

CASE REPORT

Flecked retina associated with ring 17 chromosome

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Abstract

We report the case of a mentally retarded male with a ring 17 chromosome who had subretinal drusen-like deposits in each eye. This is the second report of flecked retina in a patient with ring 17 chromosome, suggesting that there may be a causal relationship between abnormalities of chromosome 17 and retinal pigment epithelial or photoreceptor dysfunction.

In inherited diseases cytogenetic abnormalities may provide the first clues to the location of the underlying genetic defect. For example, the association between interstitial deletions and ocular diseases such as retinoblastoma,¹ aniridia,² and choroideraemia³ has led to the localisation of the genetic loci for these conditions.

Ring chromosomes are thought to form by breaks occurring in both arms of a chromosome with fusion of the proximal ends leading to loss of the distal fragments.⁴ This loss of chromatin may give rise to major dysmorphogenesis and mental retardation, sometimes with specific phenotypic features associated with terminal deletions of these same chromosomes. However, in many patients with ring chromosomes that have no visible loss of chromatin there are only minor anomalies, and the main phenotypic features are growth failure and mental retardation, regardless of which chromosome forms the ring. This has led to the suggestion that part or all of the phenotype in such patients may result from the altered structure or instability at mitosis of

the ring chromosome, rather than loss of chromatin.⁴

We describe a patient with ring 17 chromosome with a flecked retina, seizures, and café au lait spots in addition to mental retardation and short stature.

Case report**CLINICAL HISTORY**

A 20-year-old male was reviewed who had been diagnosed 10 years previously as having peripheral neurofibromatosis (now classified NF-1). The parents were concerned lest any other family members might be at risk.

He was the first born child of non-consanguineous parents aged 21 and 18 years. His birth weight was 2.40 kg. Motor and mental development was retarded, and at age 5 he developed epilepsy. He attended a special school and at age 10 was admitted to hospital for investigation of epilepsy. At that time he had pigmented patches over his body. A diagnosis of NF-1 was made in view of his severe mental retardation, fits, and skin pigmentation. A skull x-ray and CT scan were normal. There was no family history of NF-1. Over the next 10 years his behavioural problems became more pronounced, necessitating long term inpatient care. Current medication included sodium valproate, carbamazepine, and thioridazine. Thioridazine had been taken for two years (not exceeding 75 mg/day), with a cumulative dose of approximately 35 g.

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Accepted for publication
23 August 1990

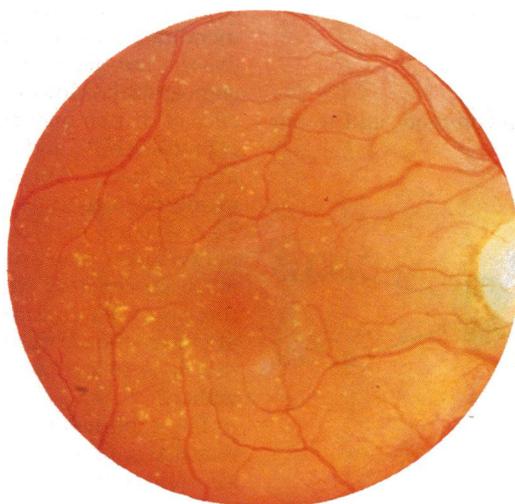


Figure 1A

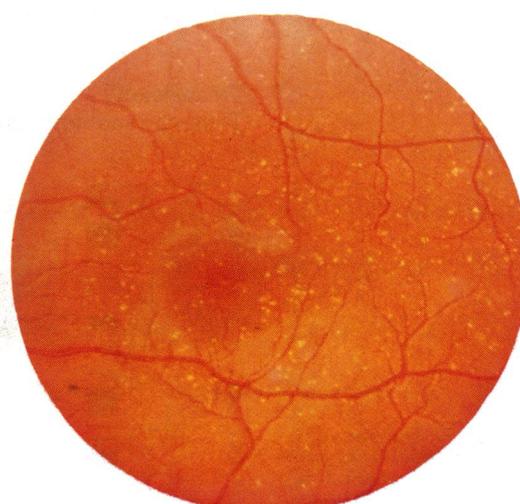


Figure 1B

Figures 1A, B Colour fundus photographs showing multiple drusen-like deposits at the posterior pole of each eye.

Figures 2A, B Fluorescein angiography showing slight masking associated with some deposits but no late hyperfluorescence.

