

Cone-Rod Dystrophy and Amelogenesis Imperfecta. Two Types: Intra and Interfamilial Variability

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Summary

- Variations in the clinical features described in the different types of retinitis pigmentosa have been frequently attributed to heterogeneity and this has been confirmed by molecular biology techniques. However, the probability that some of these phenotypes are the result of variable expressions of the same genetic defect, or observation of the same disorder at different stages of its natural history, is less documented.
- The newly described oculo-dental syndrome of cone-rod dystrophy and amelogenesis imperfecta (Jalili and Smith 1988) shows the whole spectrum of macular changes reported in cone-rod dystrophy demonstrating wide intersibship, intrasibship and interfamilial variability.

THIS SYNDROME

1. Severe photophobia and nystagmus
2. Visual impairment
3. Total colour blindness
4. Absence of night blindness
5. Absent flicker (photopic) responses of the ERG, gradual loss of rod responses
6. Autosomal recessive inheritance

PATIENTS

- Aged 3 months to 50 years
- Living in separate regions of the Gaza strip.
- From 3 unrelated pedigrees.
 - Pedigree A: 16 sibships (30 patients)
(from Khan Younis rural region)
 - Pedigree B: 1 sibship (3 patients)
(from Gaza City)
 - Pedigree C: 1 sibship (1 patient)
(from Rafah)



Cone-Rod Dystrophy
with
Amelogenesis Imperfecta

Dental Phenotypes

What is amelogenesis imperfecta ?

- It is a heterogenous group of genetically inherited disorders of enamel formation.
- Two phenotypes:
 - hypocalcified
 - hypomineralised
- In the Hypocalcified Type (this syndrome); the enamel is of normal thickness at eruption, although softer, and wears away rapidly

Evolution of teeth morphology: (1) Teeth initially pitted



Evolution of teeth morphology:

(2) further loss of enamel and staining



Evolution of teeth morphology:

(3) Linear morphological pattern in subtype 1b



Evolution of teeth morphology: (4) Final loss of teeth



Cone-Rod Dystrophy & Amelogenesis
Imperfecta: Two Types IK Jalili

Evolution of teeth morphology:

Type 2: similar morphology with anterior open bite



Cone-Rod Dystrophy
with
Amelogenesis Imperfecta

Ocular Phenotypes

RESULTS

Two distinct types, each with two subtypes, which differed in presentation, retinal features and electrophysiological criteria were found.

TYPE 1 MACULAR DYSTROPHY TYPE

Subtype 1a: Bull's Eye Lesion progressing to excavation

Pedigree A: 12 sibships/21 patients,

Pedigree C: 1 patient

Subtype 1b: Atrophic Macular Lesion

Pedigree A: 2 sibships/6 patients

TYPE 2 DIFFUSE TYPE (Normal looking macula)

Pedigree B (3 patients)

TYPE 1 - MACULAR DYSTROPHY TYPE

- Macular lesion in the first few months of life.
- Pigmentary clumping appears by the second decade
- Vision - 6/36 to No PL
- Presentations:
 - Nystagmus mean age 5 months
 - Photophobia mean age 1 year
 - Visual impairment mean age 2.3 years
- Rod responses were intact initially, but became extinguished by the end of the second decade.

