Case Report

Retinal Degenerative Disease (Retinitis Pigmentosa) Associated with Nonocular Abnormalities: A Case Series in Niger

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Abstract

Retinitis pigmentosa (RP) is a genetic abnormality affecting the retina cells and is responsible for a progressive visual impairment which at the end results in an irreversible blindness. In some rare cases, this inherited disease can be associated with other systemic abnormalities. In this report, three different families were presented with familial syndromic RP: Usher syndrome (RP and congenital deafness) reported in three members of the same family: RP associated with Marfan syndrome and RP associated with macular dystrophy in two siblings. All our patients are children from first-degree consanguineous marriages with no previous history of blindness or eye disease in each family. This case series demonstrates the variability of systemic associations with RP and its occurrence in consanguineous marriages.

Keywords: Maculopathy, marfan syndrome, Niger, syndromic retinitis pigmentosa, usher syndrome

Introduction

Degenerative malfunction of retinal cells (cones and rods) also known as retinitis pigmentosa (RP) is a hereditary disease responsible for premature degradation of visual function in carrier patients. The natural evolution is toward a so-called legal blindness which sets in gradually over the years.[1] Although known primarily to affect the eyes, RP is found to include other systemic abnormalities and therefore there is a syndromic form which is reported in about 30% of affected patients.[2]

In this report, the author presents three families, each presenting a different systemic association to RP.

Patients and Methods

The author carried out a 3-year retrospective study between January 2013 and January 2016 on syndromic forms of RP. Three families were enrolled each carrying a different association with RP. A family of RP associated with congenital deafness in three siblings was included, a case of association with Marfan syndrome (MFS) and a case of association with macular dystrophy. Isolated cases of RP were not considered. Each patient had a complete ophthalmologic examination and some available investigations (visual field, retinal photography, color vision, and electroretinogram). The patient with MFS was also observed by the cardiologist and the orthopedic surgeon. The patients with Usher syndrome were managed together with the Ear, Nose, and Throat (ENT) team.

The study involved seven patients (two girls and five boys). The mean age was 12 years with range of 3 years to 24 years.

The following associations were found: MFS, deafness, and macular dystrophy.

Family 1

A family of 12 children in a first-degree consanguineous marriage presented with the complaint that three of the children had poor vision and deafness.

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All members of the family had an ophthalmologic examination, and three among them had abnormal results.

The first born, a young boy of 20 years complained of progressive reduction in vision since childhood with associated photophobia as well as deafness since birth.

He had a history of delayed childhood developmental milestones especially walking (first steps at 3 years) and nyctalopia since the age of 5 years. At presentation, he had a stationary visual acuity 6/30 at right eye and 6/60 for the left eye (using Snellen chart). Intraocular pressure was 10 mmHg in both eyes.

A slit lamp examination of both eyes revealed normal anterior segments, and fundoscopy showed bony spicule-like pigmentation, attenuation of retinal vessels, and significant macular dystrophy. Visual field was narrow and color vision test was impaired. ENT examination confirmed a profound and congenital deafness.

The second child was also affected; he was 17 years at presentation. There was a history of photophobia, nyctalopia, and delayed sitting and walking skills. His visual acuity was 6/60 in both eyes. Clinical and other investigations findings were the same as his brother's findings.

The last born of the family, a girl of 3 years had also been deaf since birth but ophthalmologic examination was normal. The other children as well as the parents had no clinical abnormality. Among extended family members, there was a positive history of deafness in the father's junior brother. Usher syndrome type 1 was diagnosed in the two brothers with respect to the ophthalmologic findings, congenital deafness and delayed childhood developmental milestones. The girl had only congenital deafness.

Family 2

A 24-year-old man presented with gradual onset of blurred vision in both eyes to the ophthalmology outpatient department. On general examination he had a tall stature (height: 170 cm), slender limbs, thin body habitus, long and slender fingers; deformities of the chest: pectus carinatum [Figure 1].

