consequent inhibit, Patched-1 triggering the Hedgehog signaling pathway.

PTCH gene, when inactivated in homozygous mechanism, conduct to genesis of tumors and consequently at the development of multiple Basal Cell Carcinomas (BCCs) and other tumors, also in the ocular district as in the present case.

Summary Statement

Gorlin syndrome is an autosomal dominant inherited condition that increases the risk of developing several tumors. Diagnosis needs to be confirmed by genetic testing focusing to the PTCH1 gene. Nystagmus, myelinated nerve fiber, basal membrane dystrophy and iris leiomyoma was founded as singular epiphenomenon of systemic disease.

Author's Contribution

PA conceived, analyzed the data, wrote, and provided critical revision of the manuscript.

Competing Interest Statement and a Financial Disclosure statement

None of the authors has any financial/conflicting interests to disclose.

Funding

For this work PA has no requested any fund.

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