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Research Article

CLINICAL RESULTS IN A ROMA FAMILY WITH adCRD AUTOSOMAL DOMINANT CONE-ROD DYSTROPHY

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ABSTRACT

Purpose: To make a clinical results of patients affected by autosomal dominant cone-rod dystrophy (adCRD).

Materials and Methods: A three-generation autosomal dominant pedigree of Romani origin with non syndromic adCRD was identified. Eight affected and 14 unaffected individuals were clinically ascertained. All affected relatives were studied. Clinical evaluation included best corrected visual acuity determination, funduscopy, Humphrey perimetry, Farnsworth Hue-28 color testing, fluoresce in angiography, and full-field electroretinogram (ERG).

Clinical Results: In the 8 examined patients from the family we found the following symptoms: All affected individuals presented reduced visual acuity (0.01 - 0.4) and photophobia with slightly variable but early age of onset (around 13 years of age). Funduscopic examination and fluorescein angiography revealed advanced changes including bone spicule-like pigment deposits in the midperiphery and macular area along with retinal atrophy. Visual fields demonstrated central scotoma and tunnel vision. Electrophysiologic examination of the patients detected an abnormal cone-rod ERG (20-30V) with photopic amplitudes more markedly reduced than the scotopic. Flicker responses were missing and Farnsworth Hue-28 test found protanopie.

Conclusion: We present a Bulgarian Romani family with typical clinical symptoms of (adCRD) and pigmentation in the macular area. Identification of the disease causing gene may eventually contribute to new knowledge on the pathogenesis of this condition.

INTRODUCTION

Cone rod dystrophies (CRDs) characterized by the loss of cone cells, the photoreceptors responsible for both central and color vision[1,2,3]. The cones and rods transform light into electric nerve messages that transfer to our brain via our optic nerve.In contrast to typical retinitis pigmentosa (known as the rod-cone dystrophies), which results from the loss of rod cells and later the cone cells, cone-rod dystrophies reflect the opposite sequence of events, where cone cells are primarily first affected with later loss of rods[,4,5,6,7]. CRDs (prevalence 1/40,000) are inherited retinal dystrophies that belong to the group of pigmentary retinopathies(8). There are more than 30 types of cone-rod dystrophy, which are distinguished by their genetic cause and their pattern of inheritance: autosomal recessive, autosomal dominant, and X-linked. Inherited forms of cone rod dystrophy are due to mutations to one of several different genes that have been linked to cone dystrophy[9,10,11]. These genes contain instructions for making certain proteins, specifically proteins that play vital roles in the development, function or overall health of cone cells[12]. The exact, underlying mechanisms that cause cone rod dystrophy are not fully understood.

Genetic diseases are determined by the combination of genes for a particular trait that are on the chromosomes received from the father and the mother.

Dominant genetic disorders occur when only a single copy of an abnormal gene is necessary for the appearance of the disease. The abnormal gene can be inherited from either parent, or can be the result of a new mutation (gene change) in the affected individual. The risk of passing the abnormal gene from

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affected parent to offspring is 50 percent for each pregnancy regardless of the sex of the resulting child. In autosomal recessive inheritance, on the other hand, a person develops the condition only when both copies of the gene don't work. That is, the gene from the mother and the gene from the father both have mutations. X-linked recessive genetic disorders are conditions caused by an abnormal gene on the X chromosome.

Purpose

To make a clinical results of patients affected by autosomal dominant cone-rod dystrophy (adCRD).

MATERIALS AND METHODS

A three-generation autosomal dominant pedigree of Romani origin with non syndromic adCRD was identified. Eight affected and 14 unaffected individuals were clinically ascertained. All affected relatives were studied.

Clinical evaluation included best corrected visual acuity determination, funduscopy, Humphrey perimetry, Farnsworth Hue-28 color testing, fluorescein angiography, and full-field electroretinogram (ERG).

Clinical Results: In the 8 examined patients from the family we found the following symptoms:

All affected individuals presented reduced visual acuity (0.01 - 0.4) and photophobia with slightly variable but early age of onset (around 13 years of age).

Funduscopic examination shows pigment deposits and various degrees of retinal atrophy in the macular region. Retinal vessels are usually normal or moderately attenuated. The optic disc is often pale at early stages, particularly on the temporal side, which accounts for the macular fibre bundle.

Fluorescein angiography revealed advanced changes including bone spicule-like pigment deposits in the midperiphery and macular area along with retinal atrophy, narrowing of the vessels, and waxy optic discs (Figure 1). Fluorescein angiography showed an atrophy of the RPE in the macular area and midperiphery.

Visual fields demonstrated central scotoma and tunnel vision. Electrophysiologic examination of the patients detected an abnormal cone-rod ERG (20-30μV) with photopic amplitudes more markedly reduced than the scotopic. Dramatic decrease of amplitudes of both a- and b-wave.