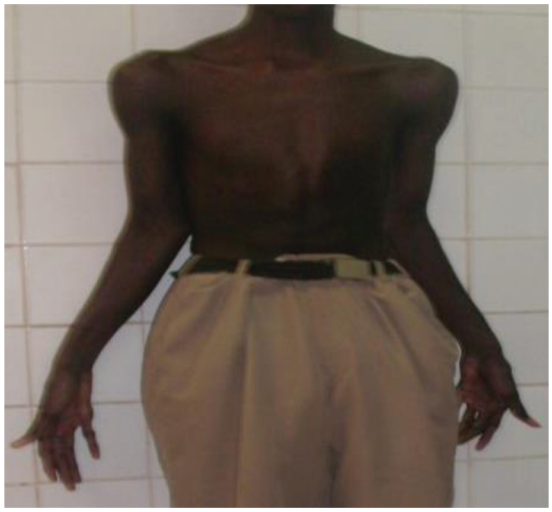

Figure 1: Marfanoid deformities of the chest and extremities.

He complained of nyctalopia and photophobia since childhood as well as poor vision. Family history outlined a late junior brother who had the same physical stature and died suddenly at the age of 10 of unknown cause and parents being first cousins (consanguineous marriage). On examination of the eyes, he had visual acuity of counting fingers at 1 m in both eyes. Slit lamp biomicroscopy showed an iridodonesis, phacodonesis, an open iridocorneal angle on gonioscopy, and intraocular pressure was 24 mmHg in the right eye and 26 mmHg in the left eye.

Anterior chamber was deep and shallow; ectopia lentis was bilateral, symmetrical, and superior. Observed retinal findings included changes of retinal pigment epithelium, bony spicule-like pigmentation, attenuation of retinal vessels, waxy disc pallor, and a cup disc ratio of 0.9. Goldman visual field analysis showed a tubular narrowing [Figure 2], significant reduction in the amplitudes of a and b waves at electroretinography [Figure 3], also scotopic system was predominant over the photopic system. Endocrinologic evaluation confirmed MFS based on Ghent nosology(clinical criteria for diagnosis of MFS). On cardiovascular examination, there was moderate aortic valve incompetence. The management of this patient was multidisciplinary with a valvuloplasty in cardiology; an intracapsular cataract extraction followed by optical rehabilitation in low vision unit as well as the prescription of beta-blockers (Timolol 0.5% (Timolo 0, 5% eye drop) twice daily) for the glaucoma. He also had orthopedic consultation and follow-up.

Family 3

The first child of this family is a girl aged 8 years; the mother noticed that she could not see at night (nyctalopia) since the age of 5 years; her school teacher also complained of her photophobic state. On examination, her visual acuity was of 6/30 in the right eye and 6/60 in the left eye. Automatic refractometry revealed hypermetropia of +2.5 diopters in both eyes. External, adnexal, as well as anterior segment examinations were normal. Vitreous examination showed a positive Shaffer sign, and significant vitreous degeneration. Fundoscopy showed bone spicule pigmentation and macular dystrophy [Figure 4] in both eyes, and there was mild disc pallor but no vascular changes. Further macular investigation tools were not available. The second patient in the family is her junior brother, aged 5 years. He started having photophobia and nyctalopia at the age of 3 years. He recently developed an esotropia of the left eye. He had a visual acuity of 6/60 in both eyes. Automatic refractometry revealed a hypermetropia of +2.50 diopters in the right eye and +5.00 diopters in the left eye. Vitreous and funduscopic changes were similar to his sister's findings.