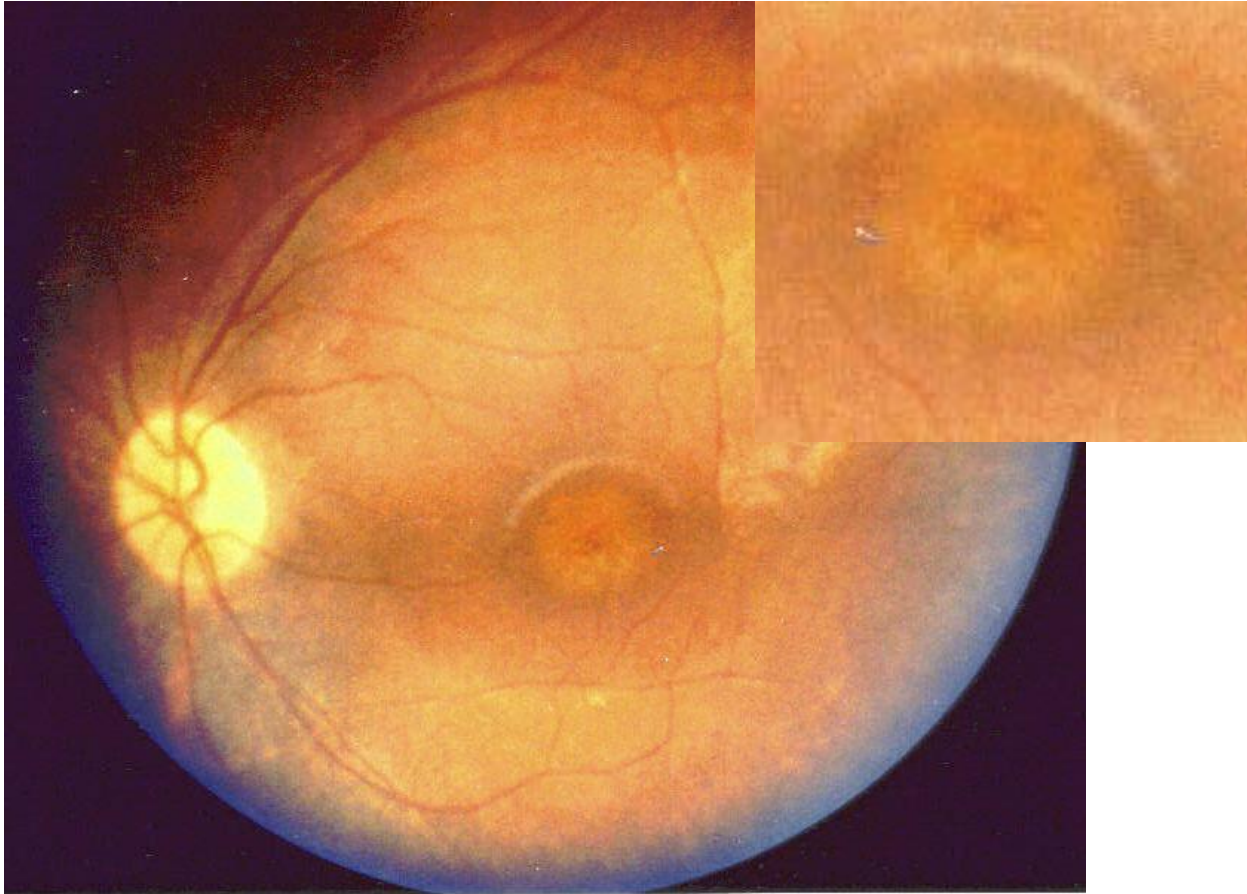
TYPE 1a: Progressive bulls eye lesion

- Onset in first 6 months of life
- Early bull's eye lesion with gradual progression to involve the neuroretina and the choroid giving rise to deeper and more circumscribed lesions