Flicker responses were missing and Farnsworth Hue-28 test found protanopia.

Distribution of visual acuity in patients with CRD (n = 8 patients, 16 eyes)

Visual acuity	0,01	0,05	0,1	0,4
Number of eyes	4	6	4	2

Distribution of perimetric findings in the patients (n = 8 patients, 16 eyes)

Perimetric defect	Tunnel visual field	Central scotoma
Number of patients (eyes)	8 (16)	8 (16)

Fluorescein Angiography of the proband

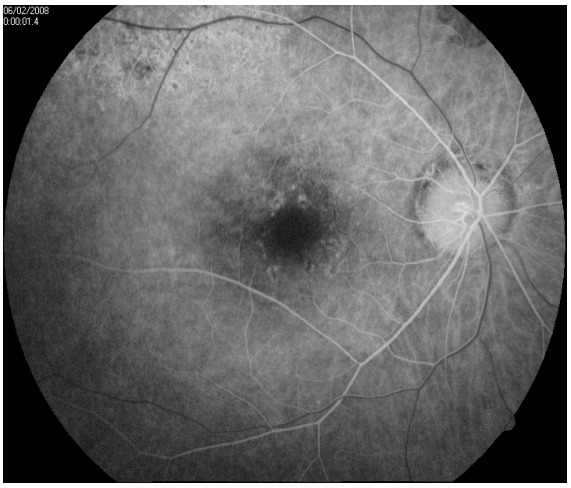

Figure 1

Discution

Clinical diagnosis is based on the early decrease of visual acuity and photophobia, lesions in fundus, hypovolted ERG traces with predominant cone involvement, and progressive worsening of these signs. In this study we report a family of Gypsy origin affected by autosomal dominant cone-rod dystrophy. The adCRD is a severe and genetically heterogeneous retinal degeneration.

The first signs and symptoms of cone-rod dystrophy, are usually decreased sharpness of visual acuity and photophobia. These features are typically followed by impaired color vision (dyschromatopsia), scotomas in the center of the visual field, and peripheral vision loss[13]. CRDs are characterized by retinal pigment deposits, predominantly localized to the macular region.

We present a Bulgarian Romani family with typical clinical symptoms of adCRD and pigmentation in the macular area. Visual field testing shows central scotomas, while periphery is spared. Predominant involvement of photopic (cones) over scotopic (rods) responses we observed the abnormal cone-rod ERG with photopic amplitudes more markedly reduced than the scotopic.

Symptoms of the following disorders can be similar to those of cone rod dystrophy. Comparisons may be useful for a differential diagnosis.

Leber's congenital amaurosis (LCA) is a rare genetic eye disorder where many different genes have been found to be involved [14]. Affected infants are often blind at birth or lose their sight within the first few of years of life. Other symptoms may include crossed eyes (strabismus); rapid, involuntary eye movements (nystagmus); unusual sensitivity to light (photophobia); clouding of the lenses of the eyes (cataracts); and/or abnormal protrusion of the front (anterior), clear portion of the eye through which light passes (cornea) (keratoconus). Leber's congenital amaurosis is usually inherited as an autosomal recessive trait.

Stargardt disease is a rare juvenile form of macular degeneration[15]. Macular degeneration is a general term for a group of eyes disorders characterized by the deterioration of the oval-shaped yellow spot (macula) near the center of the

retina. Central vision is usually affected in most cases and affected individuals may have trouble reading or have spots in their field of vision. Later in the course of the disease, the ability to perceive color is affected. Stargardt disease is inherited as an autosomal recessive trait.

Syndromic cone rod dystrophies

There are a few syndromes in which retinal degeneration characteristically features CRDs rather than typical RP. These syndromes include Bardet-Biedl syndrome, Refsum disease, Batten disease, NARP syndrome and spinocerebellar ataxia type 7.

Bardet Biedl syndrome (BBS) is an autosomal recessive disease with a prevalence ranging from 1/13,500 to 1/60,000. It associates retinal dystrophy with postaxial polydactyly, obesity, hypogenitalism, mental retardation or mild psychomotor delay, and renal abnormalities that can lead to renal failure[16].

Spinocerebellar Ataxia Type 7 is an autosomal dominant spinocerebellar degeneration due to expansions of polyglutamine in the ataxinprotein[17]. The retinal disease often begins with granular macula progressively spreading out to the whole retina, while the macula becomes atrophic.

In general, CRDs are more severe than RCDs because the loss of patients' autonomy occurs earlier[18].

CONCLUSION

In this study we report a family of Romani origin affected by autosomal dominant cone-rod dystrophy. Identification of the disease causing gene may eventually contribute to new knowledge on the pathogenesis of this condition. The authors have not conflict of interest.

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