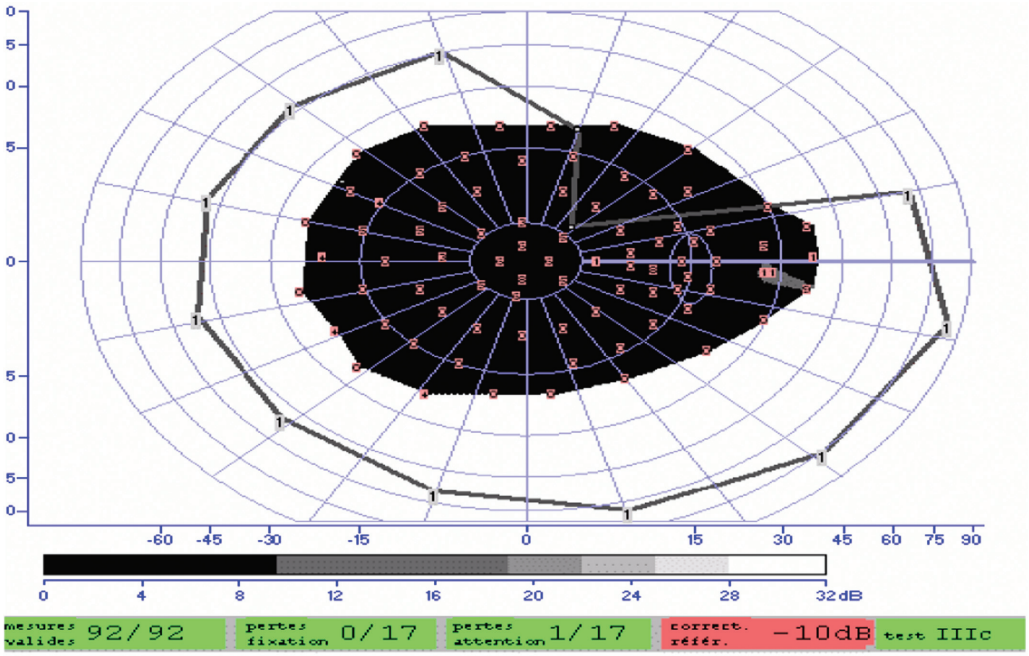

Figure 2: Visual field with tubular narrowing.

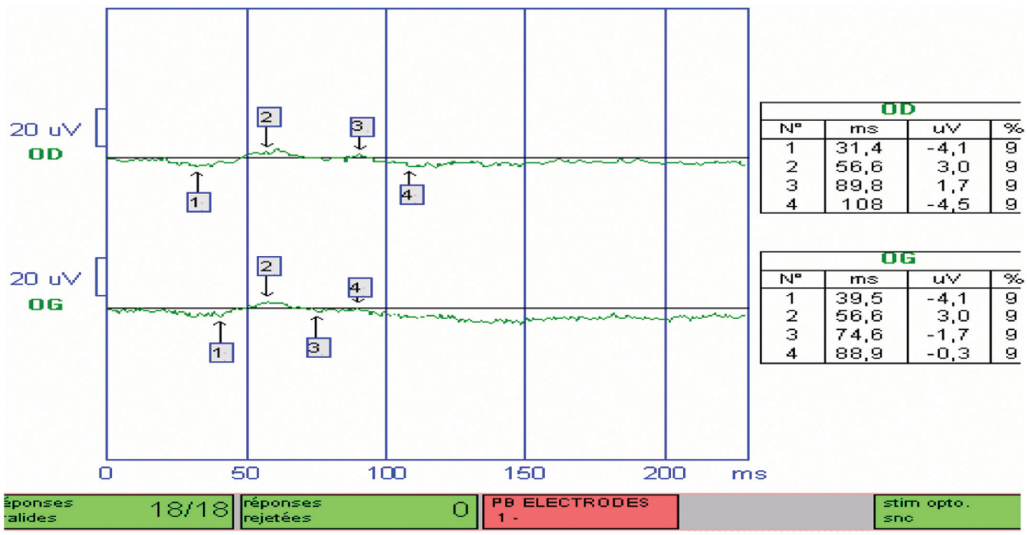

Figure 3: Electroretinography with reduced a and b waves.

Management in both cases was correction of hypermetropia with positive spherical photochromic glasses, and vitamin B complex supplementation. Pediatric examination found no other abnormality in both children. Examination of both parents was uneventful, and first-degree consanguineous marriage was reported.

Discussion

As an inherited disorder, RP is transmitted by various modes: autosomal dominant, autosomal recessive, or X-linked recessive.[3] The prevalence of this disease worldwide is about 1/4000.[2] In African countries such as Cameroun and Congo, the hospital prevalence is about 1.6/1000.[3,4] In our series, RP affected more males than females. This is in accordance with the findings of Kaya-Ganziami *et al.*[4] in Congo (63.6% were males) and Ukponmwan and Atamah[5] in Nigeria (66.6% were males), whereas equal proportions of males and females was reported by Eballe *et al.*[3] in Cameroun.