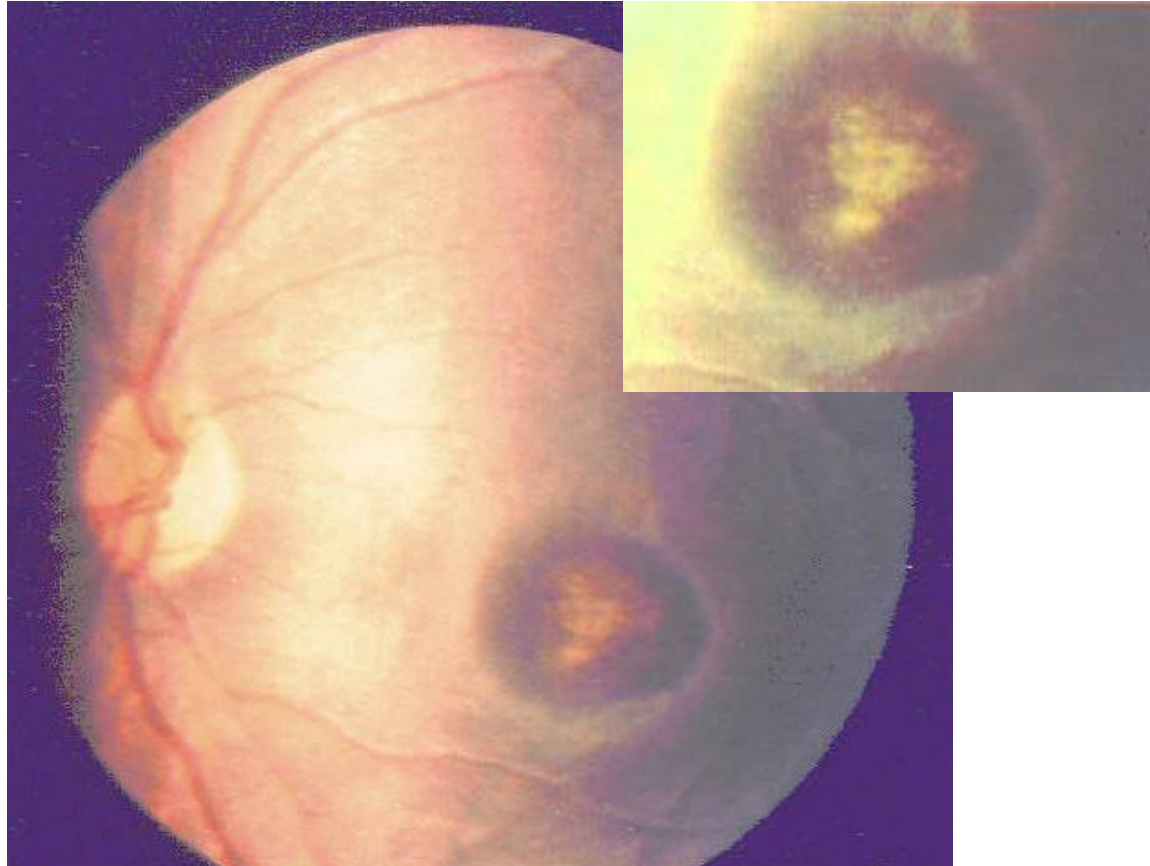
Evolution of Macular Lesion in Type 1a

- Faint annular zones of pigment epithelial atrophy 'bull's eye lesion'
- Choroidovascular involvement, with variable degrees of excavation
- Posterior staphyloma (coloboma)

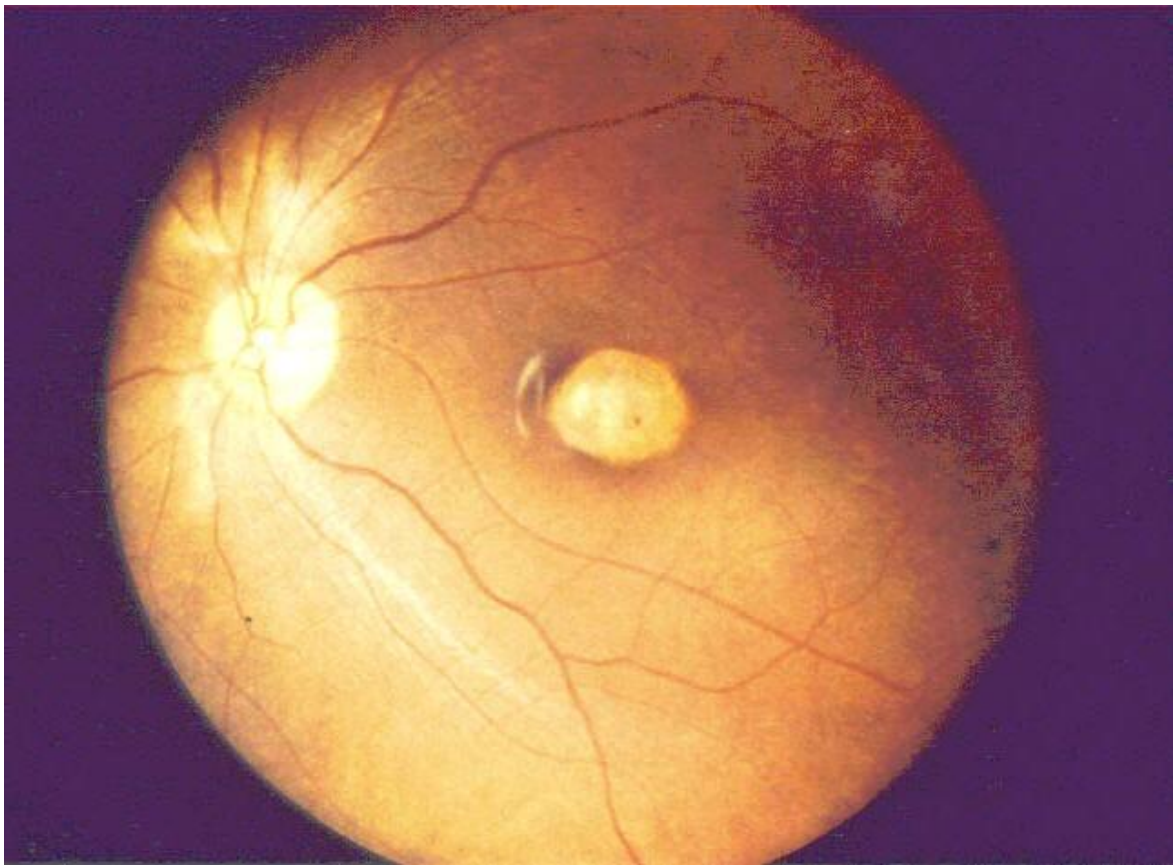
Macular Lesion in Type 1a: Bull's eye lesion