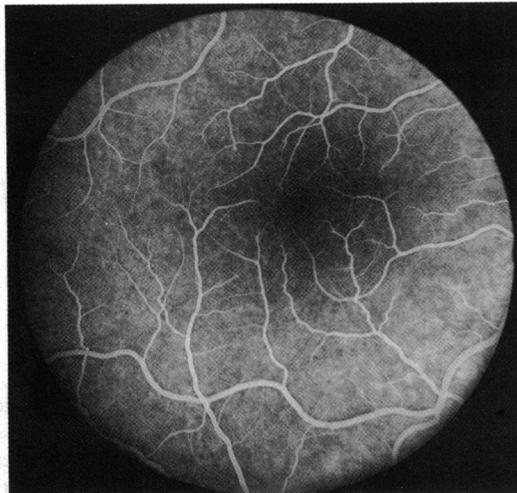


Figure 2A

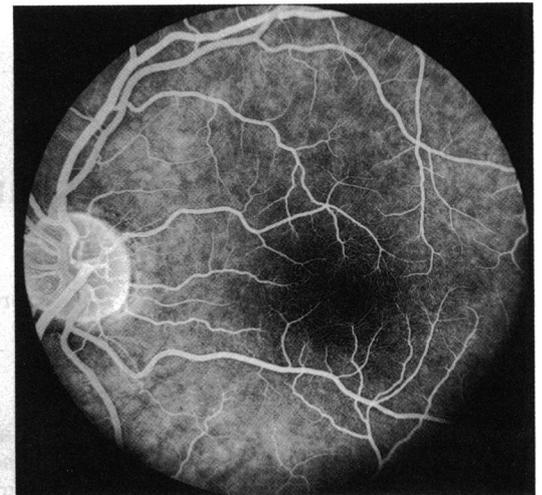


Figure 2B

EXAMINATION

At age 20 he was of short stature, 161 cm (<3rd centile), with a head circumference of 53 cm (10th centile), and weight 43.2 kg (<3rd centile). He had numerous café au lait spots, with four axillary freckles but no cutaneous neurofibromata. Visual acuity appeared to be good in each eye, with accurate assessment limited by the patient's mental retardation. The anterior segment was normal on examination, with no Lisch nodules. Retinal examination revealed multiple yellow flecks at both posterior poles at the level of the retinal pigment epithelium (RPE) similar to drusen (Figs 1A, B). Fundus fluorescein angiography (Figs 2A, B) showed normal choroidal and retinal vascular filling, with slight masking associated with some of the deposits at the posterior pole but no late hyperfluorescence.

Flash electroretinography (ERG) was normal bilaterally; the pattern ERG was found to be normal in one eye, but poor co-operation limited further investigations. Cytogenetic analysis revealed the karyotype 46,XY,r(17)(p13.3q25.3), with no visible deletion of the ring chromosome (Fig 3). Magnetic resonance imaging (MRI) of the brain gave normal results.

Parents and siblings were healthy, with no stigmata of NF and no retinal abnormalities. The mother's chromosomes were normal, but the father declined to have his examined.

Discussion

Ring chromosomes are uncommon, and to our

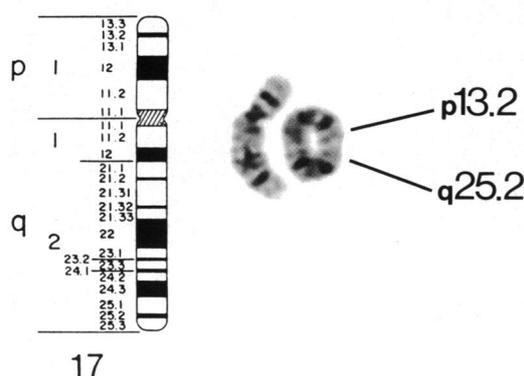


Figure 3 Idiogram and G-banded partial karyotype showing chromosome 17 in this patient. The bands p13.2 and q25.2 are indicated.

knowledge there have been only 11 reported cases of ring 17 chromosome. Common though non-specific features associated with this abnormality include mental and motor retardation, seizures, and short stature.⁵ Three cases of ring 17 chromosome have been described with Miller-Dieker lissencephaly,^{6,7} which has been mapped to the p13.3 portion of chromosome 17. Our patient had no brain abnormality on MRI scan. Multiple café au lait spots are seen in NF-1 and have also been described in patients with ring chromosomes, including chromosome 17. Although the NF-1 gene has been mapped to chromosome 17,⁸ the absence of neurofibromata or Lisch nodules⁹ in this case make the diagnosis of NF-1 unlikely.

The unusual eye findings in our patient resemble those in the 10-year-old girl with ring 17 chromosome described by Ono *et al.*¹⁰ She had numerous yellowish red retinal deposits, not associated with night blindness, and a normal ERG; her condition had been diagnosed as retinitis punctata albescens. This may not have been the correct diagnosis: retinitis punctata albescens has drusen-like deposits in the mid peripheral fundus with impairment of retinal function, and it is thought to be an early form of retinitis pigmentosa, not a distinct clinical entity.^{11,12} Our case has small yellow subretinal deposits at the level of the RPE or Bruch's membrane, which were similar in appearance to drusen but failed to fluoresce on fluorescein angiography. However, the degree of fluorescence of drusen may be related to their chemical composition,¹³ and some may show little fluorescence.¹⁴ Abnormal deposits in Bruch's membrane may cause a similar fundus picture.¹⁵ Thioridazine may cause a pigmentary retinopathy, rather than drusen-like change, which has not been reported with the low dosage used in this case.¹⁶ We consider that our patient and that of Ono *et al.* have the same retinal dystrophy and that it is related to their chromosomal abnormality.

The ophthalmic examination of mentally retarded patients, particularly in the presence of a chromosomal abnormality, may reveal relevant pathology. Some causes of flecked retina are known to be associated with crystalline deposi-

tion of an exogenous substance present in excess (as in oxalosis), but others (such as dominant drusen) may be caused by an isolated abnormality of receptor or RPE metabolism leading to an accumulation of abnormal material within the RPE or Bruch's membrane.¹⁶ This is the second report of flecked retina in patients with ring 17 chromosome, suggesting that loci on chromosome 17 may be involved in the regulation of retinal pigment epithelial or photoreceptor function. Most causes of flecked retina are inherited,¹⁷ but the underlying genetic defects are unknown. Chromosome 17 may be worthy of further investigation.

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