In general, this disease manifests during the second or third decade of life except in the syndromic forms where the onset is earlier, sometimes in the first few years of life as reported in our clinical cases.[5,6] The average patient age in this series is 12 years with extremes of 3 years and 24 years, which is lower than that found in other series. Eballe *et al.*[3] in Cameroun, Ukponmwan and Atamah[5] in Nigeria, and Tsujikawa *et al.*[6] in Japan, who reported an average age at diagnosis of 43.3, 36.7, and 35.1 years, respectively. The early onset of

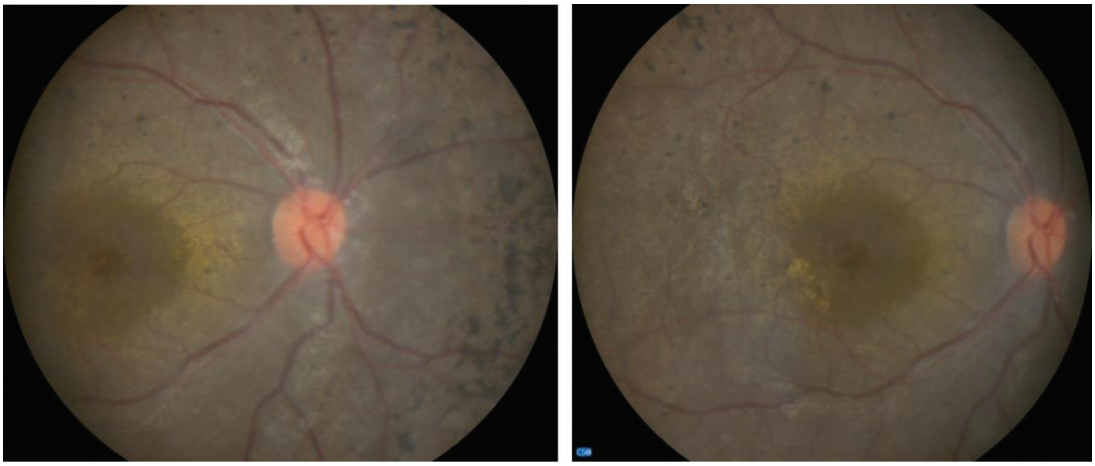

Figure 4: Fundoscopy showing bone spicule pigmentation and macular dystrophy.

RP in our series is related to its syndromic form, it is said that RP has an early onset when occurring in association with other diseases.[7]

In Usher syndrome, RP is associated with sensorineural hearing loss and in some cases, vestibular malfunction, similar to our case report.[1,8] The prevalence rate in most studies varies from 3 to 6/100,000.[9,10] Usher syndrome is clinically classified into three different types according to the age of onset of symptoms, our patients fit into the type 1 which is the most severe form (born deaf, do not develop intelligible speech, vestibular problems, and are thought to develop night blindness in infancy or early childhood).

Currently, no treatment gives relevant satisfaction to patients and clinicians in Usher syndrome; hearing aids and cochlear implantation are proposed in some cases but the visual problem remains unsolved.[9]

The MFS is a musculoskeletal-inherited disease which may include retinal degeneration in its clinical course. The mode of transmission is autosomal dominant and affects mostly the eye, the heart, the muscles, and the skeletal systems giving patients a so-called Marfanoid look. The clinical diagnosis is based on criteria enumerated by Ghent.[11] MFS has a prevalence of approximately 5 per 100,000 live births. These patients present a classical lens ectopia which is bilateral and symmetrical, sometimes cataract, myopia, retinal detachment, and glaucoma are reported in the course of the disease.[12]

The association of MFS with RP is rare, but association of RP with ectopia lenses without systemic abnormalities have been reported by some authors.[13-15] A multidisciplinary approach is needed in these cases just as is observed in this study.[16]

Macular abnormalities mostly cystoid macular edema and macular hole are frequently reported in patients presenting RP, even though the macular area is initially spared, some macular changes have been observed in the late stages.[17,18] Macular abnormality was observed by Testa *et al.*[19] in 45.1% of patients, Thobani *et al.*[20] in 60.4%, and Musarella and MacDonald.[21] in 36.08%. In our clinical case, the limitation in investigative tools did not allow further specifications of the macular lesions.

The common point in all the cases we have presented is consanguinity of the parents. Currently, scientific studies are oriented toward the discovery of health implications of consanguineous marriages. This social practice reported in some racial groups seems to play an important role in the occurrence of certain rare diseases and congenital anomalies, including rare ocular diseases.[22]

Conclusion

Although a well-known hereditary disease and responsible for legal blindness, RP is still under study with new technologies emerging day by day. Its association with nonocular signs gives the syndromic form. Among populations with a high degree of consanguineous relationships, this should be considered as a public health problem and a multi-approach strategy should be considered as well as a genetic counseling in affected cases.

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Conflicts of interest

There are no conflicts of interest.

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