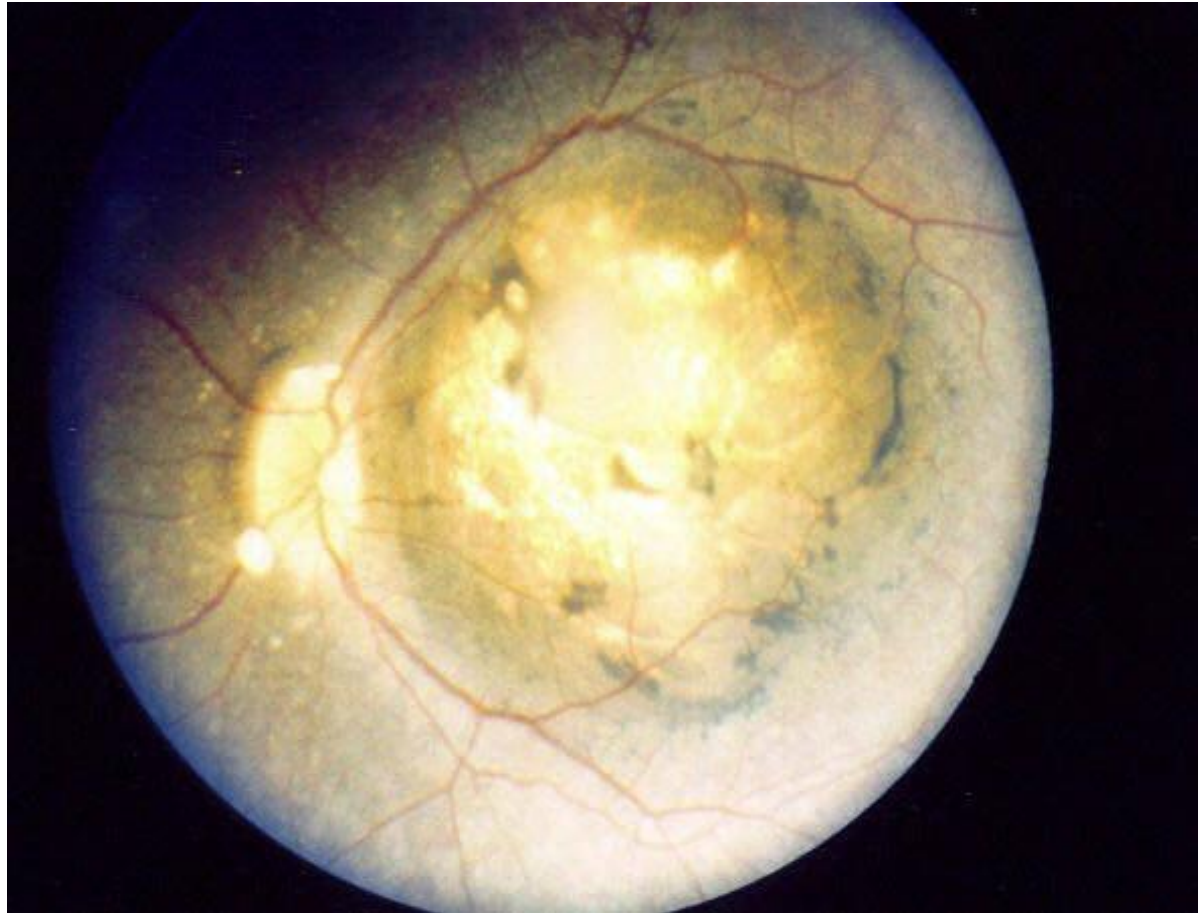
Macular Lesion in Type 1a: Lesions become more confluent.



Macular Lesion in Type 1a: Chorioretinal atrophy



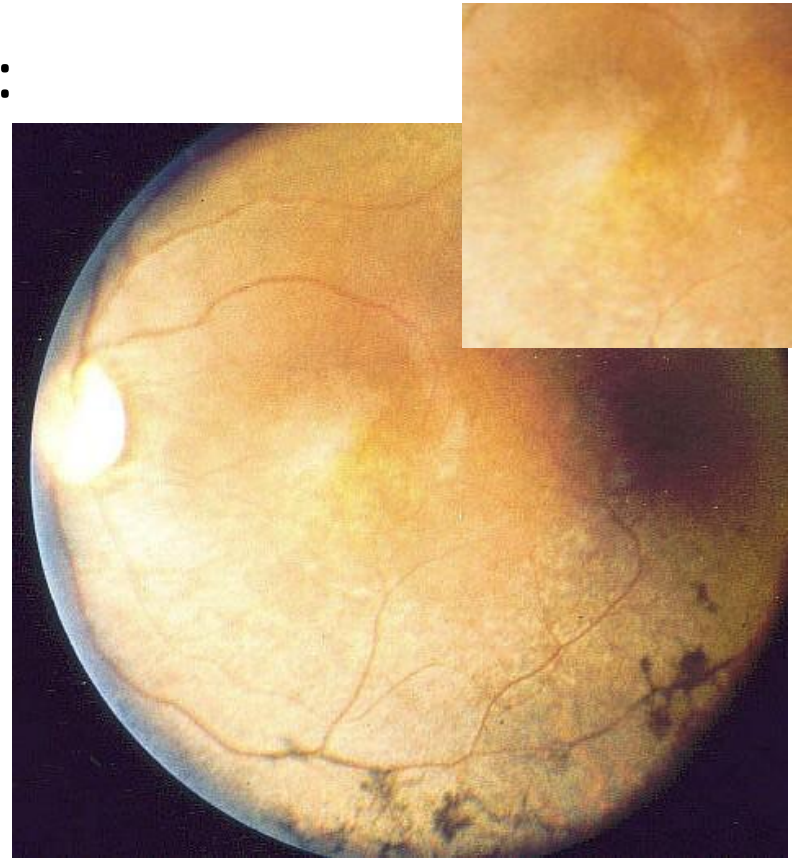
Macular Lesion in Type 1a: Further excavation leading to posterior staphyloma



Macular Lesion Type 1b: Atrophic Macular Degeneration with classical RP like picture in 1 sibship (1b)

Macular lesion appeared as:

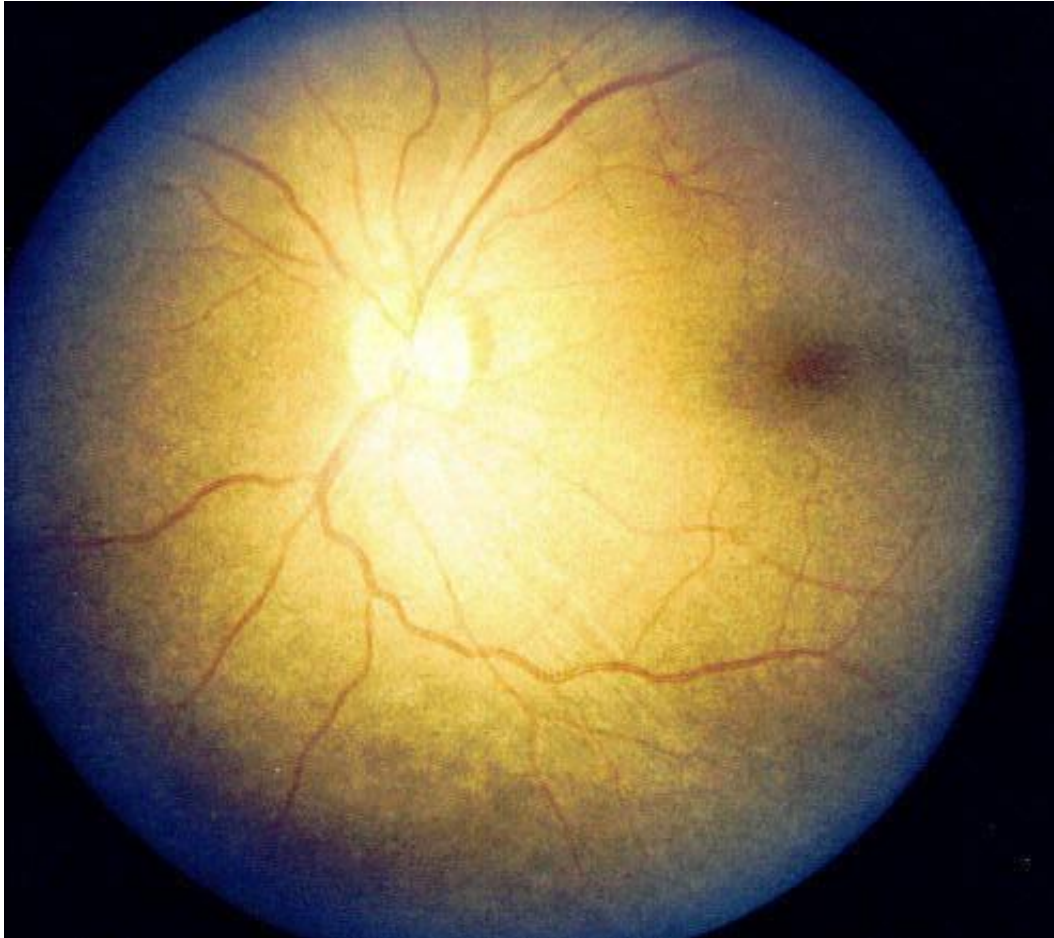
- Faint
- Non-circumscribed
- Pigment epithelial atrophy increased in size and density with age
- No excavation



CRDAI Diffuse Type (Type 2)

- Normal looking macula in the eldest (11 yrs)
- Cone and rod impairment from an early age which varied with the subtypes
- Extinguished ERG by age 11 yrs.

Type 2 of the CRDAI: no obvious ophthalmological retinal changes.



Differential Diagnosis Type 1

Cone Dystrophy

Congenital areolar central dystrophy

[\(Iqbal M, Jalili IK\)](#)

Congenital coloboma (sibling C)

Rod cone dystrophies

Differential Diagnosis - Type 2

- Achromatopsia
- Congenital amaurosis of the Cone-Rod
[\(Jalili 1989\)](#)

CONCLUSION

- The association features an unusual variability of the phenotypic expression suggesting the existence of different alleles at the same genetic locus, and demonstrating the importance of the individual's genetic environment in modifying the genetic lesion.
- If the common denominator of the enamel defect in these pedigrees did not exist, and we were unable to establish the relationship among the various sibships in the extended pedigree by extensive investigation, we would have assumed heterogeneity. Clinical variability alone should not, therefore, indicate heterogeneity in retinitis pigmentosa.
- Pedigree B is unrelated to Pedigree A suggesting a different expression of the gene.

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